Dossier zur Nutzenbewertung gemäß § 35a SGB V

Trastuzumab deruxtecan (Enhertu®)

Daiichi Sankyo Deutschland GmbH

Anhang 4-G

Erwachsene Patienten mit inoperablem oder metastasiertem HR-positivem, HER2-low oder HER2-ultralow Brustkrebs, die mindestens eine endokrine Therapie in der metastasierten Situation erhalten haben und die für eine endokrine Therapie als nächste Therapielinie nicht in Frage kommen

Analysen für das Nutzendossier

Stand: 23.04.2025

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Anhang 4-G 1. Analysen DESTINY-Breast06: Mortalität – FAS

Anhang 4-G 1.1 Gesamtüberleben

Tabelle 2.3.1 Gesamtüberleben (OS) – FAS

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Data Intelligence - Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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Statistical analyses for AMNOG (HTA Germany)

Table 2.3.1 Overall survival (OS) - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	161 (36.9)	28.9 [26.4; 32.7]	174 (40.5)	27.4 [23.9; 29.9]	0.8142 [0.6566; 1.0089] 0.0603	0.0600
Subjects with censoring event	275 (63.1)		256 (59.5)			
Still in survival follow-up	265 (60.8)		223 (51.9)			
Withdrawn consent	10 (2.3)		33 (7.7)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04DEC2024 3:23; Program name: T.2.3.1_OS_FAS.sas; Output name: T.2.3.1_OS_FAS.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.3.2 Gesamtüberleben (OS) – Subgruppenanalyse – FAS

Table 2.3.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Age at randomization						0.2170
<65 years of age	101 / 302 (33.4)	30.2 [27.7; 33.7]	118 / 297 (39.7)	27.4 [24.2; 30.2]	0.7365 [0.5637; 0.9603] 0.0236	
≥65 years of age	60 / 134 (44.8)	26.4 [21.2; 31.8]	56 / 133 (42.1)	27.7 [20.5; NE]	1.0027 [0.6964; 1.4459] 0.9887	
Race						0.3705
Asian	49 / 154 (31.8)	33.1 [28.9; NE]	51 / 151 (33.8)	29.9 [27.1; NE]	0.9142 [0.6166; 1.3543] 0.6548	
White	94 / 231 (40.7)	26.3 [24.1; 31.8]	95 / 230 (41.3)	24.7 [21.3; NE]	0.8244 [0.6187; 1.0981] 0.1857	
Other	18 / 51 (35.3)	NE [21.2; NE]	28 / 49 (57.1)	19.9 [16.9; 28.7]	0.5522 [0.2984; 0.9976] 0.0489	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 06SEP2024 5:17; Program name: T.2.3.2_OS_FAS_SUB.sas; Output name: T.2.3.2_OS_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.3.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.3994
Asia	50 / 149 (33.6)	33.1 [27.9; NE]	48 / 147 (32.7)	30.2 [27.1; NE]	0.9844 [0.6619; 1.4656] 0.9387	
Europe	88 / 227 (38.8)	26.3 [24.0; 32.7]	98 / 213 (46.0)	24.2 [20.5; 27.9]	0.6978 [0.5210; 0.9328] 0.0148	
Rest of the World	23 / 60 (38.3)	28.4 [25.7; NE]	28 / 70 (40.0)	27.7 [19.4; NE]	0.8329 [0.4748; 1.4464] 0.5173	
HER2 IHC expression						0.1145
IHC 1+	96 / 239 (40.2)	26.4 [23.8; 33.7]	93 / 234 (39.7)	27.7 [23.5; NE]	0.9685 [0.7277; 1.2894] 0.8262	
IHC 2+/ISH-	36 / 117 (30.8)	NE [25.7; NE]	53 / 118 (44.9)	24.4 [21.4; 30.1]	0.5671 [0.3682; 0.8636] 0.0080	
IHC >0 <1+	25 / 76 (32.9)	29.5 [27.9; NE]	28 / 76 (36.8)	27.4 [19.4; NE]	0.7513 [0.4338; 1.2944] 0.3008	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.3.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9544
Yes	147 / 394 (37.3)	28.4 [26.0; 32.5]	160 / 389 (41.1)	27.1 [23.1; 29.9]	0.8128 [0.6492; 1.0168] 0.0693	
No	14 / 42 (33.3)	33.7 [29.5; NE]	14 / 41 (34.1)	NE [24.4; NE]	0.8111 [0.3814; 1.7234] 0.5796	
Prior Taxane Use In The Non-Metastatic Setting						0.2952
Yes	71 / 179 (39.7)	28.9 [23.8; 33.1]	72 / 177 (40.7)	28.7 [23.5; 30.2]	0.9223 [0.6638; 1.2811] 0.6280	
No	90 / 257 (35.0)	28.9 [26.3; 33.7]	102 / 253 (40.3)	26.2 [21.8; 29.9]	0.7408 [0.5570; 0.9837] 0.0377	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.3.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.8016
1	27 / 65 (41.5)	25.7 [20.3; NE]	32 / 82 (39.0)	24.4 [18.5; NE]	0.8688 [0.5160; 1.4510] 0.5915	
2	106 / 295 (35.9)	29.5 [26.4; 33.1]	119 / 288 (41.3)	27.1 [23.5; 29.9]	0.7792 [0.5990; 1.0123] 0.0613	
>=3	27 / 75 (36.0)	NE [24.1; NE]	22 / 58 (37.9)	30.1 [21.8; NE]	0.9605 [0.5472; 1.7045] 0.8889	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.3.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status I						0.7280
ER+, PR missing	6 / 12 (50.0)	32.7 [14.9; NE]	5 / 10 (50.0)	23.9 [3.0; NE]	0.7841 [0.2152; 2.8665] 0.7036	
ER+, PR+	93 / 253 (36.8)	28.4 [26.0; 32.5]	96 / 237 (40.5)	27.7 [22.5; NE]	0.8666 [0.6513; 1.1534] 0.3260	
ER+, PR-	59 / 167 (35.3)	30.1 [26.4; NE]	72 / 181 (39.8)	27.1 [21.7; 30.1]	0.7176 [0.5066; 1.0133] 0.0592	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.3.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.8170
ER <=10%	8 / 21 (38.1)	NE [17.3; NE]	7 / 14 (50.0)	24.2 [7.9; NE]	0.6368 [0.2247; 1.8400] 0.3869	
ER >10%	135 / 364 (37.1)	29.5 [26.3; 33.1]	141 / 355 (39.7)	27.4 [23.5; 30.1]	0.8336 [0.6579; 1.0558] 0.1304	
Positive	18 / 51 (35.3)	28.4 [24.1; NE]	26 / 61 (42.6)	27.7 [21.3; NE]	0.6988 [0.3754; 1.2722] 0.2435	
Endocrine Resistance						0.7573
Primary	52 / 128 (40.6)	27.7 [22.2; 28.9]	62 / 140 (44.3)	24.4 [18.8; NE]	0.7849 [0.5408; 1.1340] 0.1975	
Secondary	109 / 308 (35.4)	31.8 [26.4; 33.7]	112 / 288 (38.9)	27.7 [24.2; 30.2]	0.8349 [0.6406; 1.0876] 0.1802	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.3.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.2145
Capecitabine	88 / 266 (33.1)	30.1 [26.4; 33.1]	96 / 257 (37.4)	27.1 [23.9; 32.1]	0.7788 [0.5823; 1.0402] 0.0897	
Nab-Paclitaxel	47 / 103 (45.6)	27.7 [21.8; NE]	42 / 105 (40.0)	28.6 [22.1; NE]	1.0868 [0.7167; 1.6536] 0.6966	
Paclitaxel	26 / 67 (38.8)	32.5 [19.9; NE]	36 / 68 (52.9)	23.5 [15.4; 30.1]	0.6137 [0.3643; 1.0178] 0.0586	
Prior anthracycline use						0.7182
Yes	75 / 199 (37.7)	30.1 [25.3; NE]	91 / 208 (43.8)	27.1 [22.1; 29.9]	0.7819 [0.5743; 1.0604] 0.1132	
No	86 / 237 (36.3)	28.4 [26.0; 32.7]	83 / 222 (37.4)	28.6 [23.5; NE]	0.8489 [0.6273; 1.1493] 0.2873	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.3.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.3362
Yes	121 / 296 (40.9)	27.8 [24.1; 30.2]	132 / 283 (46.6)	22.1 [19.9; 26.8]	0.7499 [0.5853; 0.9598] 0.0219	
No	40 / 140 (28.6)	33.7 [28.9; NE]	42 / 147 (28.6)	30.1 [28.7; NE]	0.9537 [0.6159; 1.4742] 0.8304	
ECOG						0.9436
0	84 / 252 (33.3)	29.5 [26.4; 33.7]	91 / 257 (35.4)	29.9 [24.2; NE]	0.8084 [0.5998; 1.0882] 0.1601	
>=1	76 / 179 (42.5)	27.7 [21.2; NE]	79 / 164 (48.2)	24.4 [19.8; 28.7]	0.8374 [0.6105; 1.1479] 0.2687	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Tabelle 2.3.3 Gesamtüberleben (OS) – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.3.3 Overall survival (OS) – Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

No output displayed as p-value >= 0.05 for all subgroups.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Abbildung 2.3.1 Gesamtüberleben OS) – Kaplan-Meier-Plot – FAS

Daiichi Sankyo Europe GmbH
Data Intelligence – Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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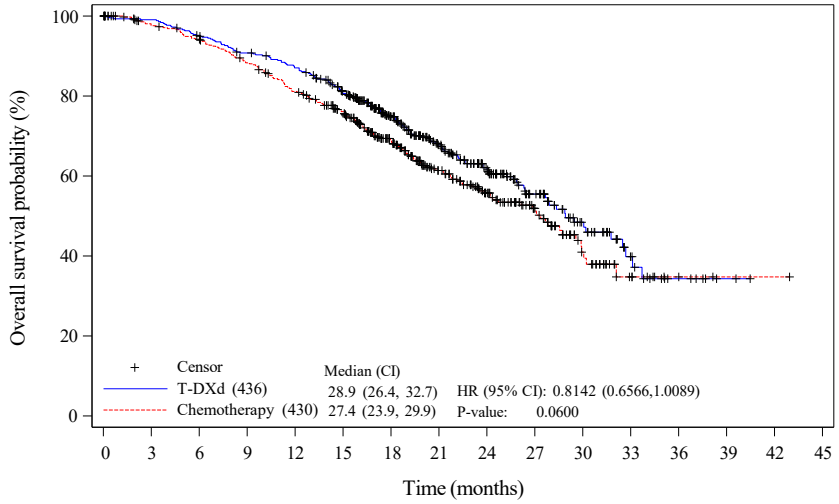
Statistical analyses for AMNOG (HTA Germany)

Figure 2.3.1 Overall survival (OS) - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:

T-DXd(436)	436	431	412	391	373	329	235	169	120	69	39	16	7	2	0
Chemotherapy (430)	430	402	387	360	328	292	210	143	101	62	27	9	3	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 03DEC2024 5:05; Program name: F.2.3.1_OS_FAS.sas; Output name: F.2.3.1_OS_FAS.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.3.2 Gesamtüberleben (OS) – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

Daiichi Sankyo Europe GmbH
Data Intelligence – Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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Statistical analyses for AMNOG (HTA Germany)

Figure 2.3.2 Overall survival (OS) - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set

No output displayed as p-value >= 0.05 for all subgroups.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 15JUL2024 8:14; Program name: F.2.3.2_OS_FAS_SUB.sas; Output name: F.2.3.2_OS_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Anhang 4-G 2. Analysen DESTINY-Breast06: Morbidität – FAS

Anhang 4-G 2.1 Progressionsfreies Überleben

Tabelle 2.4.1 Progressionsfreies Überleben (PFS) gemäß RECIST 1.1 gemäß BICR – FAS

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Final
Statistical analyses for AMNOG (HTA Germany)

Table 2.4.1 Progression-Free Survival (PFS) according to RECIST 1.1 by BICR - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	269 (61.7)	13.2 [12.0; 15.2]	271 (63.0)	8.1 [7.0; 9.0]	0.6376 [0.5379; 0.7558] <.0001	<.0001
Subjects with censoring event	167 (38.3)		159 (37.0)			
Censored RECIST progression	8 (1.8)		10 (2.3)			
Censored death	29 (6.7)		33 (7.7)			
Progression-free at time of analysis	122 (28.0)		92 (21.4)			
Withdrawn consent	8 (1.8)		24 (5.6)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
BICR: Blinded Independent Central Review; CI: confidence interval; HR: hazard ratio

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04DEC2024 3:25; Program name: T.2.4.1_PFS_BICR_FAS.sas; Output name: T.2.4.1_PFS_BICR_FAS.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.4.2 Progressionsfreies Überleben (PFS) gemäß RECIST 1.1 gemäß BICR – Subgruppenanalyse – FAS

Table 2.4.2 Progression-Free Survival (PFS) according to RECIST 1.1 by BICR - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Age at randomization						0.2844
<65 years of age	186 / 302 (61.6)	13.3 [11.8; 15.3]	186 / 297 (62.6)	7.4 [6.9; 8.6]	0.5902 [0.4806; 0.7247] <.0001	
≥65 years of age	83 / 134 (61.9)	13.1 [9.7; 15.6]	85 / 133 (63.9)	8.5 [7.1; 11.5]	0.7467 [0.5505; 1.0124] 0.0585	
Race						0.5790
Asian	88 / 154 (57.1)	15.2 [12.9; 19.4]	101 / 151 (66.9)	8.2 [6.9; 9.7]	0.5932 [0.4443; 0.7906] 0.0003	
White	148 / 231 (64.1)	13.0 [11.0; 15.1]	142 / 230 (61.7)	8.2 [6.9; 9.6]	0.6855 [0.5434; 0.8649] 0.0013	
Other	33 / 51 (64.7)	15.0 [9.7; 17.5]	28 / 49 (57.1)	7.1 [5.4; 13.8]	0.5185 [0.3087; 0.8761] 0.0117	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
BICR: Blinded Independent Central Review; CI: confidence interval; HR: hazard ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 14:46; Program name: T.2.4.2_PFS_BICR_FAS_SUB.sas; Output name: T.2.4.2_PFS_BICR_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.4.2 Progression-Free Survival (PFS) according to RECIST 1.1 by BICR - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.3219
Asia	88 / 149 (59.1)	15.2 [12.4; 19.3]	96 / 147 (65.3)	8.2 [6.9; 9.7]	0.6456 [0.4822; 0.8635] 0.0030	
Europe	143 / 227 (63.0)	13.5 [11.1; 15.4]	139 / 213 (65.3)	7.3 [6.6; 8.3]	0.5678 [0.4481; 0.7195] <.0001	
Rest of the World	38 / 60 (63.3)	11.3 [9.6; 13.3]	36 / 70 (51.4)	11.0 [6.8; 13.2]	0.8649 [0.5463; 1.3716] 0.5294	
HER2 IHC expression						0.0274
IHC 1+	157 / 239 (65.7)	13.1 [11.0; 15.2]	150 / 234 (64.1)	8.2 [7.1; 9.8]	0.7342 [0.5862; 0.9197] 0.0069	
IHC 2+/ISH-	65 / 117 (55.6)	15.2 [12.2; 21.4]	80 / 118 (67.8)	7.0 [6.2; 8.4]	0.4304 [0.3076; 0.5996] <.0001	
IHC >0 <1+	44 / 76 (57.9)	13.2 [9.8; 17.3]	39 / 76 (51.3)	8.3 [5.8; 15.2]	0.7790 [0.5050; 1.2063] 0.2567	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
BICR: Blinded Independent Central Review; CI: confidence interval; HR: hazard ratio; NE: not estimable

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Run date: 04SEP2024 14:46; Program name: T.2.4.2_PFS_BICR_FAS_SUB.sas; Output name: T.2.4.2_PFS_BICR_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.4.2 Progression-Free Survival (PFS) according to RECIST 1.1 by BICR - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8471
Yes	248 / 394 (62.9)	13.1 [11.3; 15.2]	247 / 389 (63.5)	7.9 [6.9; 8.6]	0.6388 [0.5349; 0.7629] <.0001	
No	21 / 42 (50.0)	16.1 [11.3; NE]	24 / 41 (58.5)	11.4 [7.1; 20.6]	0.5908 [0.3245; 1.0676] 0.0771	
Prior Taxane Use In The Non-Metastatic Setting						0.9496
Yes	112 / 179 (62.6)	12.9 [9.9; 14.0]	117 / 177 (66.1)	7.3 [6.3; 9.3]	0.6339 [0.4880; 0.8230] 0.0005	
No	157 / 257 (61.1)	15.1 [11.4; 16.5]	154 / 253 (60.9)	8.4 [7.1; 9.7]	0.6335 [0.5060; 0.7932] 0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
BICR: Blinded Independent Central Review; CI: confidence interval; HR: hazard ratio; NE: not estimable

Table 2.4.2 Progression-Free Survival (PFS) according to RECIST 1.1 by BICR - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1935
1	33 / 65 (50.8)	15.2 [9.7; 19.1]	55 / 82 (67.1)	6.9 [5.5; 8.4]	0.4500 [0.2873; 0.6943] 0.0003	
2	188 / 295 (63.7)	13.2 [11.4; 15.3]	179 / 288 (62.2)	8.3 [7.1; 9.8]	0.6989 [0.5690; 0.8587] 0.0006	
>=3	47 / 75 (62.7)	12.0 [8.7; 17.3]	36 / 58 (62.1)	8.3 [6.4; 11.3]	0.6348 [0.4082; 0.9937] 0.0429	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
BICR: Blinded Independent Central Review; CI: confidence interval; HR: hazard ratio; NE: not estimable

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Run date: 04SEP2024 14:46; Program name: T.2.4.2_PFS_BICR_FAS_SUB.sas; Output name: T.2.4.2_PFS_BICR_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.4.2 Progression-Free Survival (PFS) according to RECIST 1.1 by BICR - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status I						0.5605
ER+, PR missing	10 / 12 (83.3)	7.6 [1.4; 16.8]	8 / 10 (80.0)	6.9 [2.7; 13.7]	0.8336 [0.3248; 2.2055] 0.7044	
ER+, PR+	155 / 253 (61.3)	13.2 [11.3; 15.3]	145 / 237 (61.2)	8.3 [6.9; 10.4]	0.6827 [0.5438; 0.8575] 0.0009	
ER+, PR-	100 / 167 (59.9)	13.5 [11.3; 16.1]	116 / 181 (64.1)	8.1 [6.9; 9.5]	0.5585 [0.4252; 0.7320] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
BICR: Blinded Independent Central Review; CI: confidence interval; HR: hazard ratio; NE: not estimable

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Table 2.4.2 Progression-Free Survival (PFS) according to RECIST 1.1 by BICR - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1558
ER <=10%	15 / 21 (71.4)	15.0 [4.2; 15.4]	12 / 14 (85.7)	4.4 [1.5; 5.5]	0.2676 [0.1078; 0.6468] 0.0019	
ER >10%	228 / 364 (62.6)	13.1 [11.3; 15.2]	220 / 355 (62.0)	8.3 [7.3; 9.7]	0.6456 [0.5355; 0.7786] <.0001	
Positive	26 / 51 (51.0)	14.5 [9.8; NE]	39 / 61 (63.9)	6.9 [4.4; 13.0]	0.5804 [0.3489; 0.9498] 0.0299	
Endocrine Resistance						0.3195
Primary	80 / 128 (62.5)	12.4 [10.3; 15.2]	98 / 140 (70.0)	6.6 [5.4; 7.4]	0.5687 [0.4214; 0.7654] 0.0002	
Secondary	189 / 308 (61.4)	13.2 [12.0; 15.5]	172 / 288 (59.7)	9.5 [8.0; 11.1]	0.6800 [0.5523; 0.8378] 0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
BICR: Blinded Independent Central Review; CI: confidence interval; HR: hazard ratio; NE: not estimable

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Table 2.4.2 Progression-Free Survival (PFS) according to RECIST 1.1 by BICR - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0106
Capecitabine	159 / 266 (59.8)	13.3 [11.4; 15.4]	159 / 257 (61.9)	8.5 [7.0; 11.3]	0.6607 [0.5298; 0.8240] 0.0002	
Nab-Paclitaxel	68 / 103 (66.0)	12.9 [8.4; 15.2]	63 / 105 (60.0)	8.3 [7.2; 11.0]	0.8041 [0.5692; 1.1374] 0.2145	
Paclitaxel	42 / 67 (62.7)	16.1 [11.1; 19.1]	49 / 68 (72.1)	6.3 [5.0; 6.9]	0.3479 [0.2230; 0.5396] <.0001	
Prior anthracycline use						0.8079
Yes	121 / 199 (60.8)	13.1 [11.1; 15.3]	128 / 208 (61.5)	8.0 [6.4; 9.8]	0.6591 [0.5129; 0.8465] 0.0010	
No	148 / 237 (62.4)	14.5 [11.3; 15.6]	143 / 222 (64.4)	8.3 [7.0; 9.7]	0.6120 [0.4851; 0.7724] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
BICR: Blinded Independent Central Review; CI: confidence interval; HR: hazard ratio; NE: not estimable

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Table 2.4.2 Progression-Free Survival (PFS) according to RECIST 1.1 by BICR - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.3692
Yes	195 / 296 (65.9)	12.2 [10.4; 13.5]	192 / 283 (67.8)	7.0 [6.4; 8.1]	0.5850 [0.4778; 0.7163] <.0001	
No	74 / 140 (52.9)	16.5 [13.2; 19.4]	79 / 147 (53.7)	11.3 [8.3; 15.2]	0.7011 [0.5094; 0.9639] 0.0279	
ECOG						0.5714
0	147 / 252 (58.3)	14.0 [12.0; 16.8]	161 / 257 (62.6)	8.3 [7.1; 10.0]	0.6082 [0.4851; 0.7619] <.0001	
>=1	119 / 179 (66.5)	12.9 [10.9; 15.2]	105 / 164 (64.0)	7.2 [5.8; 8.9]	0.6880 [0.5281; 0.8974] 0.0053	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
BICR: Blinded Independent Central Review; CI: confidence interval; HR: hazard ratio; NE: not estimable

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Tabelle 2.4.3 Progressionsfreies Überleben (PFS) gemäß RECIST 1.1 gemäß BICR – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.4.3 Progression-Free Survival (PFS) according to RECIST 1.1 by BICR - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
HER2 IHC expression					.	0.0274
IHC 1+	157 / 239 (65.7)	13.1 [11.0; 15.2]	150 / 234 (64.1)	8.2 [7.1; 9.8]	0.7342 [0.5862; 0.9197] 0.0069	
IHC 2+/ISH-	65 / 117 (55.6)	15.2 [12.2; 21.4]	80 / 118 (67.8)	7.0 [6.2; 8.4]	0.4304 [0.3076; 0.5996] <.0001	
IHC >0 <1+	44 / 76 (57.9)	13.2 [9.8; 17.3]	39 / 76 (51.3)	8.3 [5.8; 15.2]	0.7790 [0.5050; 1.2063] 0.2567	
T-Dxd Vs. Each Investigator's Choice Chemotherapy					.	0.0106
Capecitabine	159 / 266 (59.8)	13.3 [11.4; 15.4]	159 / 257 (61.9)	8.5 [7.0; 11.3]	0.6607 [0.5298; 0.8240] 0.0002	
Nab-Paclitaxel	68 / 103 (66.0)	12.9 [8.4; 15.2]	63 / 105 (60.0)	8.3 [7.2; 11.0]	0.8041 [0.5692; 1.1374] 0.2145	
Paclitaxel	42 / 67 (62.7)	16.1 [11.1; 19.1]	49 / 68 (72.1)	6.3 [5.0; 6.9]	0.3479 [0.2230; 0.5396] <.0001	

N: number of patients in analysis set, Nsub: number of patients in subgroup category; n: number of patients with events; %: proportion of number of patients in subgroup category
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
BICR: Blinded Independent Central Review; CI: confidence interval; HR: hazard ratio; NE: not estimable

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Run date: 04SEP2024 14:49; Program name: T.2.4.3_PFS_BICR_FAS_SUB_SIG.sas; Output name: T.2.4.3_PFS_BICR_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.4.1 Progressionsfreies Überleben (PFS) gemäß RECIST 1.1 gemäß BICR – Kaplan-Meier-Plot – FAS

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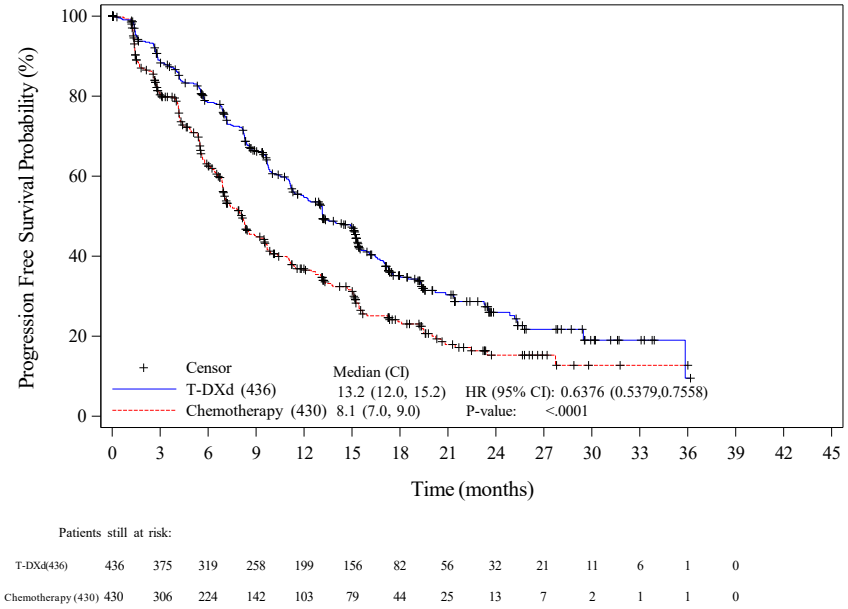
Figure 2.4.1 Progression-Free Survival (PFS) according to RECIST 1.1 by BICR - Kaplan-Meier plot - Full Analysis Set



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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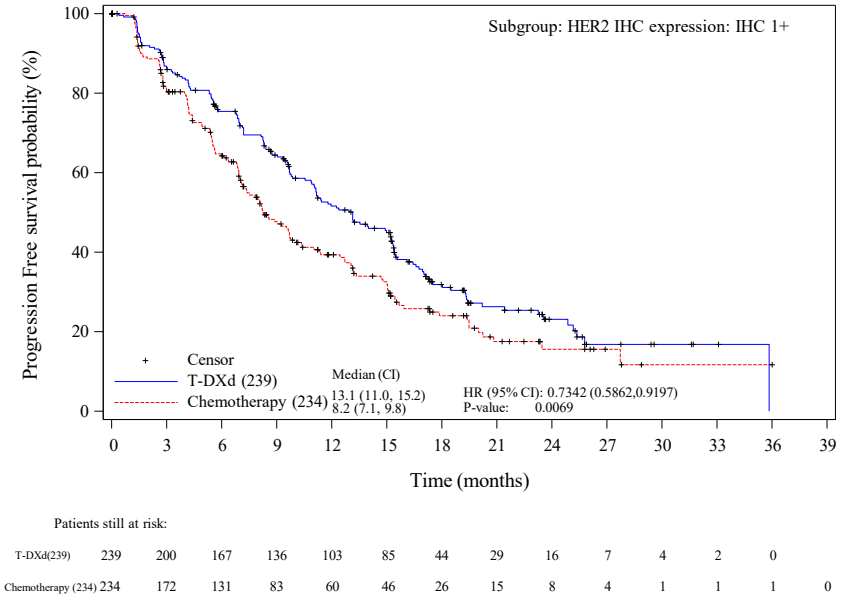
Abbildung 2.4.2 Progressionsfreies Überleben (PFS) gemäß RECIST 1.1 gemäß BICR – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

Figure 2.4.2 Kaplan-Meier plot of Progression free survival - Kaplan-Meier Plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. BICR: Blinded Independent Central Review; CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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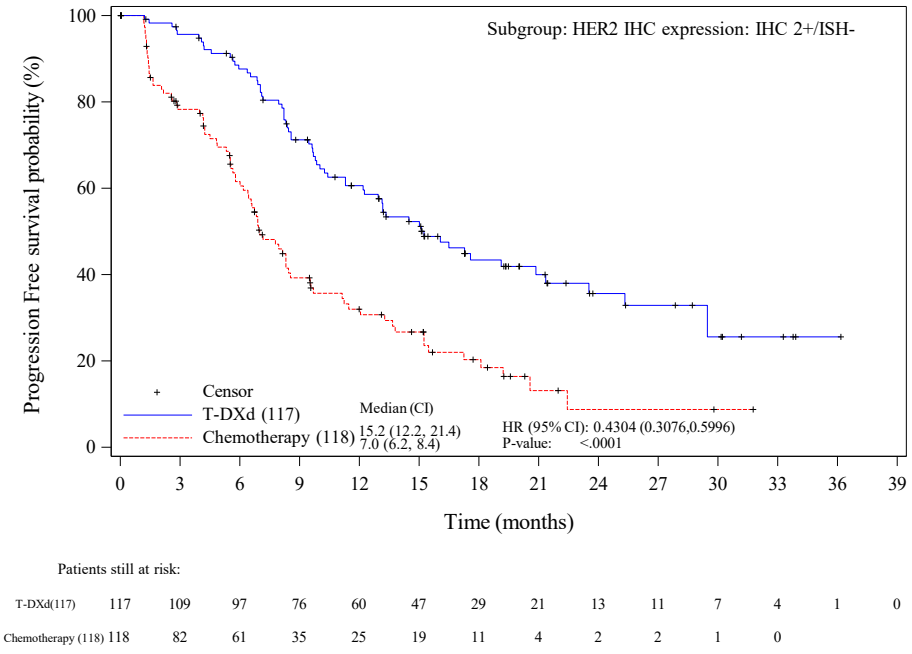
Figure 2.4.2 Kaplan-Meier plot of Progression free survival - Kaplan-Meier Plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. BICR: Blinded Independent Central Review; CI: confidence interval
NE: Not estimable

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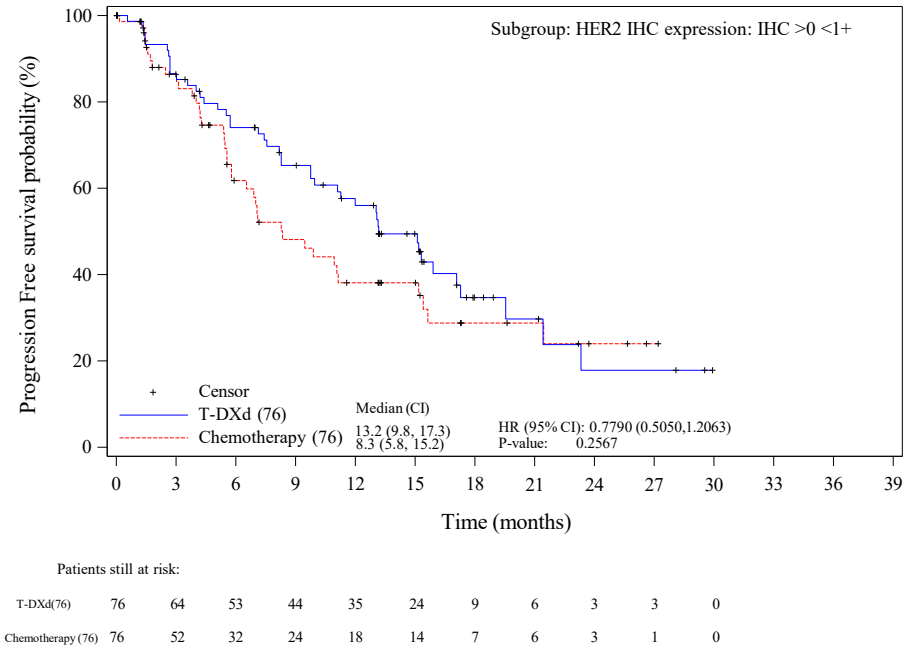
Figure 2.4.2 Kaplan-Meier plot of Progression free survival - Kaplan-Meier Plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. BICR: Blinded Independent Central Review; CI: confidence interval
NE: Not estimable

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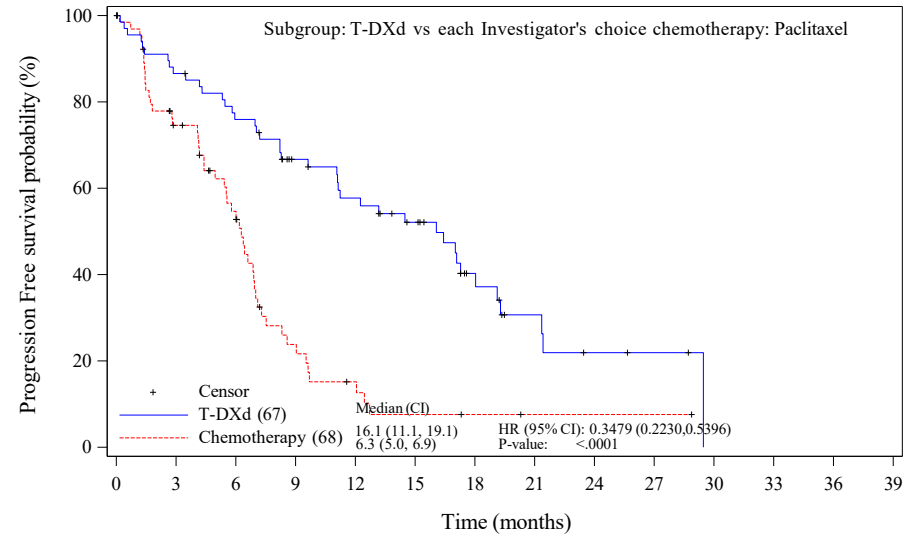
Figure 2.4.2 Kaplan-Meier plot of Progression free survival - Kaplan-Meier Plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. BICR: Blinded Independent Central Review; CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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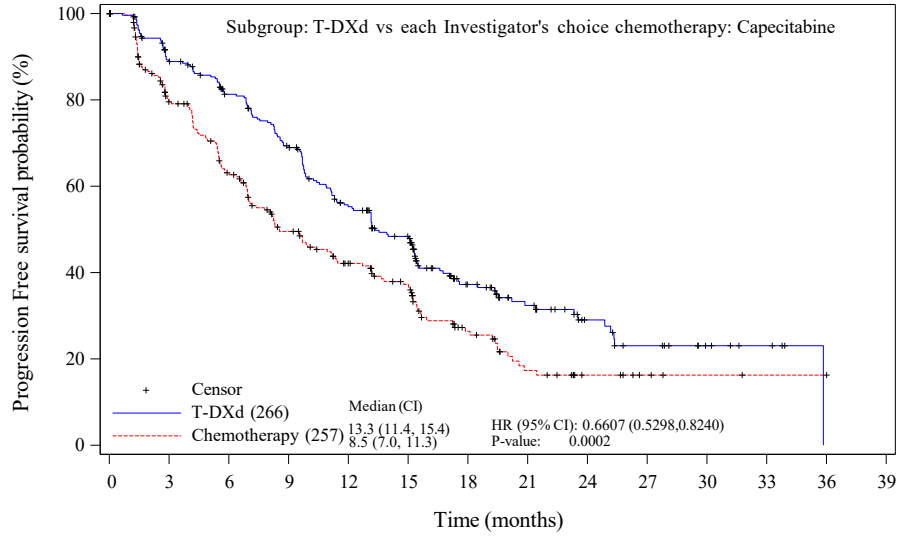
Figure 2.4.2 Kaplan-Meier plot of Progression free survival - Kaplan-Meier Plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. BICR: Blinded Independent Central Review; CI: confidence interval
NE: Not estimable

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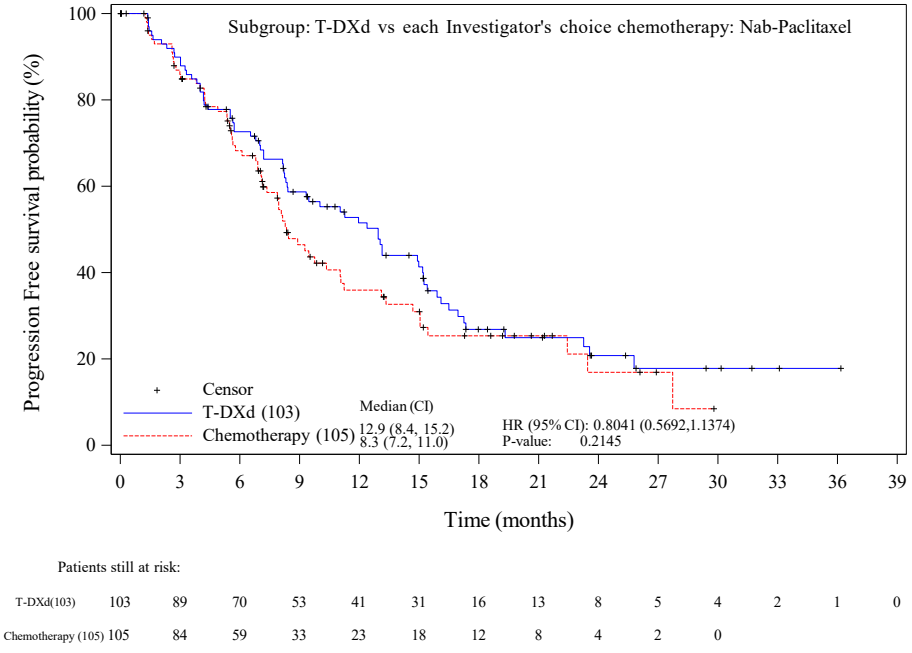
Figure 2.4.2 Kaplan-Meier plot of Progression free survival - Kaplan-Meier Plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from stratified Cox proportional hazards model and two-sided p-value is based on stratified log-rank test. BICR: Blinded Independent Central Review; CI: confidence interval
NE: Not estimable

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Tabelle 2.5.1 Progressionsfreies Überleben 2 gemäß Prüfarzt – FAS

Table 2.5.1 Progression-Free Survival 2 by Investigator - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	228 (52.3)	20.3 [18.9; 23.8]	278 (64.7)	14.7 [13.5; 15.9]	0.6180 [0.5181; 0.7363] <.0001	<.0001
Subjects with censoring event	208 (47.7)		152 (35.3)			
No first subsequent cancer therapy prior to latest	5 (1.1)		2 (0.5)			
Second progression-free at time of analysis	196 (45.0)		125 (29.1)			
Withdrawn consent	7 (1.6)		25 (5.8)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Abbildung 2.5.1 Progressionsfreies Überleben 2 gemäß Prüfarzt – Kaplan-Meier-Plot – FAS

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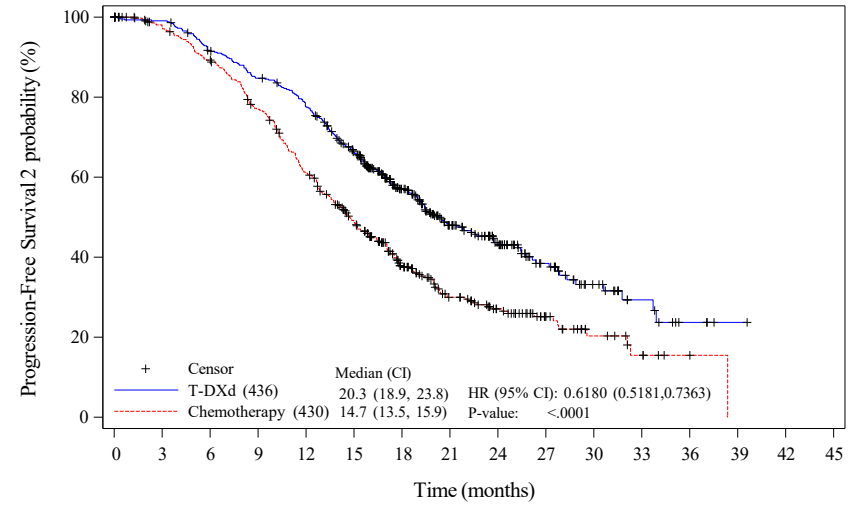
Figure 2.5.1 Progression-Free Survival 2 by Investigator - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:

T-DXd(436)	436	431	396	365	332	268	176	115	78	43	23	11	4	1	0
Chemotherapy (430)	430	399	365	311	244	183	109	69	48	26	12	6	2	0	

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Anhang 4-G 2.2 Tumoransprechen

Anhang 4-G 2.2.1 Objektive Ansprechrate

Tabelle 2.6.1 Objektive Ansprechrate (ORR) gemäß RECIST 1.1 – FAS

Table 2.6.1 Objective Response Rate (ORR) according to RECIST 1.1 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy			
	n (%) [95% CI] [a]	n (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [c]	RD [95% CI] [d]	p-value [b]
ORR by BICR	268 (61.5) [56.7; 66.1]	158 (36.7) [32.2; 41.5]	2.76 [2.10; 3.64]	1.67 [1.45; 1.93]	0.25 [0.18; 0.31]	<.0001
ORR by Investigator Assessment	268 (61.5) [56.7; 66.1]	167 (38.8) [34.2; 43.6]	2.52 [1.92; 3.32]	1.58 [1.38; 1.82]	0.23 [0.16; 0.29]	<.0001
Confirmed ORR by BICR	250 (57.3) [52.5; 62.0]	134 (31.2) [26.8; 35.8]	2.98 [2.26; 3.94]	1.84 [1.56; 2.16]	0.26 [0.20; 0.33]	<.0001
Confirmed ORR by Investigator Assessment	245 (56.2) [51.4; 60.9]	132 (30.7) [26.4; 35.3]	2.91 [2.20; 3.85]	1.83 [1.55; 2.16]	0.25 [0.19; 0.32]	<.0001

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. OR and associated two-sided 95% profile likelihood CI based on a logistic regression model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. p-value based on twice the change in log-likelihood. In case of zero cells a correction value of 0.5 is added to each cell frequency of the corresponding 2x2 contingency table.
c. Derived on percentage point scale based on the 2x2 contingency table with associated asymptotic two-sided CI. In case of zero cells a correction value of 0.5 is added to each cell frequency of the corresponding 2x2 contingency table.
d. Derived on percentage point scale based on the 2x2 contingency table with associated asymptomatic two-sided CI
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

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Tabelle 2.6.2 Objektive Ansprechrate (ORR) gemäß RECIST 1.1 – Subgruppenanalyse – FAS

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
ORR by BICR							
Age at randomization							0.1303
<65 years of age	194 / 302 (64.2) [58.5; 69.6]	106 / 297 (35.7) [30.2; 41.4]	3.24 [2.32; 4.52]	1.80 [1.51; 2.14]	0.29 [0.21; 0.37]	<.0001	
>=65 years of age	74 / 134 (55.2) [46.4; 63.8]	52 / 133 (39.1) [30.8; 47.9]	1.92 [1.18; 3.13]	1.41 [1.09; 1.83]	0.16 [0.04; 0.29]	0.0084	
Race							0.8290
Asian	96 / 154 (62.3) [54.2; 70.0]	53 / 151 (35.1) [27.5; 43.3]	3.06 [1.92; 4.88]	1.78 [1.38; 2.28]	0.27 [0.16; 0.39]	<.0001	
White	141 / 231 (61.0) [54.4; 67.4]	86 / 230 (37.4) [31.1; 44.0]	2.62 [1.80; 3.82]	1.63 [1.34; 1.99]	0.24 [0.14; 0.33]	<.0001	
Other	31 / 51 (60.8) [46.1; 74.2]	19 / 49 (38.8) [25.2; 53.8]	2.45 [1.10; 5.47]	1.57 [1.03; 2.37]	0.22 [0.01; 0.43]	0.0286	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

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Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Region							0.6017
Asia	92 / 149 (61.7) [53.4; 69.6]	54 / 147 (36.7) [28.9; 45.1]	2.78 [1.74; 4.45]	1.68 [1.31; 2.15]	0.25 [0.13; 0.37]	<.0001	
Europe	140 / 227 (61.7) [55.0; 68.0]	83 / 213 (39.0) [32.4; 45.9]	2.52 [1.72; 3.70]	1.58 [1.30; 1.93]	0.23 [0.13; 0.32]	<.0001	
Rest of the World	36 / 60 (60.0) [46.5; 72.4]	21 / 70 (30.0) [19.6; 42.1]	3.50 [1.69; 7.24]	2.00 [1.32; 3.02]	0.30 [0.12; 0.48]	0.0006	
HER2 IHC expression							0.2266
IHC 1+	143 / 239 (59.8) [53.3; 66.1]	93 / 234 (39.7) [33.4; 46.3]	2.26 [1.56; 3.26]	1.51 [1.25; 1.82]	0.20 [0.11; 0.29]	<.0001	
IHC 2+/ISH-	72 / 117 (61.5) [52.1; 70.4]	41 / 118 (34.7) [26.2; 44.1]	3.00 [1.77; 5.11]	1.77 [1.33; 2.36]	0.27 [0.14; 0.40]	<.0001	
IHC >0 <1+	51 / 76 (67.1) [55.4; 77.5]	24 / 76 (31.6) [21.4; 43.3]	4.42 [2.24; 8.73]	2.13 [1.47; 3.07]	0.36 [0.19; 0.52]	<.0001	
Prior CDK4/6 inhibitor use							0.8036
Yes	246 / 394 (62.4) [57.4; 67.2]	146 / 389 (37.5) [32.7; 42.6]	2.77 [2.07; 3.69]	1.66 [1.43; 1.93]	0.25 [0.18; 0.32]	<.0001	
No	22 / 42 (52.4) [36.4; 68.0]	12 / 41 (29.3) [16.1; 45.5]	2.66 [1.08; 6.57]	1.79 [1.03; 3.12]	0.23 [0.00; 0.46]	0.0334	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Prior Taxane Use In The Non-Metastatic Setting							0.3596
Yes	118 / 179 (65.9) [58.5; 72.8]	75 / 177 (42.4) [35.0; 50.0]	2.63 [1.71; 4.04]	1.56 [1.27; 1.90]	0.24 [0.13; 0.34]	<.0001	
No	150 / 257 (58.4) [52.1; 64.5]	83 / 253 (32.8) [27.1; 39.0]	2.87 [2.00; 4.12]	1.78 [1.45; 2.18]	0.26 [0.17; 0.34]	<.0001	
Number of prior lines of endocrine therapy in the metastatic setting							0.3629
1	43 / 65 (66.2) [53.4; 77.4]	26 / 82 (31.7) [21.9; 42.9]	4.21 [2.11; 8.42]	2.09 [1.45; 3.00]	0.34 [0.18; 0.51]	<.0001	
2	174 / 295 (59.0) [53.1; 64.7]	109 / 288 (37.8) [32.2; 43.7]	2.36 [1.69; 3.29]	1.56 [1.31; 1.86]	0.21 [0.13; 0.29]	<.0001	
>=3	50 / 75 (66.7) [54.8; 77.1]	23 / 58 (39.7) [27.0; 53.4]	3.04 [1.49; 6.20]	1.68 [1.18; 2.40]	0.27 [0.09; 0.45]	0.0020	
ER/PR status I							0.1279
ER+, PR+	158 / 253 (62.5) [56.2; 68.4]	80 / 237 (33.8) [27.8; 40.2]	3.26 [2.25; 4.73]	1.85 [1.51; 2.26]	0.29 [0.20; 0.38]	<.0001	
ER+, PR-	102 / 167 (61.1) [53.2; 68.5]	75 / 181 (41.4) [34.2; 49.0]	2.22 [1.44; 3.41]	1.47 [1.19; 1.82]	0.20 [0.09; 0.31]	0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
ER/PR status II							0.9076
ER <=10%	11 / 21 (52.4) [29.8; 74.3]	4 / 14 (28.6) [8.4; 58.1]	2.75 [0.65; 11.62]	1.83 [0.73; 4.62]	0.24 [-0.14; 0.62]	0.1693	
ER >10%	230 / 364 (63.2) [58.0; 68.2]	133 / 355 (37.5) [32.4; 42.7]	2.86 [2.12; 3.88]	1.69 [1.44; 1.97]	0.26 [0.18; 0.33]	<.0001	
Positive	27 / 51 (52.9) [38.5; 67.1]	21 / 61 (34.4) [22.7; 47.7]	2.14 [1.00; 4.59]	1.54 [1.00; 2.37]	0.19 [-0.01; 0.38]	0.0496	
Endocrine Resistance							0.0922
Primary	83 / 128 (64.8) [55.9; 73.1]	45 / 140 (32.1) [24.5; 40.6]	3.89 [2.34; 6.47]	2.02 [1.54; 2.65]	0.33 [0.21; 0.45]	<.0001	
Secondary	185 / 308 (60.1) [54.4; 65.6]	113 / 288 (39.2) [33.6; 45.1]	2.33 [1.68; 3.24]	1.53 [1.29; 1.81]	0.21 [0.13; 0.29]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
T-DXd vs. each Investigatorï¿½s choice chemotherapy							0.5006
Capecitabine	166 / 266 (62.4) [56.3; 68.2]	90 / 257 (35.0) [29.2; 41.2]	3.08 [2.16; 4.40]	1.78 [1.47; 2.16]	0.27 [0.19; 0.36]	<.0001	
Nab-Paclitaxel	63 / 103 (61.2) [51.1; 70.6]	44 / 105 (41.9) [32.3; 51.9]	2.18 [1.25; 3.80]	1.46 [1.11; 1.92]	0.19 [0.05; 0.34]	0.0056	
Paclitaxel	39 / 67 (58.2) [45.5; 70.2]	24 / 68 (35.3) [24.1; 47.8]	2.55 [1.27; 5.12]	1.65 [1.13; 2.41]	0.23 [0.05; 0.41]	0.0079	
Prior anthracycline use							0.2437
Yes	127 / 199 (63.8) [56.7; 70.5]	86 / 208 (41.3) [34.6; 48.4]	2.50 [1.68; 3.73]	1.54 [1.27; 1.87]	0.22 [0.13; 0.32]	<.0001	
No	141 / 237 (59.5) [52.9; 65.8]	72 / 222 (32.4) [26.3; 39.0]	3.06 [2.09; 4.49]	1.83 [1.48; 2.28]	0.27 [0.18; 0.36]	<.0001	
Liver metastases							0.0523
Yes	197 / 296 (66.6) [60.9; 71.9]	124 / 283 (43.8) [38.0; 49.8]	2.55 [1.82; 3.57]	1.52 [1.30; 1.77]	0.23 [0.14; 0.31]	<.0001	
No	71 / 140 (50.7) [42.1; 59.3]	34 / 147 (23.1) [16.6; 30.8]	3.42 [2.06; 5.68]	2.19 [1.57; 3.07]	0.28 [0.16; 0.39]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
ECOG							0.6815
0	166 / 252 (65.9) [59.7; 71.7]	99 / 257 (38.5) [32.5; 44.8]	3.08 [2.15; 4.42]	1.71 [1.43; 2.04]	0.27 [0.19; 0.36]	<.0001	
>=1	98 / 179 (54.7) [47.2; 62.2]	56 / 164 (34.1) [26.9; 41.9]	2.33 [1.51; 3.61]	1.60 [1.25; 2.06]	0.21 [0.10; 0.31]	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
ORR by Investigator Assessment							
Age at randomization							0.0276
<65 years of age	190 / 302 (62.9) [57.2; 68.4]	106 / 297 (35.7) [30.2; 41.4]	3.06 [2.19; 4.26]	1.76 [1.48; 2.10]	0.27 [0.19; 0.35]	<.0001	
>=65 years of age	78 / 134 (58.2) [49.4; 66.7]	61 / 133 (45.9) [37.2; 54.7]	1.64 [1.01; 2.67]	1.27 [1.00; 1.60]	0.12 [0.00; 0.25]	0.0439	
Race							0.6679
Asian	90 / 154 (58.4) [50.2; 66.3]	57 / 151 (37.7) [30.0; 46.0]	2.32 [1.47; 3.67]	1.55 [1.21; 1.98]	0.21 [0.09; 0.32]	0.0003	
White	141 / 231 (61.0) [54.4; 67.4]	91 / 230 (39.6) [33.2; 46.2]	2.39 [1.65; 3.48]	1.54 [1.28; 1.87]	0.21 [0.12; 0.31]	<.0001	
Other	37 / 51 (72.5) [58.3; 84.1]	19 / 49 (38.8) [25.2; 53.8]	4.17 [1.80; 9.68]	1.87 [1.27; 2.76]	0.34 [0.13; 0.54]	0.0007	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Region							0.5484
Asia	87 / 149 (58.4) [50.0; 66.4]	58 / 147 (39.5) [31.5; 47.8]	2.15 [1.35; 3.43]	1.48 [1.16; 1.88]	0.19 [0.07; 0.31]	0.0011	
Europe	142 / 227 (62.6) [55.9; 68.9]	85 / 213 (39.9) [33.3; 46.8]	2.52 [1.71; 3.69]	1.57 [1.29; 1.90]	0.23 [0.13; 0.32]	<.0001	
Rest of the World	39 / 60 (65.0) [51.6; 76.9]	24 / 70 (34.3) [23.3; 46.6]	3.56 [1.72; 7.35]	1.90 [1.30; 2.75]	0.31 [0.13; 0.49]	0.0005	
HER2 IHC expression							0.2240
IHC 1+	139 / 239 (58.2) [51.6; 64.5]	94 / 234 (40.2) [33.8; 46.8]	2.07 [1.43; 2.99]	1.45 [1.20; 1.75]	0.18 [0.09; 0.27]	<.0001	
IHC 2+/ISH-	78 / 117 (66.7) [57.4; 75.1]	49 / 118 (41.5) [32.5; 51.0]	2.82 [1.66; 4.79]	1.61 [1.25; 2.06]	0.25 [0.12; 0.38]	0.0001	
IHC >0 <1+	50 / 76 (65.8) [54.0; 76.3]	24 / 76 (31.6) [21.4; 43.3]	4.17 [2.12; 8.20]	2.08 [1.44; 3.01]	0.34 [0.18; 0.50]	<.0001	
Prior CDK4/6 inhibitor use							0.9917
Yes	242 / 394 (61.4) [56.4; 66.3]	151 / 389 (38.8) [33.9; 43.9]	2.51 [1.88; 3.35]	1.58 [1.37; 1.83]	0.23 [0.16; 0.30]	<.0001	
No	26 / 42 (61.9) [45.6; 76.4]	16 / 41 (39.0) [24.2; 55.5]	2.54 [1.05; 6.15]	1.59 [1.01; 2.49]	0.23 [0.00; 0.46]	0.0383	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Prior Taxane Use In The Non-Metastatic Setting							0.2548
Yes	118 / 179 (65.9) [58.5; 72.8]	67 / 177 (37.9) [30.7; 45.4]	3.18 [2.06; 4.90]	1.74 [1.40; 2.16]	0.28 [0.18; 0.39]	<.0001	
No	150 / 257 (58.4) [52.1; 64.5]	100 / 253 (39.5) [33.5; 45.8]	2.14 [1.51; 3.05]	1.48 [1.23; 1.78]	0.19 [0.10; 0.28]	<.0001	
Number of prior lines of endocrine therapy in the metastatic setting							0.8005
1	41 / 65 (63.1) [50.2; 74.7]	30 / 82 (36.6) [26.2; 48.0]	2.96 [1.51; 5.82]	1.72 [1.23; 2.42]	0.26 [0.09; 0.44]	0.0015	
2	177 / 295 (60.0) [54.2; 65.6]	113 / 288 (39.2) [33.6; 45.1]	2.32 [1.67; 3.24]	1.53 [1.29; 1.81]	0.21 [0.12; 0.29]	<.0001	
>=3	49 / 75 (65.3) [53.5; 76.0]	23 / 58 (39.7) [27.0; 53.4]	2.87 [1.41; 5.83]	1.65 [1.15; 2.36]	0.26 [0.08; 0.44]	0.0033	
ER/PR status I							0.1212
ER+, PR+	150 / 253 (59.3) [53.0; 65.4]	80 / 237 (33.8) [27.8; 40.2]	2.86 [1.98; 4.13]	1.76 [1.43; 2.16]	0.26 [0.17; 0.34]	<.0001	
ER+, PR-	109 / 167 (65.3) [57.5; 72.5]	84 / 181 (46.4) [39.0; 54.0]	2.17 [1.41; 3.34]	1.41 [1.16; 1.70]	0.19 [0.08; 0.30]	0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
ER/PR status II							0.7104
ER <=10%	11 / 21 (52.4) [29.8; 74.3]	4 / 14 (28.6) [8.4; 58.1]	2.75 [0.65; 11.62]	1.83 [0.73; 4.62]	0.24 [-0.14; 0.62]	0.1693	
ER >10%	231 / 364 (63.5) [58.3; 68.4]	140 / 355 (39.4) [34.3; 44.7]	2.67 [1.97; 3.61]	1.61 [1.38; 1.87]	0.24 [0.17; 0.31]	<.0001	
Positive	26 / 51 (51.0) [36.6; 65.2]	23 / 61 (37.7) [25.6; 51.0]	1.72 [0.81; 3.65]	1.35 [0.89; 2.06]	0.13 [-0.07; 0.33]	0.1603	
Endocrine Resistance							0.1522
Primary	84 / 128 (65.6) [56.7; 73.8]	50 / 140 (35.7) [27.8; 44.2]	3.44 [2.08; 5.68]	1.84 [1.42; 2.37]	0.30 [0.18; 0.42]	<.0001	
Secondary	184 / 308 (59.7) [54.0; 65.3]	117 / 288 (40.6) [34.9; 46.5]	2.17 [1.56; 3.01]	1.47 [1.24; 1.74]	0.19 [0.11; 0.27]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
T-DXd vs. each Investigatorï¿½s choice chemotherapy							0.3825
Capecitabine	162 / 266 (60.9) [54.8; 66.8]	97 / 257 (37.7) [31.8; 44.0]	2.57 [1.81; 3.66]	1.61 [1.34; 1.94]	0.23 [0.14; 0.32]	<.0001	
Nab-Paclitaxel	65 / 103 (63.1) [53.0; 72.4]	48 / 105 (45.7) [36.0; 55.7]	2.03 [1.17; 3.54]	1.38 [1.07; 1.78]	0.17 [0.03; 0.32]	0.0120	
Paclitaxel	41 / 67 (61.2) [48.5; 72.9]	22 / 68 (32.4) [21.5; 44.8]	3.30 [1.63; 6.69]	1.89 [1.28; 2.80]	0.29 [0.11; 0.46]	0.0008	
Prior anthracycline use							0.5199
Yes	132 / 199 (66.3) [59.3; 72.9]	83 / 208 (39.9) [33.2; 46.9]	2.97 [1.98; 4.45]	1.66 [1.37; 2.02]	0.26 [0.17; 0.36]	<.0001	
No	136 / 237 (57.4) [50.8; 63.8]	84 / 222 (37.8) [31.4; 44.6]	2.21 [1.52; 3.22]	1.52 [1.24; 1.85]	0.20 [0.10; 0.29]	<.0001	
Liver metastases							0.3840
Yes	193 / 296 (65.2) [59.5; 70.6]	122 / 283 (43.1) [37.3; 49.1]	2.47 [1.77; 3.46]	1.51 [1.29; 1.77]	0.22 [0.14; 0.30]	<.0001	
No	75 / 140 (53.6) [45.0; 62.0]	45 / 147 (30.6) [23.3; 38.7]	2.62 [1.61; 4.24]	1.75 [1.31; 2.33]	0.23 [0.11; 0.35]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
ECOG							0.7454
0	156 / 252 (61.9) [55.6; 67.9]	102 / 257 (39.7) [33.7; 46.0]	2.47 [1.73; 3.53]	1.56 [1.30; 1.87]	0.22 [0.13; 0.31]	<.0001	
>=1	109 / 179 (60.9) [53.3; 68.1]	61 / 164 (37.2) [29.8; 45.1]	2.63 [1.70; 4.07]	1.64 [1.30; 2.06]	0.24 [0.13; 0.35]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Confirmed ORR by BICR							
Age at randomization							0.0544
<65 years of age	181 / 302 (59.9) [54.2; 65.5]	87 / 297 (29.3) [24.2; 34.8]	3.61 [2.57; 5.07]	2.05 [1.68; 2.50]	0.31 [0.23; 0.39]	<.0001	
>=65 years of age	69 / 134 (51.5) [42.7; 60.2]	47 / 133 (35.3) [27.3; 44.1]	1.94 [1.19; 3.17]	1.46 [1.10; 1.93]	0.16 [0.04; 0.29]	0.0079	
Race							0.5657
Asian	92 / 154 (59.7) [51.5; 67.6]	49 / 151 (32.5) [25.1; 40.5]	3.09 [1.93; 4.94]	1.84 [1.41; 2.40]	0.27 [0.16; 0.39]	<.0001	
White	128 / 231 (55.4) [48.8; 61.9]	73 / 230 (31.7) [25.8; 38.2]	2.67 [1.83; 3.91]	1.75 [1.40; 2.18]	0.24 [0.14; 0.33]	<.0001	
Other	30 / 51 (58.8) [44.2; 72.4]	12 / 49 (24.5) [13.3; 38.9]	4.40 [1.87; 10.38]	2.40 [1.40; 4.13]	0.34 [0.14; 0.54]	0.0005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Region							0.8796
Asia	88 / 149 (59.1) [50.7; 67.0]	49 / 147 (33.3) [25.8; 41.6]	2.89 [1.80; 4.63]	1.77 [1.36; 2.31]	0.26 [0.14; 0.37]	<.0001	
Europe	129 / 227 (56.8) [50.1; 63.4]	66 / 213 (31.0) [24.8; 37.7]	2.93 [1.98; 4.34]	1.83 [1.46; 2.31]	0.26 [0.16; 0.35]	<.0001	
Rest of the World	33 / 60 (55.0) [41.6; 67.9]	19 / 70 (27.1) [17.2; 39.1]	3.28 [1.58; 6.82]	2.03 [1.30; 3.17]	0.28 [0.10; 0.46]	0.0013	
HER2 IHC expression							0.3347
IHC 1+	131 / 239 (54.8) [48.3; 61.2]	77 / 234 (32.9) [26.9; 39.3]	2.47 [1.70; 3.59]	1.67 [1.34; 2.07]	0.22 [0.13; 0.31]	<.0001	
IHC 2+/ISH-	70 / 117 (59.8) [50.4; 68.8]	37 / 118 (31.4) [23.1; 40.5]	3.26 [1.91; 5.58]	1.91 [1.41; 2.59]	0.28 [0.15; 0.42]	<.0001	
IHC >0 <1+	47 / 76 (61.8) [50.0; 72.8]	20 / 76 (26.3) [16.9; 37.7]	4.54 [2.28; 9.04]	2.35 [1.55; 3.56]	0.36 [0.19; 0.52]	<.0001	
Prior CDK4/6 inhibitor use							0.8343
Yes	228 / 394 (57.9) [52.8; 62.8]	123 / 389 (31.6) [27.0; 36.5]	2.97 [2.22; 3.98]	1.83 [1.55; 2.17]	0.26 [0.19; 0.33]	<.0001	
No	22 / 42 (52.4) [36.4; 68.0]	11 / 41 (26.8) [14.2; 42.9]	3.00 [1.20; 7.52]	1.95 [1.09; 3.49]	0.26 [0.03; 0.48]	0.0181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Prior Taxane Use In The Non-Metastatic Setting							0.9844
Yes	110 / 179 (61.5) [53.9; 68.6]	59 / 177 (33.3) [26.4; 40.8]	3.19 [2.07; 4.92]	1.84 [1.45; 2.34]	0.28 [0.18; 0.39]	<.0001	
No	140 / 257 (54.5) [48.2; 60.7]	75 / 253 (29.6) [24.1; 35.7]	2.84 [1.97; 4.09]	1.84 [1.47; 2.29]	0.25 [0.16; 0.34]	<.0001	
Number of prior lines of endocrine therapy in the metastatic setting							0.8395
1	38 / 65 (58.5) [45.6; 70.6]	24 / 82 (29.3) [19.7; 40.4]	3.40 [1.71; 6.75]	2.00 [1.35; 2.96]	0.29 [0.12; 0.46]	0.0004	
2	165 / 295 (55.9) [50.1; 61.7]	89 / 288 (30.9) [25.6; 36.6]	2.84 [2.02; 3.99]	1.81 [1.48; 2.21]	0.25 [0.17; 0.33]	<.0001	
>=3	46 / 75 (61.3) [49.4; 72.4]	21 / 58 (36.2) [24.0; 49.9]	2.79 [1.38; 5.68]	1.69 [1.15; 2.49]	0.25 [0.07; 0.43]	0.0042	
ER/PR status I							0.0083
ER+, PR+	147 / 253 (58.1) [51.8; 64.3]	61 / 237 (25.7) [20.3; 31.8]	4.00 [2.73; 5.87]	2.26 [1.78; 2.87]	0.32 [0.24; 0.41]	<.0001	
ER+, PR-	95 / 167 (56.9) [49.0; 64.5]	71 / 181 (39.2) [32.1; 46.7]	2.04 [1.33; 3.13]	1.45 [1.16; 1.81]	0.18 [0.07; 0.29]	0.0010	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
ER/PR status II							0.9231
ER <=10%	11 / 21 (52.4) [29.8; 74.3]	4 / 14 (28.6) [8.4; 58.1]	2.75 [0.65; 11.62]	1.83 [0.73; 4.62]	0.24 [-0.14; 0.62]	0.1693	
ER >10%	212 / 364 (58.2) [53.0; 63.4]	114 / 355 (32.1) [27.3; 37.2]	2.95 [2.17; 4.00]	1.81 [1.52; 2.16]	0.26 [0.19; 0.33]	<.0001	
Positive	27 / 51 (52.9) [38.5; 67.1]	16 / 61 (26.2) [15.8; 39.1]	3.16 [1.43; 6.99]	2.02 [1.23; 3.31]	0.27 [0.07; 0.46]	0.0040	
Endocrine Resistance							0.1215
Primary	74 / 128 (57.8) [48.8; 66.5]	36 / 140 (25.7) [18.7; 33.8]	3.96 [2.36; 6.64]	2.25 [1.64; 3.09]	0.32 [0.20; 0.44]	<.0001	
Secondary	176 / 308 (57.1) [51.4; 62.7]	98 / 288 (34.0) [28.6; 39.8]	2.59 [1.85; 3.60]	1.68 [1.39; 2.03]	0.23 [0.15; 0.31]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
T-DXd vs. each Investigatorï¿½s choice chemotherapy							0.2408
Capecitabine	154 / 266 (57.9) [51.7; 63.9]	79 / 257 (30.7) [25.2; 36.8]	3.10 [2.16; 4.44]	1.88 [1.53; 2.32]	0.27 [0.19; 0.36]	<.0001	
Nab-Paclitaxel	58 / 103 (56.3) [46.2; 66.1]	39 / 105 (37.1) [27.9; 47.1]	2.18 [1.25; 3.80]	1.52 [1.12; 2.05]	0.19 [0.05; 0.33]	0.0057	
Paclitaxel	38 / 67 (56.7) [44.0; 68.8]	16 / 68 (23.5) [14.1; 35.4]	4.26 [2.03; 8.93]	2.41 [1.50; 3.88]	0.33 [0.16; 0.50]	<.0001	
Prior anthracycline use							0.6968
Yes	116 / 199 (58.3) [51.1; 65.2]	68 / 208 (32.7) [26.4; 39.5]	2.88 [1.92; 4.31]	1.78 [1.42; 2.24]	0.26 [0.16; 0.35]	<.0001	
No	134 / 237 (56.5) [50.0; 62.9]	66 / 222 (29.7) [23.8; 36.2]	3.08 [2.09; 4.52]	1.90 [1.51; 2.40]	0.27 [0.18; 0.36]	<.0001	
Liver metastases							0.0368
Yes	182 / 296 (61.5) [55.7; 67.1]	106 / 283 (37.5) [31.8; 43.4]	2.67 [1.91; 3.73]	1.64 [1.38; 1.96]	0.24 [0.16; 0.32]	<.0001	
No	68 / 140 (48.6) [40.0; 57.2]	28 / 147 (19.0) [13.0; 26.3]	4.01 [2.37; 6.81]	2.55 [1.75; 3.71]	0.30 [0.18; 0.41]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
ECOG							0.5117
0	157 / 252 (62.3) [56.0; 68.3]	84 / 257 (32.7) [27.0; 38.8]	3.40 [2.36; 4.90]	1.91 [1.56; 2.33]	0.30 [0.21; 0.38]	<.0001	
>=1	89 / 179 (49.7) [42.2; 57.3]	48 / 164 (29.3) [22.4; 36.9]	2.39 [1.53; 3.73]	1.70 [1.28; 2.25]	0.20 [0.10; 0.31]	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Confirmed ORR by Investigator Assessment							
Age at randomization							0.0107
<65 years of age	175 / 302 (57.9) [52.2; 63.6]	81 / 297 (27.3) [22.3; 32.7]	3.67 [2.61; 5.18]	2.12 [1.72; 2.62]	0.31 [0.23; 0.39]	<.0001	
>=65 years of age	70 / 134 (52.2) [43.4; 60.9]	51 / 133 (38.3) [30.1; 47.2]	1.76 [1.08; 2.86]	1.36 [1.04; 1.78]	0.14 [0.01; 0.26]	0.0229	
Race							0.4186
Asian	85 / 154 (55.2) [47.0; 63.2]	48 / 151 (31.8) [24.5; 39.9]	2.64 [1.66; 4.22]	1.74 [1.32; 2.28]	0.23 [0.12; 0.35]	<.0001	
White	128 / 231 (55.4) [48.8; 61.9]	72 / 230 (31.3) [25.4; 37.7]	2.73 [1.86; 3.99]	1.77 [1.42; 2.21]	0.24 [0.15; 0.33]	<.0001	
Other	32 / 51 (62.7) [48.1; 75.9]	12 / 49 (24.5) [13.3; 38.9]	5.19 [2.19; 12.32]	2.56 [1.50; 4.38]	0.38 [0.18; 0.58]	0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Region							0.5536
Asia	81 / 149 (54.4) [46.0; 62.5]	48 / 147 (32.7) [25.2; 40.9]	2.46 [1.53; 3.94]	1.66 [1.26; 2.19]	0.22 [0.10; 0.33]	0.0002	
Europe	128 / 227 (56.4) [49.7; 62.9]	65 / 213 (30.5) [24.4; 37.2]	2.94 [1.99; 4.36]	1.85 [1.46; 2.33]	0.26 [0.16; 0.35]	<.0001	
Rest of the World	36 / 60 (60.0) [46.5; 72.4]	19 / 70 (27.1) [17.2; 39.1]	4.03 [1.93; 8.42]	2.21 [1.43; 3.42]	0.33 [0.15; 0.51]	0.0002	
HER2 IHC expression							0.4439
IHC 1+	133 / 239 (55.6) [49.1; 62.1]	74 / 234 (31.6) [25.7; 38.0]	2.71 [1.86; 3.95]	1.76 [1.41; 2.19]	0.24 [0.15; 0.33]	<.0001	
IHC 2+/ISH-	70 / 117 (59.8) [50.4; 68.8]	41 / 118 (34.7) [26.2; 44.1]	2.80 [1.65; 4.75]	1.72 [1.29; 2.30]	0.25 [0.12; 0.38]	0.0001	
IHC >0 <1+	41 / 76 (53.9) [42.1; 65.5]	17 / 76 (22.4) [13.6; 33.4]	4.07 [2.01; 8.21]	2.41 [1.51; 3.85]	0.32 [0.16; 0.48]	<.0001	
Prior CDK4/6 inhibitor use							0.7114
Yes	221 / 394 (56.1) [51.0; 61.1]	118 / 389 (30.3) [25.8; 35.2]	2.93 [2.19; 3.94]	1.85 [1.55; 2.20]	0.26 [0.19; 0.33]	<.0001	
No	24 / 42 (57.1) [41.0; 72.3]	14 / 41 (34.1) [20.1; 50.6]	2.57 [1.06; 6.25]	1.67 [1.02; 2.76]	0.23 [0.00; 0.46]	0.0366	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Prior Taxane Use In The Non-Metastatic Setting							0.1125
Yes	105 / 179 (58.7) [51.1; 66.0]	48 / 177 (27.1) [20.7; 34.3]	3.81 [2.44; 5.95]	2.16 [1.65; 2.84]	0.32 [0.21; 0.42]	<.0001	
No	140 / 257 (54.5) [48.2; 60.7]	84 / 253 (33.2) [27.4; 39.4]	2.41 [1.68; 3.45]	1.64 [1.33; 2.02]	0.21 [0.12; 0.30]	<.0001	
Number of prior lines of endocrine therapy in the metastatic setting							0.8609
1	38 / 65 (58.5) [45.6; 70.6]	24 / 82 (29.3) [19.7; 40.4]	3.40 [1.71; 6.75]	2.00 [1.35; 2.96]	0.29 [0.12; 0.46]	0.0004	
2	161 / 295 (54.6) [48.7; 60.4]	89 / 288 (30.9) [25.6; 36.6]	2.69 [1.91; 3.77]	1.77 [1.44; 2.16]	0.24 [0.16; 0.32]	<.0001	
>=3	45 / 75 (60.0) [48.0; 71.1]	19 / 58 (32.8) [21.0; 46.3]	3.08 [1.50; 6.31]	1.83 [1.21; 2.77]	0.27 [0.09; 0.45]	0.0019	
ER/PR status I							0.2002
ER+, PR+	134 / 253 (53.0) [46.6; 59.2]	61 / 237 (25.7) [20.3; 31.8]	3.25 [2.22; 4.76]	2.06 [1.61; 2.63]	0.27 [0.19; 0.36]	<.0001	
ER+, PR-	104 / 167 (62.3) [54.5; 69.6]	68 / 181 (37.6) [30.5; 45.1]	2.74 [1.78; 4.23]	1.66 [1.33; 2.07]	0.25 [0.14; 0.35]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
ER/PR status II							0.8588
ER <=10%	10 / 21 (47.6) [25.7; 70.2]	4 / 14 (28.6) [8.4; 58.1]	2.27 [0.54; 9.61]	1.67 [0.65; 4.27]	0.19 [-0.19; 0.57]	0.2667	
ER >10%	212 / 364 (58.2) [53.0; 63.4]	111 / 355 (31.3) [26.5; 36.4]	3.07 [2.26; 4.16]	1.86 [1.56; 2.22]	0.27 [0.20; 0.34]	<.0001	
Positive	23 / 51 (45.1) [31.1; 59.7]	17 / 61 (27.9) [17.1; 40.8]	2.13 [0.97; 4.66]	1.62 [0.98; 2.68]	0.17 [-0.02; 0.37]	0.0592	
Endocrine Resistance							0.1555
Primary	76 / 128 (59.4) [50.3; 68.0]	38 / 140 (27.1) [20.0; 35.3]	3.92 [2.35; 6.55]	2.19 [1.61; 2.97]	0.32 [0.20; 0.44]	<.0001	
Secondary	169 / 308 (54.9) [49.1; 60.5]	94 / 288 (32.6) [27.3; 38.4]	2.51 [1.80; 3.50]	1.68 [1.38; 2.04]	0.22 [0.14; 0.30]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
T-DXd vs. each Investigatorï¿½s choice chemotherapy							0.0600
Capecitabine	151 / 266 (56.8) [50.6; 62.8]	77 / 257 (30.0) [24.4; 36.0]	3.07 [2.14; 4.40]	1.89 [1.53; 2.35]	0.27 [0.18; 0.35]	<.0001	
Nab-Paclitaxel	58 / 103 (56.3) [46.2; 66.1]	42 / 105 (40.0) [30.6; 50.0]	1.93 [1.11; 3.36]	1.41 [1.05; 1.88]	0.16 [0.02; 0.31]	0.0189	
Paclitaxel	36 / 67 (53.7) [41.1; 66.0]	13 / 68 (19.1) [10.6; 30.5]	4.91 [2.27; 10.63]	2.81 [1.64; 4.81]	0.35 [0.18; 0.51]	<.0001	
Prior anthracycline use							0.5094
Yes	117 / 199 (58.8) [51.6; 65.7]	63 / 208 (30.3) [24.1; 37.0]	3.28 [2.18; 4.94]	1.94 [1.53; 2.46]	0.29 [0.19; 0.38]	<.0001	
No	128 / 237 (54.0) [47.4; 60.5]	69 / 222 (31.1) [25.1; 37.6]	2.60 [1.78; 3.82]	1.74 [1.38; 2.18]	0.23 [0.14; 0.32]	<.0001	
Liver metastases							0.1991
Yes	176 / 296 (59.5) [53.6; 65.1]	99 / 283 (35.0) [29.4; 40.9]	2.73 [1.95; 3.82]	1.70 [1.41; 2.04]	0.24 [0.16; 0.33]	<.0001	
No	69 / 140 (49.3) [40.7; 57.9]	33 / 147 (22.4) [16.0; 30.1]	3.36 [2.02; 5.59]	2.20 [1.56; 3.10]	0.27 [0.15; 0.38]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.2 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
ECOG							0.7628
0	142 / 252 (56.3) [50.0; 62.6]	80 / 257 (31.1) [25.5; 37.2]	2.86 [1.99; 4.11]	1.81 [1.46; 2.24]	0.25 [0.16; 0.34]	<.0001	
>=1	100 / 179 (55.9) [48.3; 63.3]	48 / 164 (29.3) [22.4; 36.9]	3.06 [1.96; 4.79]	1.91 [1.46; 2.50]	0.27 [0.16; 0.37]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 06SEP2024 4:27; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.6.3 Objektive Ansprechrate (ORR) gemäß RECIST 1.1 – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.6.3 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
ORR by Investigator Assessment							
Age at randomization							0.0276
<65 years of age	190 / 302 (62.9) [57.2; 68.4]	106 / 297 (35.7) [30.2; 41.4]	3.06 [2.19; 4.26]	1.76 [1.48; 2.10]	0.27 [0.19; 0.35]	<.0001	
>=65 years of age	78 / 134 (58.2) [49.4; 66.7]	61 / 133 (45.9) [37.2; 54.7]	1.64 [1.01; 2.67]	1.27 [1.00; 1.60]	0.12 [0.00; 0.25]	0.0439	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 22JUL2024 5:11; Program name: T.2.6.3_ORR_BICR_FAS_SUB_SIG.sas; Output name: T.2.6.3_ORR_BICR_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.3 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Confirmed ORR by BICR							
ER/PR status I							0.0083
ER+, PR+	147 / 253 (58.1) [51.8; 64.3]	61 / 237 (25.7) [20.3; 31.8]	4.00 [2.73; 5.87]	2.26 [1.78; 2.87]	0.32 [0.24; 0.41]	<.0001	
ER+, PR-	95 / 167 (56.9) [49.0; 64.5]	71 / 181 (39.2) [32.1; 46.7]	2.04 [1.33; 3.13]	1.45 [1.16; 1.81]	0.18 [0.07; 0.29]	0.0010	
Liver metastases							0.0368
Yes	182 / 296 (61.5) [55.7; 67.1]	106 / 283 (37.5) [31.8; 43.4]	2.67 [1.91; 3.73]	1.64 [1.38; 1.96]	0.24 [0.16; 0.32]	<.0001	
No	68 / 140 (48.6) [40.0; 57.2]	28 / 147 (19.0) [13.0; 26.3]	4.01 [2.37; 6.81]	2.55 [1.75; 3.71]	0.30 [0.18; 0.41]	<.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 22JUL2024 5:11; Program name: T.2.6.3_ORR_BICR_FAS_SUB_SIG.sas; Output name: T.2.6.3_ORR_BICR_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.6.3 Objective Response Rate (ORR) according to RECIST 1.1 - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy				Interaction
	n / Nsub (%) [95% CI] [a]	n / Nsub (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [b]	RD [95% CI] [b]	p-value [c]	p-value [d]
Confirmed ORR by Investigator Assessment							
Age at randomization							0.0107
<65 years of age	175 / 302 (57.9) [52.2; 63.6]	81 / 297 (27.3) [22.3; 32.7]	3.67 [2.61; 5.18]	2.12 [1.72; 2.62]	0.31 [0.23; 0.39]	<.0001	
>=65 years of age	70 / 134 (52.2) [43.4; 60.9]	51 / 133 (38.3) [30.1; 47.2]	1.76 [1.08; 2.86]	1.36 [1.04; 1.78]	0.14 [0.01; 0.26]	0.0229	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. Estimates derived based on 2x2 contingency table with associated asymptotic two-sided 95% CI
c. Two-sided p-value derived from unstratified Cochran-Mantel-Haenszel test
d. Two-sided p-value from Cochrane's Q test for homogeneity of the treatment effect across subgroups
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; ORR: objective response rate; RD: risk difference; RR: relative risk

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 22JUL2024 5:11; Program name: T.2.6.3_ORR_BICR_FAS_SUB_SIG.sas; Output name: T.2.6.3_ORR_BICR_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Anhang 4-G 2.2.2 Dauer des Ansprechens

Tabelle 2.7.1 Dauer des Ansprechens (DoR) gemäß BICR – FAS

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Table 2.7.1 Duration of Response (DoR) by BICR - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n / NR(%)	Median [95% CI] in months [a]	n / NR(%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	156 / 268 (58.2)	13.7 [11.8; 15.4]	99 / 158 (62.7)	7.3 [6.0; 10.8]	0.5918 [0.4589; 0.7669] <.0001	0.0001
Subjects with censoring event	112 / 268 (41.8)		59 / 158 (37.3)			
Censored RECIST progression	5 / 268 (1.9)		3 / 158 (1.9)			
Censored death	14 / 268 (5.2)		12 / 158 (7.6)			
Progression-free at time of analysis	90 / 268 (33.6)		39 / 158 (24.7)			
Withdrawn consent	3 / 268 (1.1)		5 / 158 (3.2)			

N: number of subjects in analysis set; NR: number of subjects with response in analysis set; n: number of subjects with event; %: proportion of number of subjects with response in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
BICR: Blinded Independent Central Review; CI: confidence interval; HR: hazard ratio

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04DEC2024 3:49; Program name: T.2.7.1_DoR_FAS.sas; Output name: T.2.7.1_DoR_FAS.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.7.1 Dauer des Ansprechens (DoR) gemäß BICR – Kaplan-Meier-Plot – FAS

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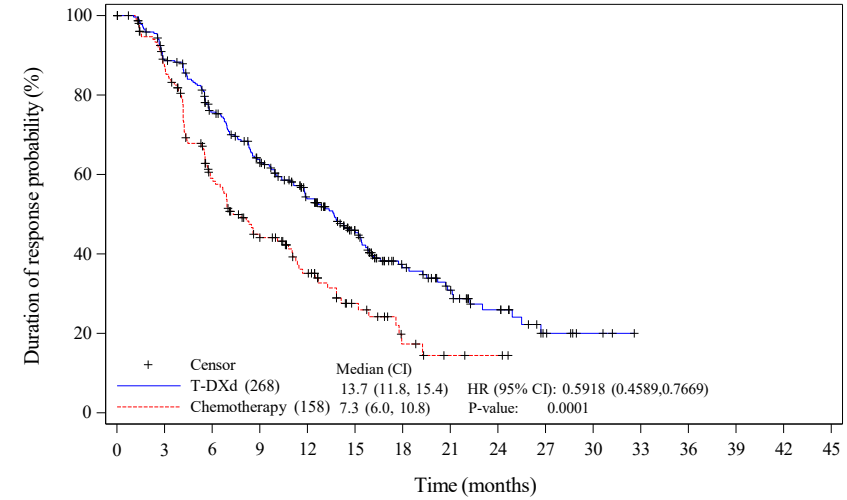
Figure 2.7.1 Duration of Response (DoR) by BICR - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:

T-DXd(268)	268	231	188	151	112	75	43	30	18	7	3	0
Chemotherapy (158)	158	129	78	53	34	17	7	3	2	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 03DEC2024 5:25; Program name: F.2.7.1_DoR_FAS.sas; Output name: F.2.7.1_DoR_FAS.rtf; DI-EG project ID: D9670C00001;

Anhang 4-G 2.2.3 Klinische Kontrollrate

Tabelle 2.8.1 Klinische Kontrollrate (DCR) – FAS

Table 2.8.1 Disease Control Rate (DCR) - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy			
	n (%) [95% CI] [a]	n (%) [95% CI] [a]	OR [95% CI] [b]	RR [95% CI] [c]	RD [95% CI] [d]	p-value [b]
DCR by BICR	350 (80.3) [76.2; 83.9]	249 (57.9) [53.1; 62.6]	2.97 [2.20; 4.05]	1.39 [1.26; 1.52]	0.22 [0.16; 0.29]	<.0001
DCR by Investigator Assessment	358 (82.1) [78.2; 85.6]	250 (58.1) [53.3; 62.8]	3.31 [2.44; 4.54]	1.41 [1.29; 1.55]	0.24 [0.18; 0.30]	<.0001

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Two-sided exact CI based on Clopper-Pearson method for single proportion
b. OR and associated two-sided 95% profile likelihood CI based on a logistic regression model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. p-value based on twice the change in log-likelihood. In case of zero cells a correction value of 0.5 is added to each cell frequency of the corresponding 2x2 contingency table.
c. Derived on percentage point scale based on the 2x2 contingency table with associated asymptotic two-sided CI. In case of zero cells a correction value of 0.5 is added to each cell frequency of the corresponding 2x2 contingency table.
d. Derived on percentage point scale based on the 2x2 contingency table with associated asymptomatic two-sided CI
BICR: blinded independent central review; CI: confidence interval; OR: odds ratio; DCR: disease control rate; RD: risk difference; RR: relative risk

Anhang 4-G 2.3 Zeit bis zur Hospitalisierung

Tabelle 2.9.1 Zeit bis zur Hospitalisierung – FAS

Table 2.9.1 Time to first hospitalization due to any reason - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	111 (25.5)	NE [NE; NE]	87 (20.2)	NE [22.1; NE]	0.8937 [0.6734; 1.1897] 0.4382	0.4378
Subjects with censoring event	325 (74.5)		343 (79.8)			
Last contact	73 (16.7)		59 (13.7)			
Last dose of study treatment + 47 days	98 (22.5)		72 (16.7)			
Start of subsequent cancer therapy	154 (35.3)		212 (49.3)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

Tabelle 2.9.2 Zeit bis zur Hospitalisierung – Subgruppenanalyse – FAS

Table 2.9.2 Time to first hospitalization due to any reason - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Age at randomization						0.7928
<65 years of age	69 / 302 (22.8)	NE [24.1; NE]	52 / 297 (17.5)	NE [19.2; NE]	0.8685 [0.6037; 1.2566] 0.4496	
≥65 years of age	42 / 134 (31.3)	NE [18.6; NE]	35 / 133 (26.3)	23.3 [14.8; NE]	0.9595 [0.6109; 1.5159] 0.8546	
Race						0.0502
Asian	44 / 154 (28.6)	NE [20.2; NE]	24 / 151 (15.9)	NE [22.1; NE]	1.4022 [0.8574; 2.3487] 0.1839	
White	56 / 231 (24.2)	NE [24.1; NE]	53 / 230 (23.0)	23.3 [19.2; NE]	0.7447 [0.5092; 1.0903] 0.1267	
Other	11 / 51 (21.6)	NE [22.6; NE]	10 / 49 (20.4)	NE [8.1; NE]	0.5400 [0.2079; 1.3856] 0.1918	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.9.2 Time to first hospitalization due to any reason - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0298
Asia	46 / 149 (30.9)	NE [17.3; NE]	25 / 147 (17.0)	NE [22.1; NE]	1.4314 [0.8843; 2.3711] 0.1496	
Europe	48 / 227 (21.1)	NE [NE; NE]	46 / 213 (21.6)	NE [NE; NE]	0.6780 [0.4490; 1.0246] 0.0624	
Rest of the World	17 / 60 (28.3)	22.6 [12.0; NE]	16 / 70 (22.9)	19.2 [14.1; NE]	0.8408 [0.4205; 1.6888] 0.6221	
HER2 IHC expression						0.5000
IHC 1+	60 / 239 (25.1)	NE [NE; NE]	42 / 234 (17.9)	NE [19.8; NE]	1.0481 [0.7065; 1.5693] 0.8160	
IHC 2+/ISH-	29 / 117 (24.8)	NE [21.7; NE]	27 / 118 (22.9)	22.1 [14.1; NE]	0.6811 [0.3981; 1.1685] 0.1579	
IHC >0 <1+	22 / 76 (28.9)	22.6 [17.3; NE]	18 / 76 (23.7)	23.3 [11.1; NE]	0.9381 [0.5015; 1.7780] 0.8406	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.9.2 Time to first hospitalization due to any reason - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8472
Yes	99 / 394 (25.1)	NE [24.1; NE]	76 / 389 (19.5)	NE [19.8; NE]	0.9176 [0.6789; 1.2449] 0.5766	
No	12 / 42 (28.6)	NE [14.5; NE]	11 / 41 (26.8)	23.3 [11.0; NE]	0.7490 [0.3245; 1.7430] 0.4933	
Prior Taxane Use In The Non-Metastatic Setting						0.9142
Yes	46 / 179 (25.7)	NE [20.2; NE]	36 / 177 (20.3)	NE [NE; NE]	0.9291 [0.5982; 1.4547] 0.7454	
No	65 / 257 (25.3)	NE [24.1; NE]	51 / 253 (20.2)	22.1 [19.2; NE]	0.8647 [0.5973; 1.2580] 0.4416	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.9.2 Time to first hospitalization due to any reason - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5703
1	18 / 65 (27.7)	22.6 [20.2; NE]	21 / 82 (25.6)	NE [13.7; NE]	0.7921 [0.4120; 1.5038] 0.4751	
2	74 / 295 (25.1)	NE [NE; NE]	58 / 288 (20.1)	NE [19.8; NE]	0.8716 [0.6165; 1.2382] 0.4385	
>=3	18 / 75 (24.0)	NE [24.1; NE]	8 / 58 (13.8)	NE [22.1; NE]	1.3690 [0.6106; 3.3528] 0.4619	
ER/PR status I						0.9535
ER+, PR missing	6 / 12 (50.0)	9.7 [2.5; NE]	4 / 10 (40.0)	NE [0.2; NE]	0.9622 [0.2741; 3.7735] 0.9527	
ER+, PR+	63 / 253 (24.9)	NE [NE; NE]	45 / 237 (19.0)	NE [19.8; NE]	0.9510 [0.6476; 1.4081] 0.7988	
ER+, PR-	42 / 167 (25.1)	NE [22.6; NE]	37 / 181 (20.4)	22.1 [19.2; NE]	0.8315 [0.5307; 1.3074] 0.4195	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 14:58; Program name: T.2.9.2_HOSP_FAS_SUB.sas; Output name: T.2.9.2_HOSP_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.9.2 Time to first hospitalization due to any reason - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2657
ER <=10%	7 / 21 (33.3)	NE [5.4; NE]	5 / 14 (35.7)	14.1 [2.2; NE]	0.5793 [0.1807; 1.9912] 0.3545	
ER >10%	89 / 364 (24.5)	NE [24.1; NE]	72 / 355 (20.3)	NE [19.8; NE]	0.8439 [0.6164; 1.1591] 0.2907	
Positive	15 / 51 (29.4)	NE [13.7; NE]	10 / 61 (16.4)	NE [22.1; NE]	1.4755 [0.6678; 3.4033] 0.3416	
Endocrine Resistance						0.8946
Primary	34 / 128 (26.6)	NE [20.2; NE]	29 / 140 (20.7)	NE [14.1; NE]	0.9124 [0.5527; 1.5167] 0.7220	
Secondary	77 / 308 (25.0)	NE [24.1; NE]	58 / 288 (20.1)	23.3 [19.8; NE]	0.8864 [0.6292; 1.2554] 0.4922	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Table 2.9.2 Time to first hospitalization due to any reason - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3469
Capecitabine	69 / 266 (25.9)	NE [24.1; NE]	57 / 257 (22.2)	23.3 [19.8; NE]	0.8689 [0.6112; 1.2400] 0.4341	
Nab-Paclitaxel	28 / 103 (27.2)	21.7 [16.4; NE]	18 / 105 (17.1)	NE [14.3; NE]	1.0654 [0.5861; 1.9848] 0.8370	
Paclitaxel	14 / 67 (20.9)	NE [NE; NE]	12 / 68 (17.6)	NE [NE; NE]	0.8090 [0.3632; 1.8201] 0.6020	
Prior anthracycline use						0.9354
Yes	53 / 199 (26.6)	NE [21.7; NE]	43 / 208 (20.7)	NE [19.2; NE]	0.9252 [0.6167; 1.3964] 0.7081	
No	58 / 237 (24.5)	NE [24.1; NE]	44 / 222 (19.8)	23.3 [19.8; NE]	0.8662 [0.5836; 1.2941] 0.4769	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 14:58; Program name: T.2.9.2_HOSP_FAS_SUB.sas; Output name: T.2.9.2_HOSP_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.9.2 Time to first hospitalization due to any reason - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.6586
Yes	72 / 296 (24.3)	NE [NE; NE]	56 / 283 (19.8)	NE [22.1; NE]	0.8899 [0.6259; 1.2715] 0.5174	
No	39 / 140 (27.9)	NE [18.6; NE]	31 / 147 (21.1)	23.3 [14.8; NE]	0.9064 [0.5634; 1.4703] 0.6862	
ECOG						0.6581
0	53 / 252 (21.0)	NE [NE; NE]	47 / 257 (18.3)	NE [19.8; NE]	0.8149 [0.5479; 1.2154] 0.3099	
>=1	55 / 179 (30.7)	24.1 [20.2; NE]	39 / 164 (23.8)	22.1 [13.7; NE]	0.9212 [0.6096; 1.4048] 0.6992	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Tabelle 2.9.3 Zeit bis zur Hospitalisierung – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.9.3 Time to first hospitalization due to any reason - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region					.	0.0298
Asia	46 / 149 (30.9)	NE [17.3; NE]	25 / 147 (17.0)	NE [22.1; NE]	1.4314 [0.8843; 2.3711] 0.1496	
Europe	48 / 227 (21.1)	NE [NE; NE]	46 / 213 (21.6)	NE [NE; NE]	0.6780 [0.4490; 1.0246] 0.0624	
Rest of the World	17 / 60 (28.3)	22.6 [12.0; NE]	16 / 70 (22.9)	19.2 [14.1; NE]	0.8408 [0.4205; 1.6888] 0.6221	

N: number of patients in analysis set, Nsub: number of patients in subgroup category; n: number of patients with events; %: proportion of number of patients in subgroup category
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 04SEP2024 15:00; Program name: T.2.9.3_HOSP_FAS_SUB_SIG.sas; Output name: T.2.9.3_HOSP_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.9.1 Zeit bis zur Hospitalisierung – Kaplan-Meier-Plot – FAS

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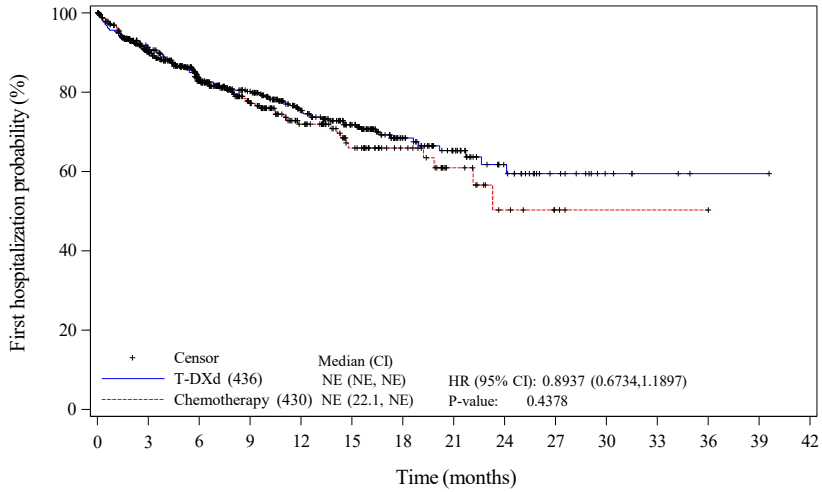
Figure 2.9.1 Time to first hospitalization due to any reason - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:

T-DXd(436)	436	372	303	252	182	135	74	49	27	14	6	3	1	1	0
Chemotherapy (430)	430	305	212	130	79	51	31	16	7	3	1	1	1	0	

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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Abbildung 2.9.2 Zeit bis zur Hospitalisierung – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

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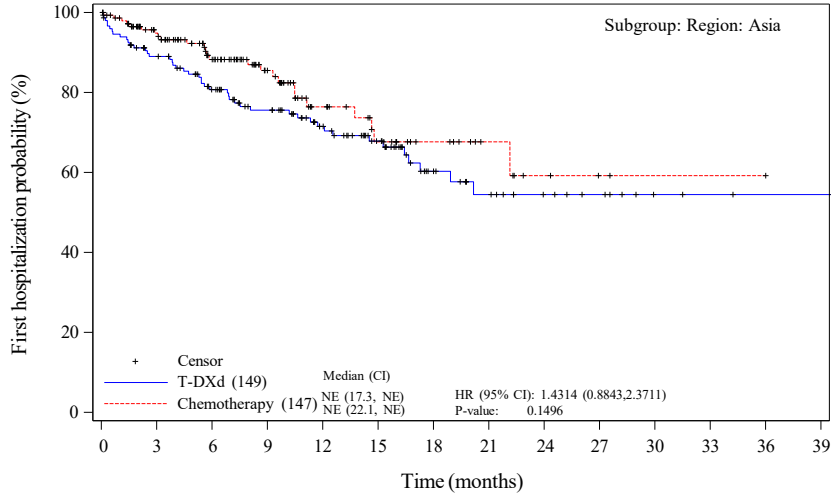
Figure 2.9.2 Time to first hospitalization due to any reason - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Patients still at risk:

T-DXd(149)	149	124	102	84	64	47	25	17	11	8	3	2	1	1
Chemotherapy (147)	147	115	85	57	32	22	14	8	4	2	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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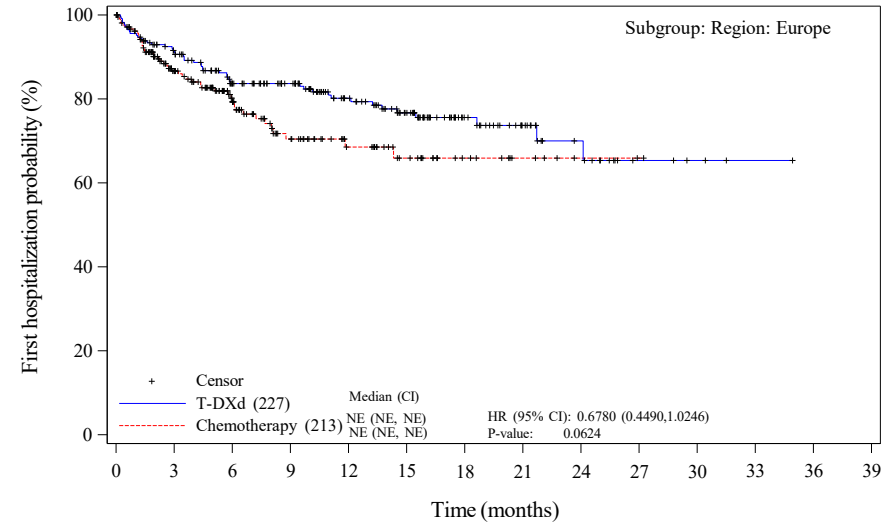
Figure 2.9.2 Time to first hospitalization due to any reason - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Patients still at risk:

T-DXd(227)	227	196	158	136	100	76	41	26	15	5	3	1	0
Chemotherapy (213)	213	140	90	54	35	23	12	6	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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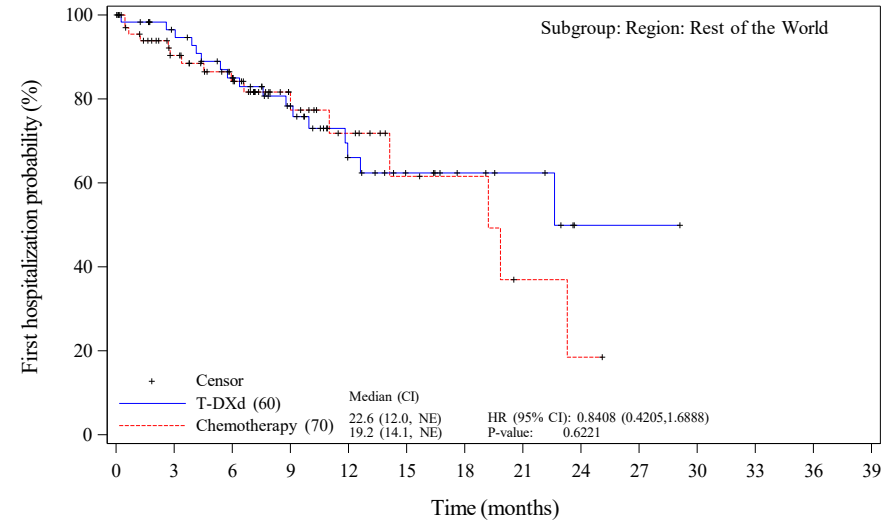
Figure 2.9.2 Time to first hospitalization due to any reason - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Patients still at risk:

T-DXd(60)	60	52	43	32	18	12	8	6	1	1	0
Chemotherapy (70)	70	50	37	19	12	6	5	2	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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Anhang 4-G 3. Analysen DESTINY-Breast06: Patientenberichtete Fragebögen – FAS

Anhang 4-G 3.1 EQ-5D-5L VAS

Tabelle 2.10.1 EQ-5D-5L VAS – Zeit bis zur bestätigten Verschlechterung – FAS

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Table 2.10.1 EQ-5D-5L VAS - Time to confirmed deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	93 (21.3)	31.1 [16.0; NE]	111 (25.8)	14.0 [9.9; NE]	0.7255 [0.5492; 0.9564] 0.0232	0.0230
Subjects with censoring event	343 (78.7)		319 (74.2)			
Baseline score not allowing for deterioration	4 (0.9)		5 (1.2)			
Deterioration after 2 or more missed assessments	1 (0.2)		2 (0.5)			
No baseline data	152 (34.9)		82 (19.1)			
No deterioration	161 (36.9)		168 (39.1)			
No evaluable visit	25 (5.7)		62 (14.4)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

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Tabelle 2.10.2 EQ-5D-5L VAS – Zeit bis zur bestätigten Verschlechterung – Subgruppenanalyse – FAS

Table 2.10.2 EQ-5D-5L VAS - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Age at randomization						0.2306
<65 years of age	70 / 302 (23.2)	20.7 [15.9; NE]	70 / 297 (23.6)	21.3 [9.9; NE]	0.8109 [0.5801; 1.1333] 0.2183	
≥65 years of age	23 / 134 (17.2)	NE [10.3; NE]	41 / 133 (30.8)	10.4 [5.5; 15.2]	0.5729 [0.3381; 0.9472] 0.0306	
Race						0.7600
Asian	49 / 154 (31.8)	31.1 [16.0; NE]	55 / 151 (36.4)	13.1 [9.0; NE]	0.6999 [0.4739; 1.0307] 0.0698	
White	39 / 231 (16.9)	20.7 [12.4; NE]	50 / 230 (21.7)	15.2 [9.6; NE]	0.8062 [0.5269; 1.2245] 0.3140	
Other	5 / 51 (9.8)	NE [10.3; NE]	6 / 49 (12.2)	9.6 [3.6; NE]	0.4449 [0.1253; 1.5130] 0.1798	
Region						0.6770
Asia	47 / 149 (31.5)	NE [16.0; NE]	54 / 147 (36.7)	13.1 [9.0; NE]	0.6978 [0.4697; 1.0328] 0.0714	
Europe	36 / 227 (15.9)	20.7 [12.4; NE]	47 / 213 (22.1)	10.4 [7.1; NE]	0.6994 [0.4497; 1.0788] 0.1057	
Rest of the World	10 / 60 (16.7)	31.1 [11.8; NE]	10 / 70 (14.3)	19.4 [9.6; NE]	0.9073 [0.3570; 2.2718] 0.8365	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.10.2 EQ-5D-5L VAS - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
HER2 IHC expression						0.2479
IHC 1+	47 / 239 (19.7)	31.1 [14.5; NE]	72 / 234 (30.8)	10.4 [6.9; 19.4]	0.6140 [0.4219; 0.8853] 0.0090	
IHC 2+/ISH-	30 / 117 (25.6)	17.3 [9.1; NE]	23 / 118 (19.5)	21.3 [10.4; NE]	1.0740 [0.6243; 1.8727] 0.7958	
IHC >0 <1+	15 / 76 (19.7)	NE [16.0; NE]	16 / 76 (21.1)	NE [9.0; NE]	0.6873 [0.3359; 1.3988] 0.2976	
Prior CDK4/6 inhibitor use						0.6499
Yes	82 / 394 (20.8)	20.7 [15.9; NE]	98 / 389 (25.2)	14.0 [9.9; 21.3]	0.7391 [0.5497; 0.9921] 0.0441	
No	11 / 42 (26.2)	NE [7.7; NE]	13 / 41 (31.7)	NE [3.4; NE]	0.6410 [0.2806; 1.4382] 0.2746	
Prior Taxane Use In The Non-Metastatic Setting						0.8865
Yes	37 / 179 (20.7)	NE [14.5; NE]	43 / 177 (24.3)	13.8 [9.6; NE]	0.7131 [0.4550; 1.1121] 0.1357	
No	56 / 257 (21.8)	20.7 [15.9; NE]	68 / 253 (26.9)	14.4 [9.1; NE]	0.7340 [0.5125; 1.0464] 0.0870	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.10.2 EQ-5D-5L VAS - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1097
1	10 / 65 (15.4)	NE [13.7; NE]	15 / 82 (18.3)	15.2 [9.1; NE]	0.5895 [0.2541; 1.3107] 0.1995	
2	59 / 295 (20.0)	31.1 [16.0; NE]	80 / 288 (27.8)	13.1 [9.0; NE]	0.6384 [0.4533; 0.8933] 0.0087	
>=3	23 / 75 (30.7)	10.3 [7.0; NE]	15 / 58 (25.9)	21.3 [10.0; NE]	1.3599 [0.7157; 2.6626] 0.3521	
ER/PR status I						0.1283
ER+, PR+	49 / 253 (19.4)	31.1 [20.7; NE]	64 / 237 (27.0)	14.0 [9.1; NE]	0.6246 [0.4280; 0.9058] 0.0127	
ER+, PR-	44 / 167 (26.3)	16.0 [10.4; NE]	43 / 181 (23.8)	13.8 [9.6; NE]	0.9203 [0.6023; 1.4073] 0.6996	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.10.2 EQ-5D-5L VAS - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9093
ER <=10%	6 / 21 (28.6)	NE [1.4; NE]	4 / 14 (28.6)	10.4 [1.4; NE]	0.7385 [0.2101; 2.8979] 0.6439	
ER >10%	77 / 364 (21.2)	20.7 [15.9; NE]	89 / 355 (25.1)	14.0 [9.6; NE]	0.7312 [0.5366; 0.9941] 0.0452	
Positive	10 / 51 (19.6)	NE [15.9; NE]	18 / 61 (29.5)	21.3 [4.9; NE]	0.5915 [0.2613; 1.2660] 0.1805	
Endocrine Resistance						0.6672
Primary	29 / 128 (22.7)	17.4 [12.4; NE]	34 / 140 (24.3)	14.0 [9.6; NE]	0.7912 [0.4783; 1.3000] 0.3572	
Secondary	64 / 308 (20.8)	31.1 [16.0; NE]	76 / 288 (26.4)	14.4 [9.0; NE]	0.7112 [0.5080; 0.9925] 0.0444	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.10.2 EQ-5D-5L VAS - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.8992
Capecitabine	54 / 266 (20.3)	31.1 [15.9; NE]	66 / 257 (25.7)	14.4 [9.6; NE]	0.7168 [0.4979; 1.0275] 0.0701	
Nab-Paclitaxel	23 / 103 (22.3)	NE [NE; NE]	26 / 105 (24.8)	NE [8.3; NE]	0.8357 [0.4731; 1.4666] 0.5294	
Paclitaxel	16 / 67 (23.9)	11.8 [6.8; NE]	19 / 68 (27.9)	9.1 [3.1; 10.4]	0.5550 [0.2749; 1.1010] 0.0881	
Prior anthracycline use						0.6341
Yes	43 / 199 (21.6)	NE [13.2; NE]	50 / 208 (24.0)	NE [9.6; NE]	0.7855 [0.5189; 1.1841] 0.2495	
No	50 / 237 (21.1)	31.1 [15.9; NE]	61 / 222 (27.5)	14.0 [9.1; 21.3]	0.6777 [0.4632; 0.9865] 0.0418	
Liver metastases						0.9092
Yes	62 / 296 (20.9)	20.7 [15.9; NE]	72 / 283 (25.4)	13.8 [9.6; NE]	0.7197 [0.5094; 1.0137] 0.0597	
No	31 / 140 (22.1)	NE [14.5; NE]	39 / 147 (26.5)	14.4 [9.1; NE]	0.7098 [0.4392; 1.1374] 0.1543	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.10.2 EQ-5D-5L VAS - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.9264
0	52 / 252 (20.6)	31.1 [14.5; NE]	69 / 257 (26.8)	13.8 [9.9; NE]	0.6895 [0.4771; 0.9899] 0.0435	
>=1	40 / 179 (22.3)	20.7 [17.3; NE]	40 / 164 (24.4)	16.6 [7.1; NE]	0.7347 [0.4724; 1.1428] 0.1703	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 15:16; Program name: T.2.10.2_EQ5D_TTCDet_FAS_SUB.sas; Output name: T.2.10.2_EQ5D_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.10.3 EQ-5D-5L VAS – Zeit bis zur bestätigten Verschlechterung – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

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Table 2.10.3 EQ-5D-5L VAS - Time to confirmed deterioration – Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

No output displayed as p-value >= 0.05 for all subgroups.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 21JUL2024 6:37; Program name: T.2.10.3_EQ5D_TTCDet_FAS_SUB_SIG.sas; Output name: T.2.10.3_EQ5D_TTCDet_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.10.1 EQ-5D-5L VAS – Zeit bis zur bestätigten Verschlechterung – Kaplan-Meier-Plot – FAS

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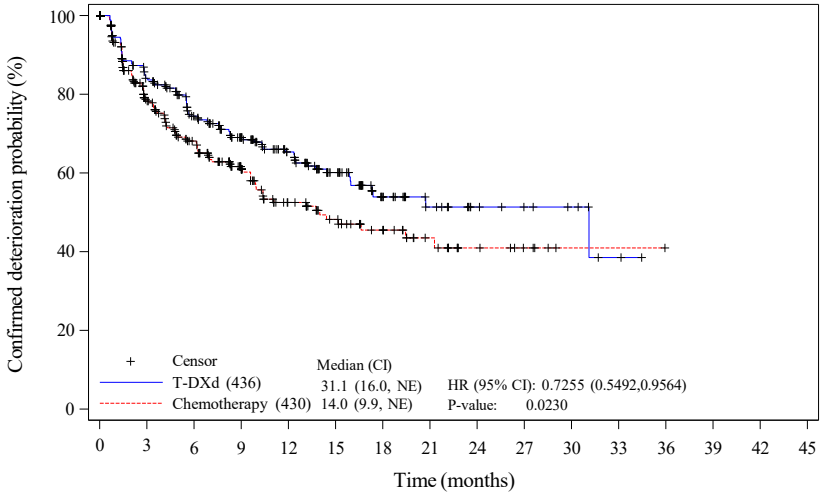
Figure 2.10.1 EQ-5D-5L VAS - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:

T-DXd(436)	436	205	161	126	95	64	32	19	11	8	6	2	0
Chemotherapy (430)	430	181	134	91	57	41	29	17	9	5	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10DEC2024 10:23; Program name: F.2.10.1_EQ5D_TTCDet_FAS.sas; Output name: F.2.10.1_EQ5D_TTCDet_FAS.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.10.2 EQ-5D-5L VAS – Zeit bis zur bestätigten Verschlechterung – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

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Figure 2.10.2 EQ-5D-5L VAS - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set

No output displayed as p-value >= 0.05 for all subgroups.

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Tabelle 2.10.4 EQ-5D-5L VAS – Zeit bis zur bestätigten Verschlechterung – Sensitivitätsanalyse – FAS

Table 2.10.4 EQ-5D-5L VAS - Time to confirmed deterioration - Sensitivity analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	76 (17.4)	NE [NE; NE]	90 (20.9)	NE [14.0; NE]	0.7402 [0.5437; 1.0051] 0.0545	0.0547
Subjects with censoring event	360 (82.6)		340 (79.1)			
Baseline score not allowing for deterioration	4 (0.9)		5 (1.2)			
Deterioration after 2 or more missed assessments	0		1 (0.2)			
No baseline data	152 (34.9)		82 (19.1)			
No deterioration	179 (41.1)		190 (44.2)			
No evaluable visit	25 (5.7)		62 (14.4)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

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Tabelle 2.10.9 EQ-5D-5L VAS – Zeit bis zur erstmaligen Verschlechterung – FAS

Table 2.10.9 EQ-5D-5L VAS - Time to first deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	141 (32.3)	8.9 [5.6; 13.1]	151 (35.1)	4.9 [4.2; 8.3]	0.8140 [0.6461; 1.0250] 0.0802	0.0815
Subjects with censoring event	295 (67.7)		279 (64.9)			
Baseline score not allowing for deterioration	4 (0.9)		5 (1.2)			
No baseline data	152 (34.9)		82 (19.1)			
No deterioration	114 (26.1)		130 (30.2)			
No evaluable visit	25 (5.7)		62 (14.4)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

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Tabelle 2.10.10 EQ-5D-5L VAS – Zeit bis zur erstmaligen Verschlechterung – Subgruppenanalyse – FAS

Table 2.10.10 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Age at randomization						0.1542
<65 years of age	104 / 302 (34.4)	8.4 [5.6; 14.7]	96 / 297 (32.3)	7.6 [4.8; 21.3]	0.9150 [0.6925; 1.2107] 0.5340	
≥65 years of age	37 / 134 (27.6)	8.9 [4.2; 18.6]	55 / 133 (41.4)	4.1 [2.1; 7.6]	0.6301 [0.4113; 0.9545] 0.0295	
Race						0.4149
Asian	78 / 154 (50.6)	8.2 [4.9; 13.9]	74 / 151 (49.0)	4.9 [3.5; 9.0]	0.8263 [0.6002; 1.1387] 0.2417	
Other	7 / 51 (13.7)	NE [8.3; NE]	9 / 49 (18.4)	4.2 [1.5; NE]	0.3818 [0.1313; 1.0618] 0.0578	
White	56 / 231 (24.2)	8.9 [4.3; NE]	68 / 230 (29.6)	6.1 [3.1; 18.8]	0.8668 [0.6061; 1.2348] 0.4283	
Region						0.9503
Asia	74 / 149 (49.7)	8.2 [4.9; 14.7]	73 / 147 (49.7)	4.9 [3.5; 9.0]	0.8116 [0.5863; 1.1237] 0.2069	
Europe	53 / 227 (23.3)	9.7 [5.6; 15.3]	61 / 213 (28.6)	4.2 [2.8; 18.8]	0.7902 [0.5441; 1.1446] 0.2118	
Rest of the World	14 / 60 (23.3)	12.4 [4.8; NE]	17 / 70 (24.3)	11.7 [4.1; NE]	0.8096 [0.3833; 1.6697] 0.5640	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.10.10 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
HER2 IHC expression						0.4230
IHC 1+	69 / 239 (28.9)	11.0 [5.5; 18.6]	92 / 234 (39.3)	4.8 [3.4; 8.3]	0.7144 [0.5207; 0.9758] 0.0340	
IHC 2+/ISH-	42 / 117 (35.9)	6.2 [4.2; 12.4]	35 / 118 (29.7)	10.0 [3.5; 21.3]	1.0330 [0.6588; 1.6298] 0.8929	
IHC >0 <1+	29 / 76 (38.2)	8.9 [4.8; 16.0]	24 / 76 (31.6)	7.6 [2.8; 20.8]	0.8599 [0.5000; 1.4930] 0.5884	
Prior CDK4/6 inhibitor use						0.7396
Yes	123 / 394 (31.2)	9.1 [5.6; 13.2]	131 / 389 (33.7)	4.9 [4.1; 9.0]	0.8234 [0.6427; 1.0543] 0.1229	
No	18 / 42 (42.9)	6.6 [3.4; NE]	20 / 41 (48.8)	4.9 [1.4; 18.8]	0.7626 [0.3991; 1.4467] 0.4052	
Prior Taxane Use In The Non-Metastatic Setting						0.7107
Yes	59 / 179 (33.0)	8.9 [5.7; 13.9]	59 / 177 (33.3)	4.9 [3.5; 22.8]	0.8583 [0.5961; 1.2358] 0.4091	
No	82 / 257 (31.9)	8.4 [4.9; 18.6]	92 / 253 (36.4)	4.8 [4.1; 8.3]	0.7839 [0.5802; 1.0572] 0.1096	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.10.10 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1095
1	21 / 65 (32.3)	8.4 [4.2; 16.7]	18 / 82 (22.0)	17.4 [2.9; NE]	1.1898 [0.6323; 2.2630] 0.5954	
2	88 / 295 (29.8)	9.8 [5.6; 14.7]	110 / 288 (38.2)	4.8 [3.6; 7.6]	0.6781 [0.5102; 0.8985] 0.0067	
>=3	31 / 75 (41.3)	4.9 [2.9; 18.6]	22 / 58 (37.9)	10.0 [3.4; NE]	1.1889 [0.6910; 2.0807] 0.5401	
ER/PR status I						0.2678
ER+, PR+	82 / 253 (32.4)	9.1 [5.6; 16.7]	88 / 237 (37.1)	4.8 [3.6; 10.0]	0.7459 [0.5506; 1.0093] 0.0566	
ER+, PR-	59 / 167 (35.3)	6.2 [4.2; 11.8]	58 / 181 (32.0)	7.7 [3.5; 13.1]	0.9495 [0.6593; 1.3681] 0.7736	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.10.10 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5394
ER >10%	113 / 364 (31.0)	8.9 [5.6; 13.2]	124 / 355 (34.9)	4.9 [4.2; 8.3]	0.7703 [0.5956; 0.9953] 0.0453	
ER <=10%	7 / 21 (33.3)	3.9 [1.3; NE]	5 / 14 (35.7)	2.8 [1.4; NE]	0.8804 [0.2781; 2.9995] 0.8161	
Positive	21 / 51 (41.2)	11.7 [4.9; 16.0]	22 / 61 (36.1)	10.0 [2.7; NE]	1.1066 [0.5978; 2.0488] 0.7409	
Endocrine Resistance						0.4941
Primary	45 / 128 (35.2)	6.2 [4.8; 16.7]	46 / 140 (32.9)	7.7 [3.1; 17.4]	0.9318 [0.6159; 1.4090] 0.7322	
Secondary	96 / 308 (31.2)	9.1 [5.7; 14.7]	104 / 288 (36.1)	4.8 [4.1; 7.7]	0.7782 [0.5883; 1.0283] 0.0769	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:08; Program name: T.2.10.10_EQ5D_TTFDet_FAS_SUB.sas; Output name: T.2.10.10_EQ5D_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.10.10 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.8014
Capecitabine	86 / 266 (32.3)	8.4 [5.0; 13.2]	96 / 257 (37.4)	4.8 [2.8; 9.6]	0.7787 [0.5805; 1.0430] 0.0931	
Nab-Paclitaxel	34 / 103 (33.0)	11.0 [5.5; NE]	36 / 105 (34.3)	6.9 [4.2; NE]	0.8599 [0.5357; 1.3781] 0.5254	
Paclitaxel	21 / 67 (31.3)	6.8 [2.1; 16.0]	19 / 68 (27.9)	4.2 [2.8; 10.0]	0.9297 [0.4944; 1.7586] 0.8147	
Prior anthracycline use						0.2932
Yes	68 / 199 (34.2)	8.2 [5.5; 11.8]	69 / 208 (33.2)	4.9 [4.2; 22.8]	0.9254 [0.6606; 1.2961] 0.6517	
No	73 / 237 (30.8)	9.8 [4.9; 16.0]	82 / 222 (36.9)	5.5 [3.1; 8.3]	0.7164 [0.5202; 0.9844] 0.0387	
Liver metastases						0.6482
Yes	90 / 296 (30.4)	9.0 [5.6; 16.0]	98 / 283 (34.6)	6.1 [3.6; 9.0]	0.7713 [0.5770; 1.0294] 0.0761	
No	51 / 140 (36.4)	8.2 [4.3; 15.3]	53 / 147 (36.1)	4.8 [3.4; 17.4]	0.8753 [0.5930; 1.2921] 0.5087	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 15:08; Program name: T.2.10.10_EQ5D_TTFDet_FAS_SUB.sas; Output name: T.2.10.10_EQ5D_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.10.10 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.5949
0	78 / 252 (31.0)	9.0 [6.2; 14.7]	94 / 257 (36.6)	6.1 [4.1; 9.9]	0.7485 [0.5516; 1.0122] 0.0593	
>=1	62 / 179 (34.6)	7.7 [4.2; 16.0]	55 / 164 (33.5)	4.8 [3.0; 10.4]	0.8674 [0.6030; 1.2511] 0.4446	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 15:08; Program name: T.2.10.10_EQ5D_TTFDet_FAS_SUB.sas; Output name: T.2.10.10_EQ5D_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.10.11 EQ-5D-5L VAS – Zeit bis zur erstmaligen Verschlechterung – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

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Table 2.10.11 EQ-5D-5L VAS - Time to first deterioration – Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

No output displayed as p-value >= 0.05 for all subgroups.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 15:11; Program name: T.2.10.11_EQ5D_TTFDet_FAS_SUB_SIG.sas; Output name: T.2.10.11_EQ5D_TTFDet_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.10.5 EQ-5D-5L VAS – Zeit bis zur erstmaligen Verschlechterung – Kaplan-Meier-Plot – FAS

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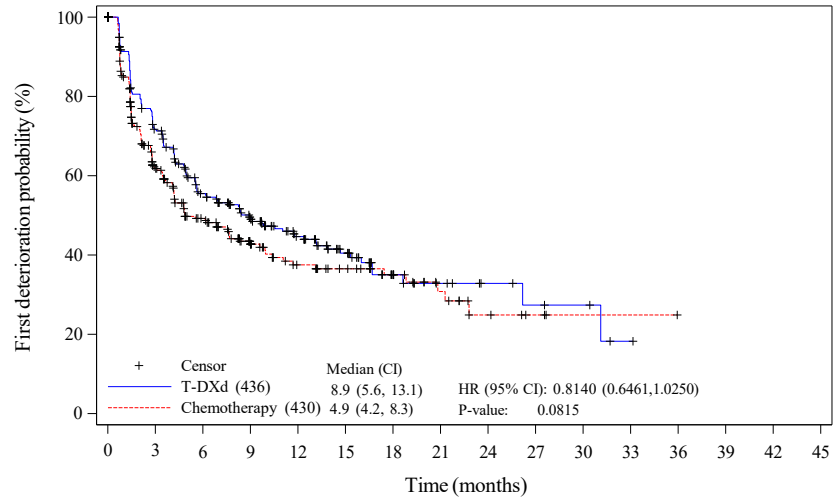
Figure 2.10.5 EQ-5D-5L VAS - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:

T-DXd(436)	436	176	122	91	64	40	17	11	7	5	4	1	0
Chemotherapy (430)	430	143	94	60	38	30	23	13	6	3	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10DEC2024 10:24; Program name: F.2.10.5_EQ5D_TTFDet.sas; Output name: F.2.10.5_EQ5D_TTFDet.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.10.6 EQ-5D-5L VAS – Zeit bis zur erstmaligen Verschlechterung – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

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Figure 2.10.6 EQ-5D-5L VAS - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set

No output displayed as p-value >= 0.05 for all subgroups.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 21JUL2024 8:02; Program name: F.2.10.6_EQ5D_TTFDet_FAS_SUB.sas; Output name: F.2.10.6_EQ5D_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.10.9 EQ-5D-5L VAS – Mean change from baseline-Plot – FAS

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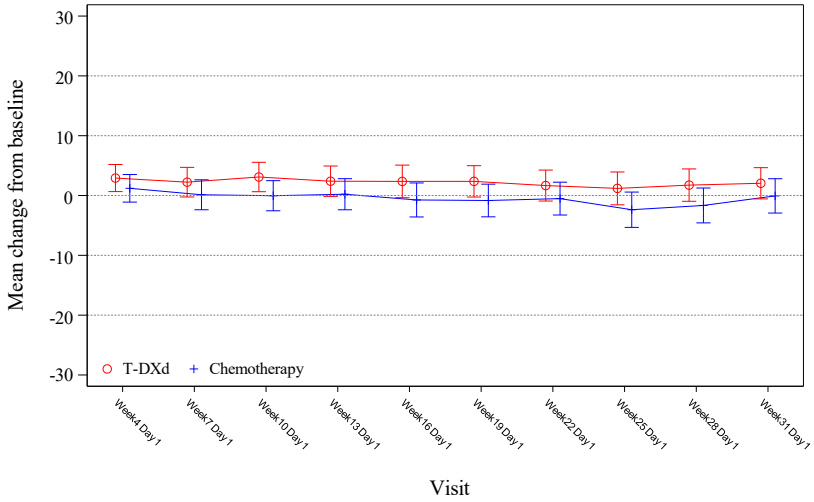
Figure 2.10.9 EQ-5D-5L VAS - Mean Change from Baseline - Full Analysis Set
EQ-5D-5L VAS
Mean baseline values: T-Dxd:72.0; Chemotherapy:70.2



Number of subjects with an observation:

T-DXd	241	227	224	208	205	199	194	187	178	166
Chemotherapy	247	234	213	201	180	182	162	141	132	116

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 29JUL2024 10:00; Program name: F.2.10.9_EQ5D_CHG_FAS.sas; Output name: F.2.10.9_EQ5D_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.10.15 EQ-5D-5L VAS – Mixed Model for Repeated Measurement – FAS

Table 2.10.15 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
EQ-5D-5L VAS			
Week 4 Day 1			
Estimated change from baseline [a]			
n	241	247	
LS Means [95% CI]	2.92 [0.66; 5.18]	1.20 [-1.10; 3.51]	
Standard error	1.15	1.17	
Difference of LS Means [95% CI]			1.72 [-0.87; 4.30]
Standard error for difference			1.32
p-value			0.1925
Hedges' g [95% CI]			0.09 [-0.08; 0.27]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 30JUL2024 4:57; Program name: T.2.10.15_EQ5D_MMRM_FAS.sas; Output name: T.2.10.15_EQ5D_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.10.15 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	227	234	
LS Means [95% CI]	2.23 [-0.24; 4.71]	0.12 [-2.38; 2.63]	
Standard error	1.26	1.27	
Difference of LS Means [95% CI]			2.11 [-0.84; 5.06]
Standard error for difference			1.50
p-value			0.1607
Hedges' g [95% CI]			0.11 [-0.07; 0.29]
Week 10 Day 1			
Estimated change from baseline [a]			
n	224	213	
LS Means [95% CI]	3.10 [0.64; 5.55]	-0.03 [-2.55; 2.48]	
Standard error	1.25	1.28	
Difference of LS Means [95% CI]			3.13 [0.19; 6.07]
Standard error for difference			1.50
p-value			0.0371
Hedges' g [95% CI]			0.17 [-0.02; 0.35]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 30JUL2024 4:57; Program name: T.2.10.15_EQ5D_MMRM_FAS.sas; Output name: T.2.10.15_EQ5D_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.10.15 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	208	201	
LS Means [95% CI]	2.39 [-0.14; 4.93]	0.22 [-2.38; 2.82]	
Standard error	1.29	1.32	
Difference of LS Means [95% CI]			2.18 [-0.91; 5.26]
Standard error for difference			1.57
p-value			0.1668
Hedges' g [95% CI]			0.12 [-0.08; 0.31]
Week 16 Day 1			
Estimated change from baseline [a]			
n	205	180	
LS Means [95% CI]	2.36 [-0.36; 5.08]	-0.74 [-3.58; 2.10]	
Standard error	1.39	1.45	
Difference of LS Means [95% CI]			3.10 [-0.34; 6.55]
Standard error for difference			1.75
p-value			0.0776
Hedges' g [95% CI]			0.16 [-0.04; 0.36]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Table 2.10.15 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	199	182	
LS Means [95% CI]	2.37 [-0.25; 4.99]	-0.83 [-3.56; 1.90]	
Standard error	1.33	1.39	
Difference of LS Means [95% CI]			3.20 [-0.07; 6.47]
Standard error for difference			1.66
p-value			0.0552
Hedges' g [95% CI]			0.17 [-0.03; 0.37]
Week 22 Day 1			
Estimated change from baseline [a]			
n	194	162	
LS Means [95% CI]	1.67 [-0.92; 4.25]	-0.52 [-3.26; 2.23]	
Standard error	1.32	1.40	
Difference of LS Means [95% CI]			2.18 [-1.07; 5.43]
Standard error for difference			1.65
p-value			0.1881
Hedges' g [95% CI]			0.12 [-0.09; 0.33]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 30JUL2024 4:57; Program name: T.2.10.15_EQ5D_MMRM_FAS.sas; Output name: T.2.10.15_EQ5D_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.10.15 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	187	141	
LS Means [95% CI]	1.19 [-1.56; 3.94]	-2.38 [-5.33; 0.58]	
Standard error	1.40	1.50	
Difference of LS Means [95% CI]			3.57 [0.01; 7.12]
Standard error for difference			1.81
p-value			0.0493
Hedges' g [95% CI]			0.19 [-0.03; 0.41]
Week 28 Day 1			
Estimated change from baseline [a]			
n	178	132	
LS Means [95% CI]	1.74 [-0.97; 4.44]	-1.66 [-4.57; 1.25]	
Standard error	1.38	1.48	
Difference of LS Means [95% CI]			3.40 [-0.09; 6.89]
Standard error for difference			1.78
p-value			0.0563
Hedges' g [95% CI]			0.19 [-0.04; 0.42]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 30JUL2024 4:57; Program name: T.2.10.15_EQ5D_MMRM_FAS.sas; Output name: T.2.10.15_EQ5D_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.10.15 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	166	116	
LS Means [95% CI]	2.05 [-0.56; 4.66]	-0.06 [-2.93; 2.81]	
Standard error	1.33	1.46	
Difference of LS Means [95% CI]			2.11 [-1.27; 5.49]
Standard error for difference			1.72
p-value			0.2205
Hedges' g [95% CI]			0.13 [-0.11; 0.36]
Average [b]			
n	258	285	
LS Means [95% CI]	2.20 [0.06; 4.34]	-0.47 [-2.69; 1.75]	
Standard error	1.09	1.13	
Difference of LS Means [95% CI]			2.67 [0.25; 5.09]
Standard error for difference			1.23
p-value			0.0306
Hedges' g [95% CI]			0.15 [-0.02; 0.31]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 30JUL2024 4:57; Program name: T.2.10.15_EQ5D_MMRM_FAS.sas; Output name: T.2.10.15_EQ5D_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.10.10 EQ-5D-5L VAS – Plot of least-square means of repeated measures analysis of change from baseline – FAS

Daiichi Sankyo Europe GmbH
Data Intelligence – Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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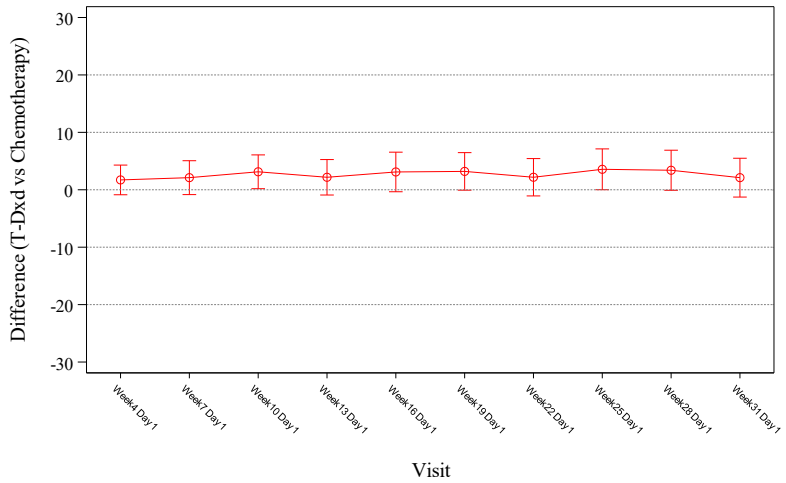
Figure 2.10.10 EQ-5D-5L VAS - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
EQ-5D-5L VAS



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 29JUL2024 10:03; Program name: F.2.10.10_EQ5D_MMRM_CHG_FAS.sas; Output name: F.2.10.10_EQ5D_MMRM_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Anhang 4-G 3.2 EORTC QLQ-C30

Tabelle 2.11.1 EORTC-QLQ-C30 – Zeit bis zur bestätigten Verschlechterung – FAS

Table 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Global Health Status	142 (32.6)	11.3 [8.3; 14.7]	137 (31.9)	10.5 [7.7; 13.3]	0.9279 [0.7333; 1.1747] 0.5329	0.5381
Functional Scales/Physical Functioning	116 (26.6)	18.0 [15.9; NE]	137 (31.9)	9.9 [6.9; 15.2]	0.7078 [0.5512; 0.9073] 0.0065	0.0062
Functional Scales/Role Functioning	152 (34.9)	10.3 [6.9; 14.6]	174 (40.5)	5.5 [4.1; 6.9]	0.7339 [0.5887; 0.9140] 0.0058	0.0057
Functional Scales/Emotional Functioning	91 (20.9)	28.2 [18.6; NE]	104 (24.2)	17.3 [12.4; NE]	0.7398 [0.5571; 0.9809] 0.0365	0.0363
Functional Scales/Cognitive Functioning	145 (33.3)	11.8 [8.3; 16.6]	143 (33.3)	9.9 [7.8; 13.8]	0.8829 [0.6999; 1.1145] 0.2934	0.2955
Functional Scales/Social Functioning	142 (32.6)	11.7 [7.6; 16.3]	149 (34.7)	7.7 [6.2; 10.4]	0.8392 [0.6659; 1.0571] 0.1366	0.1355
Symptom Scales/Fatigue	175 (40.1)	4.3 [3.4; 7.7]	201 (46.7)	2.9 [2.2; 4.2]	0.7692 [0.6253; 0.9453] 0.0127	0.0127
Symptom Scales/Nausea and Vomiting	178 (40.8)	3.5 [2.8; 5.6]	132 (30.7)	13.8 [7.7; 21.5]	1.6375 [1.3085; 2.0544] <.0001	<.0001
Symptom Scales/Pain	105 (24.1)	22.0 [17.2; NE]	157 (36.5)	6.3 [4.8; 9.6]	0.5068 [0.3938; 0.6495] <.0001	<.0001

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP*. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test*.
*: The following parameters were analysed using a stratified Cox proportional hazards model (hazard ratio) and a stratified log-rank test (two-sided p-value): Symptom Scales/Fatigue. Otherwise unstratified analyses have been conducted.
CI: confidence interval; HR: hazard ratio; NE: not estimable.

Table 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Dyspnoea	98 (22.5)	20.0 [19.3; NE]	107 (24.9)	20.8 [13.1; NE]	0.7686 [0.5831; 1.0121] 0.0610	0.0603
Common Symptoms/Insomnia	96 (22.0)	NE [17.3; NE]	108 (25.1)	15.2 [12.4; NE]	0.7628 [0.5782; 1.0047] 0.0543	0.0534
Common Symptoms/Appetite Loss	152 (34.9)	8.3 [5.0; 11.7]	125 (29.1)	13.8 [9.6; 16.1]	1.3450 [1.0621; 1.7063] 0.0141	0.0147
Common Symptoms/Constipation	147 (33.7)	9.2 [5.5; 12.5]	96 (22.3)	22.0 [15.9; NE]	1.7575 [1.3610; 2.2799] <.0001	<.0001
Common Symptoms/Diarrhea	101 (23.2)	29.0 [17.2; NE]	101 (23.5)	16.5 [13.9; 23.4]	0.8605 [0.6511; 1.1380] 0.2909	0.2934
Common Symptoms/Financial Difficulties	83 (19.0)	NE [26.3; NE]	93 (21.6)	20.1 [15.1; NE]	0.7694 [0.5704; 1.0361] 0.0846	0.0836

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP*. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test*.
*: The following parameters were analysed using a stratified Cox proportional hazards model (hazard ratio) and a stratified log-rank test (two-sided p-value): Symptom Scales/Fatigue. Otherwise unstratified analyses have been conducted.
CI: confidence interval; HR: hazard ratio; NE: not estimable.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 02DEC2024 3:48; Program name: T.2.11.1_EORTC_TTCDet_FAS.sas; Output name: T.2.11.1_EORTC_TTCDet_FAS.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.11.2 EORTC-QLQ-C30 – Zeit bis zur bestätigten Verschlechterung – Subgruppenanalyse – FAS

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Global Health Status						
Age at randomization						0.3086
<65 years of age	100 / 302 (33.1)	11.3 [8.2; 15.9]	90 / 297 (30.3)	12.4 [7.7; 20.7]	1.0063 [0.7559; 1.3413] 0.9702	
>=65 years of age	42 / 134 (31.3)	10.4 [5.0; 24.1]	47 / 133 (35.3)	9.0 [4.1; 11.1]	0.7797 [0.5116; 1.1841] 0.2456	
Race						0.6420
Asian	65 / 154 (42.2)	12.4 [7.7; 20.7]	65 / 151 (43.0)	9.0 [4.8; 21.3]	0.8703 [0.6161; 1.2304] 0.4344	
White	69 / 231 (29.9)	8.9 [5.6; 15.9]	65 / 230 (28.3)	10.6 [7.5; 15.2]	1.0563 [0.7520; 1.4855] 0.7514	
Other	8 / 51 (15.7)	12.4 [7.6; NE]	7 / 49 (14.3)	11.1 [2.0; NE]	0.6950 [0.2473; 1.9986] 0.4832	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.8005
Asia	63 / 149 (42.3)	12.4 [7.7; 20.7]	63 / 147 (42.9)	10.4 [4.8; 21.3]	0.8756 [0.6167; 1.2443] 0.4629	
Europe	65 / 227 (28.6)	10.3 [7.4; 12.4]	57 / 213 (26.8)	11.1 [7.6; 15.2]	1.0178 [0.7125; 1.4581] 0.9226	
Rest of the World	14 / 60 (23.3)	29.7 [2.1; NE]	17 / 70 (24.3)	11.0 [3.4; NE]	0.8889 [0.4218; 1.8297] 0.7480	
HER2 IHC expression						0.2194
IHC 1+	81 / 239 (33.9)	10.4 [6.9; 17.4]	86 / 234 (36.8)	8.2 [4.2; 11.0]	0.8533 [0.6288; 1.1575] 0.3083	
IHC 2+/ISH-	40 / 117 (34.2)	9.9 [5.6; 13.3]	29 / 118 (24.6)	21.3 [7.7; NE]	1.3502 [0.8394; 2.1986] 0.2157	
IHC >0 <1+	20 / 76 (26.3)	16.6 [12.4; NE]	21 / 76 (27.6)	13.3 [5.6; NE]	0.7531 [0.4051; 1.3957] 0.3668	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1630
Yes	125 / 394 (31.7)	11.4 [8.9; 15.9]	124 / 389 (31.9)	10.4 [6.9; 13.1]	0.8688 [0.6770; 1.1151] 0.2692	
No	17 / 42 (40.5)	8.3 [1.4; NE]	13 / 41 (31.7)	NE [4.8; NE]	1.5505 [0.7555; 3.2574] 0.2349	
Prior Taxane Use In The Non-Metastatic Setting						0.3810
Yes	59 / 179 (33.0)	11.1 [7.4; 14.6]	65 / 177 (36.7)	7.6 [4.3; 12.4]	0.7803 [0.5451; 1.1145] 0.1731	
No	83 / 257 (32.3)	11.8 [7.7; 29.7]	72 / 253 (28.5)	13.3 [9.9; 25.5]	1.0169 [0.7411; 1.3983] 0.9191	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.7344
1	18 / 65 (27.7)	14.6 [4.9; NE]	23 / 82 (28.0)	9.9 [3.4; 19.5]	0.8180 [0.4345; 1.5164] 0.5193	
2	99 / 295 (33.6)	11.1 [7.6; 14.7]	95 / 288 (33.0)	10.4 [6.9; 12.4]	0.9352 [0.7049; 1.2416] 0.6446	
>=3	25 / 75 (33.3)	11.4 [6.8; NE]	18 / 58 (31.0)	21.3 [7.6; NE]	1.1118 [0.6088; 2.0714] 0.7254	
ER/PR status I						0.3945
ER+, PR+	82 / 253 (32.4)	12.4 [7.6; 20.7]	79 / 237 (33.3)	10.5 [5.6; 13.1]	0.8733 [0.6405; 1.1915] 0.3936	
ER+, PR-	59 / 167 (35.3)	11.1 [7.7; 13.3]	53 / 181 (29.3)	12.5 [6.3; 25.5]	1.0804 [0.7447; 1.5715] 0.6827	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7683
ER <=10%	7 / 21 (33.3)	16.6 [0.7; NE]	5 / 14 (35.7)	4.2 [0.8; NE]	0.8369 [0.2509; 2.9171] 0.7582	
ER >10%	116 / 364 (31.9)	11.1 [8.2; 14.7]	112 / 355 (31.5)	10.4 [7.6; 12.5]	0.9173 [0.7067; 1.1914] 0.5160	
Positive	19 / 51 (37.3)	14.6 [4.3; NE]	20 / 61 (32.8)	19.5 [2.1; NE]	0.9872 [0.5222; 1.8599] 0.9835	
Endocrine Resistance						0.4964
Primary	43 / 128 (33.6)	10.3 [5.0; NE]	42 / 140 (30.0)	10.4 [4.8; NE]	1.0559 [0.6889; 1.6195] 0.8004	
Secondary	99 / 308 (32.1)	11.3 [8.3; 15.9]	94 / 288 (32.6)	10.6 [7.5; 15.9]	0.8831 [0.6652; 1.1731] 0.3905	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.8293
Capecitabine	82 / 266 (30.8)	11.8 [9.9; 20.7]	76 / 257 (29.6)	12.5 [9.0; 21.3]	0.9761 [0.7139; 1.3362] 0.8792	
Nab-Paclitaxel	37 / 103 (35.9)	12.4 [5.6; NE]	40 / 105 (38.1)	9.9 [4.8; 15.2]	0.8950 [0.5696; 1.4023] 0.6260	
Paclitaxel	23 / 67 (34.3)	7.6 [2.9; 15.9]	21 / 68 (30.9)	4.1 [2.7; 13.1]	0.7533 [0.4119; 1.3838] 0.3647	
Prior anthracycline use						0.8287
Yes	66 / 199 (33.2)	11.1 [7.0; 13.3]	73 / 208 (35.1)	9.0 [4.8; 12.4]	0.8968 [0.6406; 1.2528] 0.5280	
No	76 / 237 (32.1)	12.4 [8.3; 29.7]	64 / 222 (28.8)	13.1 [7.7; 21.3]	0.9646 [0.6912; 1.3503] 0.8325	
Liver metastases						0.0553
Yes	82 / 296 (27.7)	12.4 [10.3; NE]	88 / 283 (31.1)	10.4 [6.9; 15.2]	0.7700 [0.5678; 1.0427] 0.0910	
No	60 / 140 (42.9)	7.7 [4.8; 11.1]	49 / 147 (33.3)	10.5 [4.8; 20.7]	1.2333 [0.8464; 1.8059] 0.2724	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.6487
0	84 / 252 (33.3)	11.8 [7.4; 16.6]	84 / 257 (32.7)	10.5 [7.6; 19.5]	0.9470 [0.6982; 1.2842] 0.7232	
>=1	57 / 179 (31.8)	10.9 [8.2; 17.4]	52 / 164 (31.7)	10.4 [4.8; 13.1]	0.8541 [0.5862; 1.2471] 0.4159	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Physical Functioning						
Age at randomization						0.7139
<65 years of age	75 / 302 (24.8)	20.7 [16.6; NE]	87 / 297 (29.3)	15.1 [9.0; 18.6]	0.6994 [0.5112; 0.9544] 0.0231	
>=65 years of age	41 / 134 (30.6)	10.5 [6.9; NE]	50 / 133 (37.6)	5.6 [4.2; 12.5]	0.7526 [0.4951; 1.1371] 0.1756	
Race						0.3689
Asian	50 / 154 (32.5)	30.4 [16.6; NE]	57 / 151 (37.7)	16.6 [7.6; 25.6]	0.6829 [0.4644; 1.0010] 0.0486	
White	57 / 231 (24.7)	16.3 [10.4; NE]	68 / 230 (29.6)	9.0 [5.5; 14.6]	0.7948 [0.5565; 1.1304] 0.1985	
Other	9 / 51 (17.6)	11.7 [2.3; NE]	12 / 49 (24.5)	4.2 [2.1; 4.9]	0.3905 [0.1480; 0.9702] 0.0394	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7018
Asia	49 / 149 (32.9)	30.4 [18.0; NE]	56 / 147 (38.1)	15.2 [7.6; 25.6]	0.6751 [0.4574; 0.9931] 0.0441	
Europe	53 / 227 (23.3)	16.6 [11.9; NE]	64 / 213 (30.0)	5.5 [4.2; 10.5]	0.6964 [0.4816; 1.0029] 0.0508	
Rest of the World	14 / 60 (23.3)	12.4 [3.7; NE]	17 / 70 (24.3)	12.5 [4.9; NE]	0.9472 [0.4574; 1.9293] 0.8710	
HER2 IHC expression						0.2973
IHC 1+	64 / 239 (26.8)	20.0 [12.4; NE]	84 / 234 (35.9)	9.0 [5.5; 15.1]	0.6649 [0.4777; 0.9206] 0.0136	
IHC 2+/ISH-	34 / 117 (29.1)	11.7 [8.3; NE]	31 / 118 (26.3)	18.6 [5.5; NE]	0.9837 [0.6031; 1.6104] 0.9451	
IHC >0 <1+	17 / 76 (22.4)	17.2 [16.6; NE]	22 / 76 (28.9)	12.5 [4.8; NE]	0.5157 [0.2679; 0.9755] 0.0391	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8101
Yes	107 / 394 (27.2)	17.2 [12.4; NE]	125 / 389 (32.1)	9.0 [5.5; 15.1]	0.7069 [0.5440; 0.9167] 0.0084	
No	9 / 42 (21.4)	NE [12.4; NE]	12 / 41 (29.3)	NE [8.3; NE]	0.6433 [0.2620; 1.5240] 0.3149	
Prior Taxane Use In The Non-Metastatic Setting						0.0558
Yes	43 / 179 (24.0)	30.4 [13.8; NE]	64 / 177 (36.2)	7.5 [4.2; 15.1]	0.5364 [0.3596; 0.7922] 0.0016	
No	73 / 257 (28.4)	17.2 [10.5; NE]	73 / 253 (28.9)	13.1 [8.3; 21.3]	0.8690 [0.6277; 1.2043] 0.3910	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5213
1	12 / 65 (18.5)	NE [11.7; NE]	21 / 82 (25.6)	9.9 [5.5; NE]	0.5359 [0.2530; 1.0828] 0.0843	
2	80 / 295 (27.1)	17.2 [13.8; NE]	91 / 288 (31.6)	10.5 [6.3; 16.6]	0.7670 [0.5662; 1.0372] 0.0827	
>=3	23 / 75 (30.7)	20.0 [10.4; NE]	24 / 58 (41.4)	6.9 [3.4; NE]	0.6329 [0.3547; 1.1267] 0.1134	
ER/PR status I						0.6675
ER+, PR+	70 / 253 (27.7)	16.6 [12.4; NE]	80 / 237 (33.8)	8.9 [4.9; 14.6]	0.6808 [0.4923; 0.9393] 0.0181	
ER+, PR-	44 / 167 (26.3)	20.0 [11.7; NE]	50 / 181 (27.6)	21.3 [7.6; NE]	0.7879 [0.5203; 1.1877] 0.2519	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4121
ER <=10%	7 / 21 (33.3)	16.6 [1.3; NE]	4 / 14 (28.6)	18.6 [1.4; NE]	1.0938 [0.3254; 4.2194] 0.8875	
ER >10%	96 / 364 (26.4)	20.0 [12.4; NE]	109 / 355 (30.7)	10.5 [7.1; 15.2]	0.7456 [0.5652; 0.9820] 0.0349	
Positive	13 / 51 (25.5)	30.4 [12.4; NE]	24 / 61 (39.3)	7.6 [2.9; NE]	0.4460 [0.2146; 0.8784] 0.0196	
Endocrine Resistance						0.3656
Primary	28 / 128 (21.9)	NE [11.9; NE]	42 / 140 (30.0)	11.7 [5.5; 16.6]	0.5875 [0.3592; 0.9461] 0.0286	
Secondary	88 / 308 (28.6)	16.6 [12.4; NE]	95 / 288 (33.0)	9.7 [4.9; 15.1]	0.7539 [0.5626; 1.0092] 0.0555	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1495
Capecitabine	73 / 266 (27.4)	18.0 [10.5; NE]	77 / 257 (30.0)	13.1 [7.6; 25.6]	0.8115 [0.5872; 1.1201] 0.2005	
Nab-Paclitaxel	26 / 103 (25.2)	NE [13.8; NE]	34 / 105 (32.4)	11.7 [5.5; NE]	0.6926 [0.4104; 1.1551] 0.1563	
Paclitaxel	17 / 67 (25.4)	15.9 [8.3; NE]	26 / 68 (38.2)	4.2 [2.2; 6.9]	0.3672 [0.1873; 0.6966] 0.0018	
Prior anthracycline use						0.2215
Yes	54 / 199 (27.1)	16.6 [11.7; NE]	74 / 208 (35.6)	6.9 [4.2; 15.1]	0.6067 [0.4235; 0.8638] 0.0055	
No	62 / 237 (26.2)	18.0 [15.9; NE]	63 / 222 (28.4)	13.1 [8.3; 21.3]	0.8259 [0.5804; 1.1747] 0.2788	
Liver metastases						0.1405
Yes	71 / 296 (24.0)	NE [12.4; NE]	94 / 283 (33.2)	8.3 [4.9; 15.1]	0.6283 [0.4591; 0.8560] 0.0029	
No	45 / 140 (32.1)	18.0 [10.5; NE]	43 / 147 (29.3)	13.1 [7.6; NE]	0.8991 [0.5907; 1.3714] 0.6213	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0571
0	63 / 252 (25.0)	20.0 [16.3; NE]	90 / 257 (35.0)	9.0 [5.5; 13.1]	0.6064 [0.4367; 0.8368] 0.0022	
>=1	52 / 179 (29.1)	13.8 [9.9; NE]	44 / 164 (26.8)	15.1 [7.5; NE]	0.9598 [0.6425; 1.4406] 0.8407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Role Functioning						
Age at randomization						0.5786
<65 years of age	104 / 302 (34.4)	11.9 [6.4; 18.6]	115 / 297 (38.7)	5.6 [4.2; 8.4]	0.7688 [0.5874; 1.0048] 0.0524	
>=65 years of age	48 / 134 (35.8)	8.3 [4.2; 13.9]	59 / 133 (44.4)	2.9 [2.1; 6.9]	0.6768 [0.4596; 0.9919] 0.0442	
Race						0.1946
Asian	76 / 154 (49.4)	7.7 [4.9; 15.3]	76 / 151 (50.3)	6.2 [4.2; 9.7]	0.8485 [0.6145; 1.1711] 0.3132	
White	67 / 231 (29.0)	11.3 [4.2; 18.6]	86 / 230 (37.4)	4.2 [2.8; 6.9]	0.7049 [0.5092; 0.9715] 0.0309	
Other	9 / 51 (17.6)	12.4 [6.4; NE]	12 / 49 (24.5)	4.1 [1.3; NE]	0.2942 [0.1104; 0.7423] 0.0074	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4861
Asia	72 / 149 (48.3)	7.8 [5.0; 16.0]	74 / 147 (50.3)	6.2 [4.2; 9.7]	0.8409 [0.6056; 1.1666] 0.2958	
Europe	63 / 227 (27.8)	11.7 [6.8; 18.6]	76 / 213 (35.7)	4.2 [2.8; 6.9]	0.6258 [0.4447; 0.8774] 0.0059	
Rest of the World	17 / 60 (28.3)	6.4 [1.4; NE]	24 / 70 (34.3)	4.1 [2.0; 9.8]	0.7513 [0.3895; 1.4110] 0.3761	
HER2 IHC expression						0.8485
IHC 1+	85 / 239 (35.6)	9.7 [4.8; 18.7]	101 / 234 (43.2)	4.2 [2.8; 6.3]	0.7280 [0.5424; 0.9749] 0.0319	
IHC 2+/ISH-	38 / 117 (32.5)	9.8 [4.8; NE]	45 / 118 (38.1)	5.6 [3.5; 9.0]	0.7157 [0.4606; 1.1060] 0.1280	
IHC >0 <1+	28 / 76 (36.8)	11.7 [3.6; NE]	27 / 76 (35.5)	8.3 [2.9; 13.1]	0.8621 [0.5031; 1.4834] 0.5803	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5754
Yes	137 / 394 (34.8)	9.9 [6.8; 14.6]	154 / 389 (39.6)	4.9 [3.5; 7.5]	0.7452 [0.5901; 0.9400] 0.0123	
No	15 / 42 (35.7)	13.9 [2.2; NE]	20 / 41 (48.8)	6.1 [1.5; 11.8]	0.6379 [0.3185; 1.2494] 0.1860	
Prior Taxane Use In The Non-Metastatic Setting						0.3447
Yes	60 / 179 (33.5)	11.3 [4.8; 18.7]	75 / 177 (42.4)	4.2 [2.2; 6.2]	0.6649 [0.4693; 0.9375] 0.0191	
No	92 / 257 (35.8)	9.7 [6.2; 15.2]	99 / 253 (39.1)	6.9 [4.2; 9.0]	0.7959 [0.5974; 1.0591] 0.1119	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0952
1	23 / 65 (35.4)	11.7 [3.6; 14.6]	22 / 82 (26.8)	6.1 [3.4; NE]	1.0844 [0.6010; 1.9615] 0.7814	
2	95 / 295 (32.2)	13.9 [7.7; 18.6]	126 / 288 (43.8)	4.2 [2.8; 6.9]	0.6205 [0.4726; 0.8117] 0.0005	
>=3	34 / 75 (45.3)	4.9 [1.5; 10.3]	25 / 58 (43.1)	6.9 [2.8; 12.4]	1.0658 [0.6380; 1.8058] 0.8330	
ER/PR status I						0.0214
ER+, PR+	81 / 253 (32.0)	11.9 [7.7; NE]	101 / 237 (42.6)	4.2 [2.8; 6.9]	0.6085 [0.4514; 0.8175] 0.0009	
ER+, PR-	70 / 167 (41.9)	6.2 [3.5; 13.9]	65 / 181 (35.9)	7.7 [4.2; 12.4]	1.0161 [0.7224; 1.4308] 0.9371	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3493
ER <=10%	7 / 21 (33.3)	4.2 [0.7; NE]	3 / 14 (21.4)	NE [0.8; NE]	1.6820 [0.4641; 7.8479] 0.4678	
ER >10%	128 / 364 (35.2)	9.1 [6.2; 12.4]	144 / 355 (40.6)	5.5 [4.1; 6.9]	0.7572 [0.5948; 0.9628] 0.0218	
Positive	17 / 51 (33.3)	15.2 [13.9; NE]	27 / 61 (44.3)	4.2 [1.9; 20.8]	0.5138 [0.2698; 0.9471] 0.0331	
Endocrine Resistance						0.1215
Primary	47 / 128 (36.7)	9.9 [3.4; 18.6]	47 / 140 (33.6)	5.5 [3.4; 9.7]	0.9906 [0.6589; 1.4891] 0.9688	
Secondary	105 / 308 (34.1)	11.3 [6.9; 15.3]	126 / 288 (43.8)	4.9 [2.9; 6.9]	0.6453 [0.4957; 0.8382] 0.0009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.4721
Capecitabine	87 / 266 (32.7)	11.7 [6.9; 18.7]	108 / 257 (42.0)	5.5 [2.8; 7.7]	0.6653 [0.4993; 0.8839] 0.0046	
Nab-Paclitaxel	38 / 103 (36.9)	11.7 [2.8; NE]	45 / 105 (42.9)	5.5 [3.4; 8.4]	0.8048 [0.5183; 1.2418] 0.3152	
Paclitaxel	27 / 67 (40.3)	7.5 [1.4; 14.5]	21 / 68 (30.9)	3.4 [2.1; 9.8]	0.9773 [0.5495; 1.7604] 0.9369	
Prior anthracycline use						0.9744
Yes	71 / 199 (35.7)	7.5 [3.6; 15.3]	87 / 208 (41.8)	4.2 [2.8; 6.1]	0.7625 [0.5540; 1.0458] 0.0907	
No	81 / 237 (34.2)	11.9 [7.7; 15.3]	87 / 222 (39.2)	6.9 [4.2; 9.0]	0.7227 [0.5320; 0.9806] 0.0347	
Liver metastases						0.6170
Yes	101 / 296 (34.1)	9.8 [5.0; 14.5]	112 / 283 (39.6)	4.8 [3.4; 7.6]	0.7657 [0.5828; 1.0045] 0.0514	
No	51 / 140 (36.4)	13.9 [6.2; NE]	62 / 147 (42.2)	5.6 [2.8; 9.0]	0.6810 [0.4671; 0.9885] 0.0421	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0130
0	77 / 252 (30.6)	15.2 [9.8; NE]	108 / 257 (42.0)	5.6 [3.0; 7.7]	0.5859 [0.4343; 0.7860] 0.0003	
>=1	74 / 179 (41.3)	6.9 [2.2; 9.9]	63 / 164 (38.4)	4.8 [3.4; 6.9]	0.9924 [0.7072; 1.3962] 0.9428	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Emotional Functioning						
Age at randomization						0.3207
<65 years of age	65 / 302 (21.5)	24.2 [18.6; NE]	65 / 297 (21.9)	18.6 [12.4; NE]	0.8148 [0.5763; 1.1520] 0.2440	
>=65 years of age	26 / 134 (19.4)	NE [17.2; NE]	39 / 133 (29.3)	15.3 [6.3; NE]	0.6169 [0.3711; 1.0088] 0.0547	
Race						0.4435
Asian	36 / 154 (23.4)	NE [24.2; NE]	47 / 151 (31.1)	NE [11.8; NE]	0.6218 [0.3995; 0.9597] 0.0314	
White	49 / 231 (21.2)	18.6 [11.8; NE]	53 / 230 (23.0)	15.3 [10.4; NE]	0.8661 [0.5852; 1.2794] 0.4672	
Other	6 / 51 (11.8)	17.2 [8.3; NE]	4 / 49 (8.2)	NE [4.1; NE]	0.9203 [0.2616; 3.6134] 0.8980	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4970
Asia	35 / 149 (23.5)	NE [24.2; NE]	45 / 147 (30.6)	NE [11.8; NE]	0.6377 [0.4068; 0.9916] 0.0451	
Europe	47 / 227 (20.7)	17.4 [15.3; NE]	45 / 213 (21.1)	15.3 [9.9; NE]	0.8866 [0.5881; 1.3382] 0.5632	
Rest of the World	9 / 60 (15.0)	NE [5.7; NE]	14 / 70 (20.0)	13.9 [8.9; NE]	0.6887 [0.2858; 1.5757] 0.3817	
HER2 IHC expression						0.2123
IHC 1+	52 / 239 (21.8)	NE [16.6; NE]	60 / 234 (25.6)	NE [11.0; NE]	0.7577 [0.5205; 1.0991] 0.1442	
IHC 2+/ISH-	21 / 117 (17.9)	28.2 [18.6; NE]	31 / 118 (26.3)	15.3 [8.9; 18.6]	0.5285 [0.2980; 0.9192] 0.0230	
IHC >0 <1+	17 / 76 (22.4)	17.4 [16.6; NE]	12 / 76 (15.8)	NE [15.2; NE]	1.2075 [0.5802; 2.5937] 0.6176	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9465
Yes	79 / 394 (20.1)	NE [17.4; NE]	91 / 389 (23.4)	17.3 [11.8; NE]	0.7412 [0.5469; 1.0023] 0.0515	
No	12 / 42 (28.6)	28.2 [11.8; NE]	13 / 41 (31.7)	15.2 [4.8; NE]	0.7350 [0.3269; 1.6360] 0.4388	
Prior Taxane Use In The Non-Metastatic Setting						0.9916
Yes	39 / 179 (21.8)	18.6 [16.2; NE]	44 / 177 (24.9)	17.3 [9.6; NE]	0.7288 [0.4705; 1.1248] 0.1514	
No	52 / 257 (20.2)	NE [19.3; NE]	60 / 253 (23.7)	18.6 [11.8; NE]	0.7465 [0.5127; 1.0832] 0.1235	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1938
1	13 / 65 (20.0)	17.4 [14.6; NE]	15 / 82 (18.3)	13.1 [9.0; NE]	0.7804 [0.3636; 1.6531] 0.5134	
2	55 / 295 (18.6)	28.2 [19.3; NE]	74 / 288 (25.7)	15.3 [10.5; NE]	0.6281 [0.4407; 0.8905] 0.0088	
>=3	22 / 75 (29.3)	NE [7.5; NE]	14 / 58 (24.1)	18.6 [11.1; NE]	1.2325 [0.6361; 2.4692] 0.5416	
ER/PR status I						0.4842
ER+, PR+	50 / 253 (19.8)	24.2 [19.3; NE]	57 / 237 (24.1)	17.3 [9.8; NE]	0.6839 [0.4662; 1.0003] 0.0491	
ER+, PR-	41 / 167 (24.6)	18.6 [16.5; NE]	43 / 181 (23.8)	15.3 [11.1; NE]	0.8206 [0.5284; 1.2716] 0.3779	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6531
ER <=10%	4 / 21 (19.0)	NE [1.4; NE]	3 / 14 (21.4)	NE [1.4; NE]	0.7221 [0.1585; 3.6787] 0.6714	
ER >10%	74 / 364 (20.3)	28.2 [17.2; NE]	88 / 355 (24.8)	15.3 [11.0; NE]	0.6962 [0.5092; 0.9493] 0.0216	
Positive	13 / 51 (25.5)	19.3 [10.3; NE]	13 / 61 (21.3)	NE [11.1; NE]	1.0345 [0.4741; 2.2571] 0.9297	
Endocrine Resistance						0.1207
Primary	31 / 128 (24.2)	17.4 [15.3; NE]	30 / 140 (21.4)	NE [9.9; NE]	1.0211 [0.6166; 1.6932] 0.9345	
Secondary	60 / 308 (19.5)	28.2 [19.3; NE]	74 / 288 (25.7)	17.2 [11.0; NE]	0.6341 [0.4489; 0.8923] 0.0086	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.9341
Capecitabine	46 / 266 (17.3)	NE [28.2; NE]	57 / 257 (22.2)	NE [15.2; NE]	0.7119 [0.4805; 1.0498] 0.0860	
Nab-Paclitaxel	27 / 103 (26.2)	24.2 [11.0; NE]	32 / 105 (30.5)	11.0 [8.3; NE]	0.7307 [0.4333; 1.2226] 0.2312	
Paclitaxel	18 / 67 (26.9)	15.3 [8.3; NE]	15 / 68 (22.1)	13.9 [4.1; NE]	0.6546 [0.3202; 1.3487] 0.2481	
Prior anthracycline use						0.5735
Yes	46 / 199 (23.1)	18.6 [16.2; NE]	51 / 208 (24.5)	17.3 [9.9; NE]	0.7988 [0.5336; 1.1926] 0.2717	
No	45 / 237 (19.0)	NE [28.2; NE]	53 / 222 (23.9)	17.2 [11.0; NE]	0.6906 [0.4618; 1.0283] 0.0674	
Liver metastases						0.9872
Yes	58 / 296 (19.6)	NE [17.2; NE]	65 / 283 (23.0)	17.2 [11.8; NE]	0.7423 [0.5188; 1.0595] 0.1002	
No	33 / 140 (23.6)	24.2 [16.6; NE]	39 / 147 (26.5)	17.3 [9.8; NE]	0.7326 [0.4580; 1.1649] 0.1874	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.8474
0	51 / 252 (20.2)	28.2 [19.3; NE]	61 / 257 (23.7)	17.3 [11.1; NE]	0.7015 [0.4810; 1.0188] 0.0616	
>=1	39 / 179 (21.8)	24.2 [16.2; NE]	42 / 164 (25.6)	17.2 [8.3; NE]	0.7475 [0.4807; 1.1592] 0.1917	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Cognitive Functioning						
Age at randomization						0.4618
<65 years of age	101 / 302 (33.4)	12.4 [8.3; 21.5]	95 / 297 (32.0)	11.8 [8.4; 16.6]	0.9396 [0.7093; 1.2460] 0.6584	
>=65 years of age	44 / 134 (32.8)	11.7 [6.9; 20.0]	48 / 133 (36.1)	8.3 [4.2; 13.8]	0.7833 [0.5147; 1.1881] 0.2519	
Race						0.0462
Asian	59 / 154 (38.3)	23.5 [11.1; NE]	70 / 151 (46.4)	8.9 [4.9; 14.6]	0.6415 [0.4494; 0.9117] 0.0129	
White	73 / 231 (31.6)	8.3 [6.2; 11.7]	66 / 230 (28.7)	11.0 [7.6; 18.0]	1.1632 [0.8334; 1.6266] 0.3751	
Other	13 / 51 (25.5)	12.4 [2.8; NE]	7 / 49 (14.3)	13.2 [2.1; NE]	1.2539 [0.5086; 3.3617] 0.6321	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0369
Asia	58 / 149 (38.9)	15.8 [11.1; NE]	67 / 147 (45.6)	9.6 [4.9; 14.6]	0.6643 [0.4632; 0.9490] 0.0239	
Europe	67 / 227 (29.5)	10.3 [7.4; 12.4]	59 / 213 (27.7)	10.3 [5.5; 22.0]	1.0110 [0.7118; 1.4399] 0.9462	
Rest of the World	20 / 60 (33.3)	6.2 [1.1; 21.5]	17 / 70 (24.3)	11.0 [7.1; NE]	1.4759 [0.7549; 2.8969] 0.2504	
HER2 IHC expression						0.1370
IHC 1+	77 / 239 (32.2)	13.8 [10.3; 23.5]	90 / 234 (38.5)	8.9 [5.5; 13.2]	0.7136 [0.5232; 0.9707] 0.0309	
IHC 2+/ISH-	38 / 117 (32.5)	10.5 [4.2; NE]	31 / 118 (26.3)	17.3 [7.0; NE]	1.2283 [0.7645; 1.9885] 0.3981	
IHC >0 <1+	29 / 76 (38.2)	8.3 [4.9; NE]	22 / 76 (28.9)	13.1 [3.6; 20.8]	1.0663 [0.6140; 1.8788] 0.8187	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5499
Yes	131 / 394 (33.2)	11.7 [8.3; 15.8]	130 / 389 (33.4)	9.8 [7.0; 13.2]	0.8546 [0.6691; 1.0916] 0.2061	
No	14 / 42 (33.3)	13.8 [4.1; NE]	13 / 41 (31.7)	20.7 [4.9; NE]	1.1133 [0.5200; 2.4003] 0.7811	
Prior Taxane Use In The Non-Metastatic Setting						0.3296
Yes	55 / 179 (30.7)	13.8 [6.9; NE]	63 / 177 (35.6)	7.6 [4.8; 18.0]	0.7859 [0.5441; 1.1320] 0.1940	
No	90 / 257 (35.0)	11.7 [8.3; 17.2]	80 / 253 (31.6)	13.1 [8.9; 16.6]	0.9712 [0.7176; 1.3164] 0.8468	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5438
1	26 / 65 (40.0)	4.2 [1.5; 16.6]	24 / 82 (29.3)	9.8 [4.9; 11.8]	1.1188 [0.6324; 1.9828] 0.7132	
2	93 / 295 (31.5)	11.8 [8.3; 23.5]	95 / 288 (33.0)	11.0 [7.6; 14.6]	0.8638 [0.6480; 1.1520] 0.3198	
>=3	26 / 75 (34.7)	12.4 [6.2; NE]	23 / 58 (39.7)	13.2 [4.2; 20.8]	0.8035 [0.4540; 1.4283] 0.4501	
ER/PR status I						0.4580
ER+, PR+	81 / 253 (32.0)	12.4 [10.3; 23.5]	79 / 237 (33.3)	9.7 [7.1; 14.4]	0.8174 [0.5986; 1.1166] 0.2028	
ER+, PR-	62 / 167 (37.1)	8.9 [5.5; 16.6]	60 / 181 (33.1)	11.8 [5.5; 17.3]	0.9914 [0.6909; 1.4224] 0.9500	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4782
ER <=10%	7 / 21 (33.3)	8.9 [1.4; NE]	6 / 14 (42.9)	2.1 [1.4; NE]	0.4156 [0.1329; 1.3390] 0.1220	
ER >10%	120 / 364 (33.0)	11.1 [7.6; 15.8]	114 / 355 (32.1)	9.9 [8.3; 14.4]	0.9201 [0.7110; 1.1916] 0.5252	
Positive	18 / 51 (35.3)	17.2 [4.9; NE]	23 / 61 (37.7)	11.8 [4.2; NE]	0.7904 [0.4151; 1.4756] 0.4611	
Endocrine Resistance						0.8158
Primary	42 / 128 (32.8)	10.4 [4.2; NE]	46 / 140 (32.9)	9.8 [4.9; 14.6]	0.9139 [0.5994; 1.3895] 0.6761	
Secondary	103 / 308 (33.4)	11.8 [8.3; 17.2]	97 / 288 (33.7)	13.1 [7.6; 17.3]	0.8557 [0.6465; 1.1332] 0.2725	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.4742
Capecitabine	88 / 266 (33.1)	12.4 [7.4; 23.5]	83 / 257 (32.3)	13.1 [7.8; 18.0]	1.0065 [0.7442; 1.3621] 0.9749	
Nab-Paclitaxel	33 / 103 (32.0)	13.8 [6.9; NE]	40 / 105 (38.1)	9.6 [4.9; 14.6]	0.7009 [0.4381; 1.1136] 0.1312	
Paclitaxel	24 / 67 (35.8)	10.5 [6.1; 14.6]	20 / 68 (29.4)	5.5 [2.2; 16.6]	0.7347 [0.4005; 1.3586] 0.3224	
Prior anthracycline use						0.5859
Yes	62 / 199 (31.2)	12.4 [7.6; NE]	72 / 208 (34.6)	8.9 [4.9; 18.0]	0.8393 [0.5945; 1.1806] 0.3140	
No	83 / 237 (35.0)	11.7 [7.4; 20.0]	71 / 222 (32.0)	11.8 [8.4; 16.6]	0.9383 [0.6825; 1.2935] 0.6944	
Liver metastases						0.7098
Yes	94 / 296 (31.8)	10.4 [6.9; 16.6]	95 / 283 (33.6)	9.3 [6.3; 13.8]	0.8600 [0.6456; 1.1453] 0.3009	
No	51 / 140 (36.4)	13.8 [8.3; 27.6]	48 / 147 (32.7)	13.2 [7.1; 20.7]	0.9279 [0.6225; 1.3850] 0.7090	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.8106
0	82 / 252 (32.5)	12.4 [8.3; 23.5]	86 / 257 (33.5)	10.3 [8.3; 13.8]	0.8664 [0.6382; 1.1755] 0.3564	
>=1	62 / 179 (34.6)	11.7 [6.2; 16.6]	54 / 164 (32.9)	9.7 [4.9; 17.3]	0.9154 [0.6341; 1.3260] 0.6390	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Social Functioning						
Age at randomization						0.6901
<65 years of age	98 / 302 (32.5)	12.5 [7.7; 17.2]	99 / 297 (33.3)	9.6 [6.2; 14.6]	0.8161 [0.6161; 1.0809] 0.1554	
>=65 years of age	44 / 134 (32.8)	11.0 [3.5; 21.4]	50 / 133 (37.6)	6.9 [4.2; 10.4]	0.9215 [0.6112; 1.3839] 0.6773	
Race						0.7498
Asian	68 / 154 (44.2)	11.0 [4.9; NE]	69 / 151 (45.7)	9.0 [4.2; 12.5]	0.8584 [0.6123; 1.2029] 0.3667	
White	65 / 231 (28.1)	11.7 [6.4; 15.9]	70 / 230 (30.4)	7.6 [5.5; 13.1]	0.8623 [0.6137; 1.2102] 0.3885	
Other	9 / 51 (17.6)	12.4 [2.1; NE]	10 / 49 (20.4)	6.8 [1.5; NE]	0.5960 [0.2354; 1.4869] 0.2549	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.9539
Asia	67 / 149 (45.0)	11.0 [5.5; NE]	67 / 147 (45.6)	9.0 [4.2; 12.5]	0.8659 [0.6155; 1.2179] 0.4000	
Europe	63 / 227 (27.8)	11.7 [6.9; 15.9]	66 / 213 (31.0)	6.8 [4.3; 9.9]	0.8164 [0.5765; 1.1550] 0.2496	
Rest of the World	12 / 60 (20.0)	NE [4.9; NE]	16 / 70 (22.9)	11.9 [3.5; NE]	0.7859 [0.3623; 1.6589] 0.5291	
HER2 IHC expression						0.1500
IHC 1+	72 / 239 (30.1)	16.3 [6.4; NE]	93 / 234 (39.7)	7.0 [4.8; 10.3]	0.7144 [0.5232; 0.9716] 0.0310	
IHC 2+/ISH-	40 / 117 (34.2)	9.8 [5.6; 15.2]	35 / 118 (29.7)	7.7 [4.3; 21.3]	0.9744 [0.6167; 1.5462] 0.9054	
IHC >0 <1+	29 / 76 (38.2)	11.0 [4.2; 18.6]	20 / 76 (26.3)	13.1 [4.9; NE]	1.2268 [0.6971; 2.2029] 0.4748	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2467
Yes	131 / 394 (33.2)	11.0 [7.0; 15.2]	132 / 389 (33.9)	8.2 [6.1; 10.4]	0.8722 [0.6843; 1.1125] 0.2654	
No	11 / 42 (26.2)	NE [4.2; NE]	17 / 41 (41.5)	7.6 [2.1; NE]	0.5903 [0.2674; 1.2496] 0.1697	
Prior Taxane Use In The Non-Metastatic Setting						0.3137
Yes	54 / 179 (30.2)	12.5 [7.7; NE]	66 / 177 (37.3)	6.8 [4.3; 11.9]	0.7217 [0.4999; 1.0372] 0.0757	
No	88 / 257 (34.2)	9.8 [6.2; 17.2]	83 / 253 (32.8)	8.9 [6.2; 13.1]	0.9271 [0.6865; 1.2535] 0.6144	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0728
1	17 / 65 (26.2)	14.6 [4.9; NE]	18 / 82 (22.0)	NE [3.5; NE]	1.0219 [0.5211; 1.9951] 0.9484	
2	88 / 295 (29.8)	15.2 [8.2; 20.0]	108 / 288 (37.5)	6.9 [4.8; 9.9]	0.6939 [0.5217; 0.9206] 0.0108	
>=3	36 / 75 (48.0)	5.1 [2.0; 9.8]	22 / 58 (37.9)	11.1 [4.2; 21.3]	1.3827 [0.8198; 2.3859] 0.2316	
ER/PR status I						0.3764
ER+, PR+	82 / 253 (32.4)	11.7 [6.3; NE]	84 / 237 (35.4)	6.9 [4.3; 10.3]	0.7970 [0.5868; 1.0822] 0.1420	
ER+, PR-	59 / 167 (35.3)	11.0 [6.3; 17.2]	59 / 181 (32.6)	10.4 [5.5; 21.3]	0.9392 [0.6523; 1.3520] 0.7275	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4416
ER <=10%	6 / 21 (28.6)	NE [1.4; NE]	5 / 14 (35.7)	4.2 [0.6; NE]	0.4956 [0.1461; 1.7574] 0.2454	
ER >10%	117 / 364 (32.1)	11.1 [6.9; 17.2]	123 / 355 (34.6)	7.6 [6.1; 10.3]	0.8299 [0.6430; 1.0705] 0.1466	
Positive	19 / 51 (37.3)	14.6 [4.2; 20.0]	21 / 61 (34.4)	16.5 [2.9; NE]	1.0616 [0.5644; 1.9845] 0.8446	
Endocrine Resistance						0.2400
Primary	44 / 128 (34.4)	9.8 [5.5; 18.6]	44 / 140 (31.4)	11.1 [3.5; NE]	1.0380 [0.6822; 1.5794] 0.8615	
Secondary	98 / 308 (31.8)	13.8 [7.6; 20.0]	105 / 288 (36.5)	7.7 [5.0; 10.3]	0.7602 [0.5757; 1.0029] 0.0494	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.4839
Capecitabine	83 / 266 (31.2)	11.9 [7.0; 20.0]	85 / 257 (33.1)	9.6 [6.9; 13.1]	0.9046 [0.6673; 1.2259] 0.5141	
Nab-Paclitaxel	38 / 103 (36.9)	11.0 [2.9; NE]	42 / 105 (40.0)	6.9 [4.8; 14.6]	0.8656 [0.5553; 1.3448] 0.5124	
Paclitaxel	21 / 67 (31.3)	14.6 [5.6; 18.6]	22 / 68 (32.4)	2.9 [2.1; 13.8]	0.5364 [0.2891; 0.9920] 0.0449	
Prior anthracycline use						0.2893
Yes	62 / 199 (31.2)	12.4 [7.0; NE]	78 / 208 (37.5)	6.3 [4.2; 10.3]	0.7466 [0.5317; 1.0437] 0.0864	
No	80 / 237 (33.8)	11.1 [6.3; 18.6]	71 / 222 (32.0)	9.9 [6.9; 21.3]	0.9419 [0.6842; 1.2998] 0.7082	
Liver metastases						0.2419
Yes	95 / 296 (32.1)	9.8 [6.4; 15.2]	105 / 283 (37.1)	6.8 [4.2; 9.6]	0.7492 [0.5657; 0.9908] 0.0413	
No	47 / 140 (33.6)	15.2 [5.1; NE]	44 / 147 (29.9)	10.4 [7.6; NE]	1.0264 [0.6796; 1.5532] 0.9072	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.3788
0	78 / 252 (31.0)	13.8 [9.8; 21.4]	89 / 257 (34.6)	8.9 [6.9; 11.1]	0.7400 [0.5439; 1.0048] 0.0523	
>=1	63 / 179 (35.2)	6.4 [4.1; 20.0]	59 / 164 (36.0)	6.2 [3.4; 11.9]	0.9507 [0.6661; 1.3589] 0.7758	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Fatigue						
Age at randomization						0.7534
<65 years of age	115 / 302 (38.1)	6.9 [3.5; 13.1]	130 / 297 (43.8)	3.6 [2.8; 4.9]	0.7871 [0.6096; 1.0151] 0.0608	
>=65 years of age	60 / 134 (44.8)	3.5 [2.2; 5.6]	71 / 133 (53.4)	2.2 [1.5; 3.5]	0.7013 [0.4939; 0.9924] 0.0435	
Race						0.2050
Asian	77 / 154 (50.0)	7.7 [3.5; 15.3]	87 / 151 (57.6)	4.2 [2.1; 5.7]	0.6990 [0.5095; 0.9564] 0.0233	
White	84 / 231 (36.4)	4.1 [2.8; 5.0]	97 / 230 (42.2)	2.9 [2.2; 4.2]	0.8863 [0.6594; 1.1885] 0.4110	
Other	14 / 51 (27.5)	1.5 [0.8; NE]	17 / 49 (34.7)	1.5 [0.8; 2.9]	0.6814 [0.3239; 1.4145] 0.2871	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4453
Asia	73 / 149 (49.0)	9.0 [3.5; 16.6]	84 / 147 (57.1)	4.2 [2.1; 6.1]	0.6999 [0.5072; 0.9631] 0.0266	
Europe	79 / 227 (34.8)	4.2 [2.8; 7.7]	89 / 213 (41.8)	2.8 [2.2; 3.6]	0.8054 [0.5925; 1.0940] 0.1617	
Rest of the World	23 / 60 (38.3)	1.4 [0.8; 6.2]	28 / 70 (40.0)	2.1 [1.3; 6.9]	0.9757 [0.5486; 1.7129] 0.9277	
HER2 IHC expression						0.1578
IHC 1+	92 / 239 (38.5)	6.2 [3.4; 10.4]	118 / 234 (50.4)	2.8 [2.1; 4.1]	0.6535 [0.4935; 0.8623] 0.0025	
IHC 2+/ISH-	50 / 117 (42.7)	4.2 [2.2; 7.7]	54 / 118 (45.8)	2.8 [2.1; 5.6]	0.8584 [0.5806; 1.2676] 0.4307	
IHC >0 <1+	32 / 76 (42.1)	3.3 [1.3; 13.9]	28 / 76 (36.8)	4.2 [2.2; 9.0]	1.0873 [0.6521; 1.8229] 0.7644	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2785
Yes	155 / 394 (39.3)	4.3 [3.3; 7.7]	178 / 389 (45.8)	3.4 [2.3; 4.2]	0.7774 [0.6248; 0.9665] 0.0215	
No	20 / 42 (47.6)	6.2 [1.3; 31.7]	23 / 41 (56.1)	2.1 [0.9; 4.1]	0.6228 [0.3323; 1.1532] 0.1274	
Prior Taxane Use In The Non-Metastatic Setting						0.4511
Yes	67 / 179 (37.4)	7.0 [4.2; 13.9]	84 / 177 (47.5)	3.4 [2.1; 4.2]	0.6816 [0.4894; 0.9452] 0.0204	
No	108 / 257 (42.0)	3.7 [2.8; 6.9]	117 / 253 (46.2)	2.8 [2.2; 4.2]	0.8135 [0.6243; 1.0597] 0.1201	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5790
1	25 / 65 (38.5)	5.0 [2.1; 18.6]	29 / 82 (35.4)	3.4 [2.1; 7.7]	0.8048 [0.4591; 1.3958] 0.4319	
2	115 / 295 (39.0)	4.3 [2.8; 9.7]	142 / 288 (49.3)	3.4 [2.1; 4.2]	0.7127 [0.5540; 0.9146] 0.0070	
>=3	35 / 75 (46.7)	4.2 [2.1; 7.7]	29 / 58 (50.0)	2.3 [1.4; 7.0]	0.9626 [0.5871; 1.5908] 0.8850	
ER/PR status I						0.8776
ER+, PR+	103 / 253 (40.7)	4.8 [2.8; 9.7]	112 / 237 (47.3)	2.8 [2.2; 4.1]	0.7455 [0.5678; 0.9775] 0.0313	
ER+, PR-	68 / 167 (40.7)	4.9 [2.8; 10.4]	81 / 181 (44.8)	3.5 [2.1; 5.6]	0.7864 [0.5649; 1.0908] 0.1450	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7361
ER <=10%	6 / 21 (28.6)	4.2 [0.7; NE]	4 / 14 (28.6)	8.9 [2.7; NE]	1.3116 [0.3729; 5.1496] 0.6833	
ER >10%	146 / 364 (40.1)	4.2 [2.9; 7.6]	168 / 355 (47.3)	3.4 [2.2; 4.2]	0.7644 [0.6101; 0.9569] 0.0173	
Positive	23 / 51 (45.1)	11.7 [2.8; 15.9]	29 / 61 (47.5)	2.2 [1.4; 4.2]	0.6770 [0.3847; 1.1782] 0.1721	
Endocrine Resistance						0.4851
Primary	50 / 128 (39.1)	4.2 [2.2; 11.8]	56 / 140 (40.0)	3.7 [2.2; 6.9]	0.8605 [0.5828; 1.2656] 0.4350	
Secondary	125 / 308 (40.6)	4.8 [2.9; 7.7]	144 / 288 (50.0)	2.8 [2.1; 4.1]	0.7188 [0.5631; 0.9161] 0.0068	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.6640
Capecitabine	101 / 266 (38.0)	4.3 [2.9; 9.8]	119 / 257 (46.3)	2.9 [2.1; 4.2]	0.7493 [0.5724; 0.9794] 0.0324	
Nab-Paclitaxel	47 / 103 (45.6)	4.2 [2.1; 13.9]	51 / 105 (48.6)	5.1 [2.8; 6.9]	0.8344 [0.5544; 1.2512] 0.3583	
Paclitaxel	27 / 67 (40.3)	5.6 [1.4; 9.1]	31 / 68 (45.6)	2.1 [0.9; 2.9]	0.5687 [0.3292; 0.9720] 0.0367	
Prior anthracycline use						0.2271
Yes	82 / 199 (41.2)	4.2 [2.8; 9.1]	94 / 208 (45.2)	3.4 [2.1; 4.8]	0.8720 [0.6445; 1.1761] 0.3644	
No	93 / 237 (39.2)	5.6 [3.3; 10.3]	107 / 222 (48.2)	2.9 [2.1; 4.2]	0.6696 [0.5042; 0.8875] 0.0047	
Liver metastases						0.3133
Yes	111 / 296 (37.5)	4.2 [2.9; 9.0]	134 / 283 (47.3)	2.8 [2.1; 4.2]	0.7053 [0.5453; 0.9104] 0.0065	
No	64 / 140 (45.7)	4.9 [2.8; 9.9]	67 / 147 (45.6)	3.5 [2.3; 4.8]	0.8646 [0.6108; 1.2232] 0.4047	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.5485
0	101 / 252 (40.1)	4.3 [2.9; 9.1]	127 / 257 (49.4)	2.9 [2.1; 4.2]	0.7220 [0.5532; 0.9397] 0.0140	
>=1	73 / 179 (40.8)	4.9 [2.2; 9.9]	71 / 164 (43.3)	3.4 [2.1; 4.9]	0.8097 [0.5800; 1.1303] 0.2082	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Nausea and Vomiting						
Age at randomization						0.8082
<65 years of age	131 / 302 (43.4)	3.4 [2.2; 4.9]	95 / 297 (32.0)	13.8 [6.9; 19.5]	1.6566 [1.2736; 2.1627] 0.0002	
>=65 years of age	47 / 134 (35.1)	7.1 [2.2; 11.8]	37 / 133 (27.8)	15.9 [7.5; NE]	1.5610 [1.0159; 2.4163] 0.0412	
Race						0.6292
Asian	89 / 154 (57.8)	3.4 [2.2; 5.6]	61 / 151 (40.4)	13.8 [7.6; NE]	1.8441 [1.3336; 2.5668] 0.0002	
White	78 / 231 (33.8)	3.6 [2.1; 7.6]	63 / 230 (27.4)	9.0 [5.7; NE]	1.5067 [1.0820; 2.1064] 0.0151	
Other	11 / 51 (21.6)	9.1 [1.4; NE]	8 / 49 (16.3)	NE [1.4; NE]	1.1888 [0.4800; 3.0773] 0.7132	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.6926
Asia	87 / 149 (58.4)	3.4 [2.2; 5.6]	60 / 147 (40.8)	13.8 [7.6; NE]	1.8355 [1.3233; 2.5629] 0.0002	
Europe	71 / 227 (31.3)	4.2 [2.1; 9.1]	53 / 213 (24.9)	15.9 [6.2; NE]	1.5317 [1.0756; 2.1962] 0.0180	
Rest of the World	20 / 60 (33.3)	2.9 [0.8; 19.4]	19 / 70 (27.1)	7.5 [2.7; NE]	1.2604 [0.6573; 2.4121] 0.4965	
HER2 IHC expression						0.8015
IHC 1+	96 / 239 (40.2)	4.2 [2.8; 7.1]	71 / 234 (30.3)	19.5 [7.7; NE]	1.7320 [1.2761; 2.3617] 0.0004	
IHC 2+/ISH-	50 / 117 (42.7)	2.8 [1.4; 7.6]	39 / 118 (33.1)	6.9 [3.5; NE]	1.4659 [0.9647; 2.2420] 0.0745	
IHC >0 <1+	32 / 76 (42.1)	3.5 [2.1; 14.6]	20 / 76 (26.3)	13.8 [6.4; NE]	1.8740 [1.0705; 3.3634] 0.0276	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4430
Yes	155 / 394 (39.3)	4.2 [2.8; 7.1]	117 / 389 (30.1)	13.8 [7.6; NE]	1.5873 [1.2497; 2.0216] 0.0001	
No	23 / 42 (54.8)	2.8 [1.4; 4.9]	15 / 41 (36.6)	15.8 [2.7; NE]	2.0776 [1.0859; 4.0972] 0.0261	
Prior Taxane Use In The Non-Metastatic Setting						0.4642
Yes	64 / 179 (35.8)	7.1 [2.2; 14.6]	56 / 177 (31.6)	10.3 [7.0; 21.5]	1.4562 [1.0163; 2.0925] 0.0409	
No	114 / 257 (44.4)	3.0 [2.1; 4.2]	76 / 253 (30.0)	13.8 [6.9; NE]	1.7338 [1.2994; 2.3266] 0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1362
1	21 / 65 (32.3)	10.3 [1.5; NE]	27 / 82 (32.9)	6.2 [2.7; NE]	0.9947 [0.5559; 1.7560] 0.9848	
2	120 / 295 (40.7)	3.5 [2.8; 6.3]	86 / 288 (29.9)	13.8 [8.2; NE]	1.7563 [1.3333; 2.3231] 0.0001	
>=3	36 / 75 (48.0)	3.0 [2.1; 11.0]	18 / 58 (31.0)	NE [2.9; NE]	1.9418 [1.1160; 3.5022] 0.0201	
ER/PR status I						0.4310
ER+, PR+	98 / 253 (38.7)	4.2 [2.7; 8.2]	75 / 237 (31.6)	13.8 [7.5; 21.5]	1.4863 [1.1017; 2.0139] 0.0097	
ER+, PR-	76 / 167 (45.5)	3.5 [2.2; 7.0]	54 / 181 (29.8)	15.9 [6.4; NE]	1.7971 [1.2707; 2.5590] 0.0008	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4138
ER <=10%	8 / 21 (38.1)	2.2 [1.3; NE]	7 / 14 (50.0)	4.8 [0.8; NE]	1.0047 [0.3584; 2.8830] 0.9924	
ER >10%	144 / 364 (39.6)	4.0 [2.8; 7.1]	106 / 355 (29.9)	13.8 [7.7; NE]	1.6259 [1.2666; 2.0939] 0.0001	
Positive	26 / 51 (51.0)	2.1 [1.4; 11.0]	19 / 61 (31.1)	19.5 [6.3; NE]	1.9856 [1.0985; 3.6576] 0.0217	
Endocrine Resistance						0.0700
Primary	48 / 128 (37.5)	4.2 [2.0; 18.0]	49 / 140 (35.0)	7.6 [4.1; 19.5]	1.2114 [0.8120; 1.8064] 0.3495	
Secondary	130 / 308 (42.2)	3.5 [2.2; 5.6]	83 / 288 (28.8)	15.9 [8.3; NE]	1.8798 [1.4303; 2.4844] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.7024
Capecitabine	108 / 266 (40.6)	3.5 [2.1; 7.1]	86 / 257 (33.5)	13.8 [7.5; 21.5]	1.5604 [1.1763; 2.0762] 0.0020	
Nab-Paclitaxel	42 / 103 (40.8)	4.2 [2.1; NE]	32 / 105 (30.5)	13.8 [5.7; NE]	1.6168 [1.0224; 2.5812] 0.0396	
Paclitaxel	28 / 67 (41.8)	3.0 [2.1; 9.1]	14 / 68 (20.6)	NE [4.3; NE]	2.0743 [1.1088; 4.0630] 0.0229	
Prior anthracycline use						0.5723
Yes	74 / 199 (37.2)	3.6 [2.2; 11.0]	58 / 208 (27.9)	15.2 [8.9; NE]	1.7184 [1.2196; 2.4329] 0.0019	
No	104 / 237 (43.9)	3.4 [2.2; 5.6]	74 / 222 (33.3)	8.3 [5.7; 19.5]	1.5329 [1.1393; 2.0728] 0.0048	
Liver metastases						0.8900
Yes	113 / 296 (38.2)	4.2 [2.2; 7.6]	81 / 283 (28.6)	15.2 [7.7; NE]	1.6572 [1.2473; 2.2106] 0.0005	
No	65 / 140 (46.4)	3.4 [2.2; 4.9]	51 / 147 (34.7)	13.8 [4.9; 21.5]	1.6274 [1.1279; 2.3611] 0.0088	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.5551
0	108 / 252 (42.9)	3.0 [2.1; 4.9]	79 / 257 (30.7)	13.8 [7.6; NE]	1.7438 [1.3061; 2.3382] 0.0001	
>=1	70 / 179 (39.1)	4.8 [2.8; 9.1]	51 / 164 (31.1)	8.9 [6.4; NE]	1.5407 [1.0757; 2.2217] 0.0182	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Pain						
Age at randomization						0.6945
<65 years of age	69 / 302 (22.8)	22.0 [17.2; NE]	107 / 297 (36.0)	7.6 [4.9; 11.1]	0.4801 [0.3517; 0.6508] <.0001	
>=65 years of age	36 / 134 (26.9)	17.2 [8.3; NE]	50 / 133 (37.6)	4.6 [3.0; 9.8]	0.5597 [0.3605; 0.8603] 0.0079	
Race						0.7982
Asian	47 / 154 (30.5)	31.7 [17.2; NE]	71 / 151 (47.0)	7.5 [4.8; 13.3]	0.4572 [0.3129; 0.6618] <.0001	
White	50 / 231 (21.6)	21.4 [12.4; NE]	76 / 230 (33.0)	6.3 [4.2; 9.9]	0.5663 [0.3930; 0.8090] 0.0016	
Other	8 / 51 (15.7)	NE [1.6; NE]	10 / 49 (20.4)	4.2 [1.9; NE]	0.5861 [0.2201; 1.5072] 0.2618	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7552
Asia	44 / 149 (29.5)	31.7 [17.2; NE]	67 / 147 (45.6)	9.1 [4.9; 14.9]	0.4533 [0.3064; 0.6640] <.0001	
Europe	47 / 227 (20.7)	21.4 [12.5; NE]	65 / 213 (30.5)	6.3 [4.2; 9.9]	0.5773 [0.3935; 0.8407] 0.0039	
Rest of the World	14 / 60 (23.3)	12.4 [1.4; NE]	25 / 70 (35.7)	4.8 [2.0; 9.6]	0.5759 [0.2899; 1.0986] 0.0888	
HER2 IHC expression						0.7128
IHC 1+	60 / 239 (25.1)	18.0 [16.6; NE]	94 / 234 (40.2)	6.3 [4.3; 9.6]	0.4907 [0.3517; 0.6794] <.0001	
IHC 2+/ISH-	27 / 117 (23.1)	21.4 [15.1; 23.4]	41 / 118 (34.7)	4.9 [3.5; 11.1]	0.4595 [0.2769; 0.7502] 0.0016	
IHC >0 <1+	17 / 76 (22.4)	NE [15.3; NE]	21 / 76 (27.6)	13.3 [4.8; 22.1]	0.6533 [0.3391; 1.2407] 0.1886	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6368
Yes	93 / 394 (23.6)	21.4 [17.2; NE]	137 / 389 (35.2)	7.6 [4.9; 9.9]	0.5111 [0.3907; 0.6658] <.0001	
No	12 / 42 (28.6)	31.7 [4.2; NE]	20 / 41 (48.8)	4.2 [2.0; 15.2]	0.4514 [0.2069; 0.9339] 0.0310	
Prior Taxane Use In The Non-Metastatic Setting						0.1888
Yes	36 / 179 (20.1)	23.4 [17.3; NE]	66 / 177 (37.3)	6.2 [4.2; 9.1]	0.4135 [0.2708; 0.6212] <.0001	
No	69 / 257 (26.8)	17.9 [12.5; NE]	91 / 253 (36.0)	6.9 [4.9; 11.1]	0.5820 [0.4235; 0.7963] 0.0006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.8296
1	11 / 65 (16.9)	31.7 [16.7; NE]	21 / 82 (25.6)	7.5 [4.2; NE]	0.4524 [0.2019; 0.9456] 0.0361	
2	74 / 295 (25.1)	22.0 [15.3; NE]	114 / 288 (39.6)	4.9 [4.1; 9.1]	0.5138 [0.3809; 0.6886] <.0001	
>=3	20 / 75 (26.7)	18.0 [12.5; NE]	22 / 58 (37.9)	9.1 [6.3; 15.9]	0.5372 [0.2884; 0.9939] 0.0439	
ER/PR status I						0.1527
ER+, PR+	55 / 253 (21.7)	23.4 [17.2; NE]	91 / 237 (38.4)	5.0 [4.1; 9.6]	0.4296 [0.3048; 0.5999] <.0001	
ER+, PR-	48 / 167 (28.7)	17.3 [12.5; NE]	62 / 181 (34.3)	8.3 [4.9; 11.9]	0.5985 [0.4045; 0.8795] 0.0084	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9075
ER <=10%	3 / 21 (14.3)	NE [4.9; NE]	3 / 14 (21.4)	NE [0.7; NE]	0.5358 [0.0988; 2.9064] 0.4388	
ER >10%	89 / 364 (24.5)	21.4 [16.7; NE]	130 / 355 (36.6)	6.3 [4.8; 9.6]	0.5197 [0.3943; 0.6818] <.0001	
Positive	13 / 51 (25.5)	NE [11.1; NE]	24 / 61 (39.3)	4.3 [2.2; 13.3]	0.4681 [0.2298; 0.9118] 0.0256	
Endocrine Resistance						0.9526
Primary	27 / 128 (21.1)	31.7 [16.6; NE]	44 / 140 (31.4)	7.5 [4.2; 16.6]	0.4985 [0.3025; 0.8054] 0.0043	
Secondary	78 / 308 (25.3)	21.4 [17.2; NE]	112 / 288 (38.9)	6.3 [4.3; 9.1]	0.5025 [0.3737; 0.6722] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.2585
Capecitabine	63 / 266 (23.7)	21.4 [16.7; NE]	100 / 257 (38.9)	5.0 [4.2; 9.0]	0.4850 [0.3514; 0.6644] <.0001	
Nab-Paclitaxel	28 / 103 (27.2)	31.7 [10.4; NE]	35 / 105 (33.3)	9.9 [6.3; NE]	0.7051 [0.4212; 1.1672] 0.1735	
Paclitaxel	14 / 67 (20.9)	23.4 [11.1; NE]	22 / 68 (32.4)	4.1 [1.8; 16.6]	0.3369 [0.1623; 0.6714] 0.0016	
Prior anthracycline use						0.9001
Yes	47 / 199 (23.6)	17.9 [16.7; NE]	75 / 208 (36.1)	6.3 [4.3; 9.1]	0.4767 [0.3260; 0.6899] 0.0001	
No	58 / 237 (24.5)	NE [14.5; NE]	82 / 222 (36.9)	6.3 [4.2; 11.1]	0.5268 [0.3741; 0.7369] 0.0002	
Liver metastases						0.3619
Yes	69 / 296 (23.3)	23.4 [14.5; NE]	108 / 283 (38.2)	4.9 [4.2; 7.6]	0.4600 [0.3358; 0.6256] <.0001	
No	36 / 140 (25.7)	18.0 [16.6; NE]	49 / 147 (33.3)	9.9 [5.0; 17.3]	0.6046 [0.3900; 0.9285] 0.0207	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.1670
0	61 / 252 (24.2)	23.4 [17.3; NE]	107 / 257 (41.6)	5.6 [4.2; 9.0]	0.4578 [0.3316; 0.6265] <.0001	
>=1	43 / 179 (24.0)	17.9 [15.3; NE]	47 / 164 (28.7)	11.1 [4.9; 16.6]	0.6418 [0.4208; 0.9761] 0.0363	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Dyspnoea						
Age at randomization						0.3090
<65 years of age	66 / 302 (21.9)	20.7 [19.3; NE]	75 / 297 (25.3)	21.3 [9.9; NE]	0.6954 [0.4972; 0.9702] 0.0316	
>=65 years of age	32 / 134 (23.9)	19.3 [11.0; NE]	32 / 133 (24.1)	20.8 [12.0; NE]	0.9521 [0.5808; 1.5608] 0.8466	
Race						0.0620
Asian	42 / 154 (27.3)	29.7 [19.3; NE]	48 / 151 (31.8)	21.3 [14.9; NE]	0.7453 [0.4902; 1.1289] 0.1638	
White	52 / 231 (22.5)	17.2 [13.1; 20.0]	49 / 230 (21.3)	20.8 [9.9; NE]	0.9259 [0.6253; 1.3735] 0.6962	
Other	4 / 51 (7.8)	NE [NE; NE]	10 / 49 (20.4)	7.0 [2.1; NE]	0.2517 [0.0682; 0.7630] 0.0132	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2554
Asia	40 / 149 (26.8)	NE [19.3; NE]	47 / 147 (32.0)	21.3 [10.3; NE]	0.7181 [0.4686; 1.0952] 0.1227	
Europe	45 / 227 (19.8)	19.3 [15.1; NE]	51 / 213 (23.9)	12.4 [7.0; NE]	0.7023 [0.4678; 1.0509] 0.0835	
Rest of the World	13 / 60 (21.7)	19.3 [6.4; NE]	9 / 70 (12.9)	NE [NE; NE]	1.4383 [0.6027; 3.5489] 0.4114	
HER2 IHC expression						0.5551
IHC 1+	52 / 239 (21.8)	29.7 [19.3; NE]	61 / 234 (26.1)	NE [12.4; NE]	0.7537 [0.5182; 1.0932] 0.1351	
IHC 2+/ISH-	26 / 117 (22.2)	20.7 [15.3; NE]	31 / 118 (26.3)	20.8 [6.3; NE]	0.6878 [0.4046; 1.1599] 0.1579	
IHC >0 <1+	19 / 76 (25.0)	17.2 [15.9; NE]	14 / 76 (18.4)	NE [9.6; NE]	1.0576 [0.5324; 2.1530] 0.8666	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3759
Yes	85 / 394 (21.6)	20.0 [19.3; NE]	97 / 389 (24.9)	20.8 [12.4; NE]	0.7374 [0.5496; 0.9875] 0.0402	
No	13 / 42 (31.0)	19.3 [8.2; NE]	10 / 41 (24.4)	NE [9.7; NE]	1.1084 [0.4864; 2.6019] 0.8072	
Prior Taxane Use In The Non-Metastatic Setting						0.4590
Yes	38 / 179 (21.2)	19.4 [17.2; NE]	48 / 177 (27.1)	14.6 [9.6; NE]	0.6793 [0.4398; 1.0419] 0.0762	
No	60 / 257 (23.3)	20.0 [16.6; NE]	59 / 253 (23.3)	21.3 [14.9; NE]	0.8368 [0.5828; 1.2017] 0.3296	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.2128
1	13 / 65 (20.0)	NE [10.5; NE]	13 / 82 (15.9)	NE [9.9; NE]	1.0531 [0.4820; 2.3004] 0.8951	
2	60 / 295 (20.3)	20.0 [19.3; NE]	76 / 288 (26.4)	15.9 [9.7; NE]	0.6449 [0.4574; 0.9053] 0.0107	
>=3	25 / 75 (33.3)	13.8 [6.9; NE]	17 / 58 (29.3)	21.3 [4.9; NE]	1.1632 [0.6322; 2.1928] 0.6287	
ER/PR status I						0.0878
ER+, PR+	52 / 253 (20.6)	29.7 [19.3; NE]	63 / 237 (26.6)	15.9 [9.0; NE]	0.6539 [0.4509; 0.9443] 0.0224	
ER+, PR-	45 / 167 (26.9)	19.3 [13.8; NE]	39 / 181 (21.5)	21.3 [14.9; NE]	1.0294 [0.6695; 1.5898] 0.8951	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4981
ER <=10%	3 / 21 (14.3)	NE [2.0; NE]	4 / 14 (28.6)	NE [1.0; NE]	0.3835 [0.0726; 1.7934] 0.2056	
ER >10%	81 / 364 (22.3)	19.4 [17.3; NE]	87 / 355 (24.5)	NE [10.3; NE]	0.7521 [0.5539; 1.0200] 0.0654	
Positive	14 / 51 (27.5)	19.3 [10.5; NE]	16 / 61 (26.2)	21.3 [14.9; NE]	1.0225 [0.4910; 2.1050] 0.9507	
Endocrine Resistance						0.9291
Primary	25 / 128 (19.5)	NE [17.2; NE]	30 / 140 (21.4)	NE [9.9; NE]	0.7648 [0.4457; 1.3008] 0.3230	
Secondary	73 / 308 (23.7)	19.4 [17.3; NE]	76 / 288 (26.4)	20.8 [12.0; NE]	0.7706 [0.5573; 1.0646] 0.1109	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.2745
Capecitabine	65 / 266 (24.4)	20.0 [15.9; NE]	64 / 257 (24.9)	20.8 [12.0; NE]	0.8809 [0.6227; 1.2477] 0.4741	
Nab-Paclitaxel	19 / 103 (18.4)	19.4 [19.3; NE]	25 / 105 (23.8)	NE [10.3; NE]	0.6897 [0.3743; 1.2501] 0.2202	
Paclitaxel	14 / 67 (20.9)	19.3 [11.1; NE]	18 / 68 (26.5)	7.6 [2.1; NE]	0.4443 [0.2072; 0.9195] 0.0274	
Prior anthracycline use						0.0445
Yes	43 / 199 (21.6)	20.0 [15.9; NE]	63 / 208 (30.3)	12.0 [4.9; NE]	0.5854 [0.3938; 0.8620] 0.0066	
No	55 / 237 (23.2)	19.4 [17.3; NE]	44 / 222 (19.8)	NE [15.9; NE]	1.0217 [0.6872; 1.5276] 0.9218	
Liver metastases						0.1712
Yes	68 / 296 (23.0)	19.3 [16.6; NE]	66 / 283 (23.3)	20.8 [14.6; NE]	0.8743 [0.6211; 1.2321] 0.4389	
No	30 / 140 (21.4)	NE [17.3; NE]	41 / 147 (27.9)	15.9 [9.0; NE]	0.5853 [0.3618; 0.9362] 0.0247	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.1440
0	51 / 252 (20.2)	29.7 [19.3; NE]	65 / 257 (25.3)	NE [9.9; NE]	0.6474 [0.4457; 0.9352] 0.0200	
>=1	46 / 179 (25.7)	17.3 [11.1; NE]	40 / 164 (24.4)	15.9 [12.0; 21.3]	0.9583 [0.6269; 1.4713] 0.8450	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Insomnia						
Age at randomization						0.9652
<65 years of age	66 / 302 (21.9)	NE [17.2; NE]	72 / 297 (24.2)	15.8 [13.9; NE]	0.7592 [0.5418; 1.0621] 0.1048	
>=65 years of age	30 / 134 (22.4)	NE [9.6; NE]	36 / 133 (27.1)	12.4 [6.3; NE]	0.7732 [0.4732; 1.2539] 0.2976	
Race						0.8099
Asian	42 / 154 (27.3)	NE [20.0; NE]	48 / 151 (31.8)	15.9 [13.8; NE]	0.7384 [0.4849; 1.1202] 0.1491	
White	46 / 231 (19.9)	NE [11.8; NE]	55 / 230 (23.9)	12.4 [5.6; NE]	0.7386 [0.4970; 1.0926] 0.1292	
Other	8 / 51 (15.7)	11.0 [9.6; NE]	5 / 49 (10.2)	13.9 [3.5; NE]	1.0835 [0.3609; 3.5904] 0.8869	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1655
Asia	41 / 149 (27.5)	NE [20.0; NE]	47 / 147 (32.0)	15.9 [13.8; NE]	0.7185 [0.4694; 1.0953] 0.1205	
Europe	40 / 227 (17.6)	NE [12.4; NE]	50 / 213 (23.5)	12.4 [4.9; NE]	0.6384 [0.4187; 0.9672] 0.0334	
Rest of the World	15 / 60 (25.0)	11.0 [2.8; NE]	11 / 70 (15.7)	NE [5.6; NE]	1.4981 [0.6913; 3.3499] 0.3081	
HER2 IHC expression						0.8318
IHC 1+	57 / 239 (23.8)	NE [11.8; NE]	62 / 234 (26.5)	15.2 [12.4; NE]	0.8049 [0.5597; 1.1554] 0.2374	
IHC 2+/ISH-	22 / 117 (18.8)	NE [12.4; NE]	28 / 118 (23.7)	21.3 [5.6; NE]	0.7008 [0.3959; 1.2245] 0.2108	
IHC >0 <1+	16 / 76 (21.1)	20.0 [20.0; NE]	18 / 76 (23.7)	13.8 [5.5; NE]	0.6676 [0.3360; 1.3146] 0.2365	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6531
Yes	85 / 394 (21.6)	NE [17.2; NE]	97 / 389 (24.9)	15.2 [12.4; NE]	0.7440 [0.5548; 0.9960] 0.0458	
No	11 / 42 (26.2)	NE [8.3; NE]	11 / 41 (26.8)	15.8 [4.9; NE]	0.9693 [0.4128; 2.2749] 0.9419	
Prior Taxane Use In The Non-Metastatic Setting						0.0318
Yes	34 / 179 (19.0)	NE [17.3; NE]	51 / 177 (28.8)	13.8 [6.3; 16.8]	0.5130 [0.3273; 0.7939] 0.0025	
No	62 / 257 (24.1)	NE [12.4; NE]	57 / 253 (22.5)	21.3 [13.8; NE]	0.9820 [0.6852; 1.4100] 0.9167	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4855
1	11 / 65 (16.9)	NE [13.8; NE]	19 / 82 (23.2)	12.4 [4.8; NE]	0.4616 [0.2064; 0.9791] 0.0433	
2	65 / 295 (22.0)	NE [17.2; NE]	71 / 288 (24.7)	15.9 [9.6; NE]	0.8117 [0.5783; 1.1375] 0.2233	
>=3	20 / 75 (26.7)	NE [7.7; NE]	17 / 58 (29.3)	21.3 [9.0; NE]	0.8793 [0.4602; 1.6994] 0.6951	
ER/PR status I						0.3237
ER+, PR+	58 / 253 (22.9)	NE [13.8; NE]	67 / 237 (28.3)	13.8 [6.9; 15.9]	0.6616 [0.4638; 0.9408] 0.0206	
ER+, PR-	37 / 167 (22.2)	NE [13.8; NE]	39 / 181 (21.5)	21.3 [12.4; NE]	0.9043 [0.5739; 1.4222] 0.6586	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.0804
ER <=10%	6 / 21 (28.6)	10.4 [1.4; NE]	2 / 14 (14.3)	NE [0.7; NE]	2.3422 [0.5389; 15.9945] 0.2796	
ER >10%	82 / 364 (22.5)	NE [13.8; NE]	88 / 355 (24.8)	15.2 [9.6; NE]	0.7975 [0.5890; 1.0786] 0.1389	
Positive	8 / 51 (15.7)	NE [20.0; NE]	18 / 61 (29.5)	16.8 [5.0; NE]	0.4120 [0.1686; 0.9198] 0.0319	
Endocrine Resistance						0.5863
Primary	27 / 128 (21.1)	NE [13.8; NE]	35 / 140 (25.0)	15.2 [8.3; 16.8]	0.6560 [0.3915; 1.0872] 0.1004	
Secondary	69 / 308 (22.4)	NE [13.8; NE]	72 / 288 (25.0)	21.3 [9.0; NE]	0.8157 [0.5852; 1.1359] 0.2243	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.7133
Capecitabine	56 / 266 (21.1)	NE [17.3; NE]	69 / 257 (26.8)	13.9 [8.3; NE]	0.7204 [0.5045; 1.0247] 0.0672	
Nab-Paclitaxel	26 / 103 (25.2)	NE [11.0; NE]	25 / 105 (23.8)	15.9 [9.6; NE]	0.9212 [0.5294; 1.6063] 0.7694	
Paclitaxel	14 / 67 (20.9)	NE [10.5; NE]	14 / 68 (20.6)	15.2 [2.8; NE]	0.7033 [0.3304; 1.4967] 0.3526	
Prior anthracycline use						0.2301
Yes	37 / 199 (18.6)	NE [NE; NE]	52 / 208 (25.0)	15.2 [9.0; NE]	0.6306 [0.4094; 0.9617] 0.0319	
No	59 / 237 (24.9)	20.0 [12.4; NE]	56 / 222 (25.2)	15.2 [9.6; NE]	0.8807 [0.6105; 1.2720] 0.4905	
Liver metastases						0.3653
Yes	59 / 296 (19.9)	NE [13.8; NE]	72 / 283 (25.4)	14.6 [9.0; NE]	0.6825 [0.4817; 0.9632] 0.0287	
No	37 / 140 (26.4)	NE [12.4; NE]	36 / 147 (24.5)	16.8 [13.8; NE]	0.9319 [0.5875; 1.4798] 0.7582	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.6455
0	61 / 252 (24.2)	NE [13.1; NE]	66 / 257 (25.7)	13.8 [8.9; NE]	0.8139 [0.5728; 1.1545] 0.2454	
>=1	35 / 179 (19.6)	NE [17.2; NE]	40 / 164 (24.4)	15.8 [14.6; NE]	0.6990 [0.4416; 1.1016] 0.1201	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Appetite Loss						
Age at randomization						0.0918
<65 years of age	105 / 302 (34.8)	8.3 [4.9; 13.9]	76 / 297 (25.6)	15.2 [10.3; NE]	1.5542 [1.1586; 2.0946] 0.0033	
>=65 years of age	47 / 134 (35.1)	8.3 [2.9; 11.7]	49 / 133 (36.8)	6.2 [3.5; 13.8]	1.0116 [0.6763; 1.5114] 0.9476	
Race						0.6255
Asian	82 / 154 (53.2)	5.1 [2.2; 9.8]	62 / 151 (41.1)	10.3 [6.2; 21.3]	1.5189 [1.0936; 2.1204] 0.0126	
White	59 / 231 (25.5)	12.4 [6.9; 17.3]	55 / 230 (23.9)	14.4 [8.3; NE]	1.1816 [0.8178; 1.7091] 0.3763	
Other	11 / 51 (21.6)	10.3 [1.4; NE]	8 / 49 (16.3)	10.4 [4.2; NE]	1.0763 [0.4327; 2.7979] 0.8741	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4545
Asia	79 / 149 (53.0)	5.1 [2.8; 9.8]	60 / 147 (40.8)	11.1 [6.3; 21.3]	1.5323 [1.0965; 2.1506] 0.0123	
Europe	59 / 227 (26.0)	9.7 [5.0; 17.3]	48 / 213 (22.5)	14.4 [8.3; NE]	1.2701 [0.8687; 1.8662] 0.2194	
Rest of the World	14 / 60 (23.3)	11.7 [2.7; NE]	17 / 70 (24.3)	13.8 [4.9; NE]	0.9012 [0.4351; 1.8352] 0.7651	
HER2 IHC expression						0.4206
IHC 1+	81 / 239 (33.9)	7.7 [4.8; 13.0]	76 / 234 (32.5)	10.3 [7.5; 15.9]	1.1781 [0.8610; 1.6126] 0.3085	
IHC 2+/ISH-	42 / 117 (35.9)	9.1 [3.1; 15.3]	27 / 118 (22.9)	15.1 [8.3; NE]	1.6912 [1.0479; 2.7761] 0.0323	
IHC >0 <1+	28 / 76 (36.8)	9.8 [2.1; 14.6]	21 / 76 (27.6)	17.2 [5.6; NE]	1.5272 [0.8680; 2.7296] 0.1403	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4659
Yes	131 / 394 (33.2)	9.1 [6.3; 13.0]	109 / 389 (28.0)	13.8 [9.6; 16.1]	1.3027 [1.0110; 1.6825] 0.0414	
No	21 / 42 (50.0)	2.1 [1.4; 9.8]	16 / 41 (39.0)	8.2 [1.5; NE]	1.5113 [0.7890; 2.9513] 0.2207	
Prior Taxane Use In The Non-Metastatic Setting						0.3168
Yes	57 / 179 (31.8)	10.4 [4.2; 13.9]	55 / 177 (31.1)	10.3 [6.9; NE]	1.1464 [0.7886; 1.6666] 0.4747	
No	95 / 257 (37.0)	6.9 [3.6; 10.3]	70 / 253 (27.7)	15.1 [9.6; 21.3]	1.4855 [1.0926; 2.0297] 0.0118	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.8763
1	20 / 65 (30.8)	11.7 [3.6; NE]	18 / 82 (22.0)	14.4 [8.2; NE]	1.3414 [0.7072; 2.5627] 0.3724	
2	108 / 295 (36.6)	5.1 [3.0; 9.7]	89 / 288 (30.9)	13.8 [7.5; 15.9]	1.4023 [1.0599; 1.8600] 0.0180	
>=3	23 / 75 (30.7)	13.1 [6.7; NE]	17 / 58 (29.3)	21.3 [7.7; NE]	1.1747 [0.6301; 2.2338] 0.6170	
ER/PR status I						0.2106
ER+, PR+	81 / 253 (32.0)	9.1 [6.7; 17.3]	70 / 237 (29.5)	13.8 [9.6; 16.1]	1.1869 [0.8626; 1.6380] 0.2996	
ER+, PR-	68 / 167 (40.7)	5.6 [2.9; 10.4]	50 / 181 (27.6)	17.2 [7.7; NE]	1.6204 [1.1268; 2.3461] 0.0089	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.8221
ER <=10%	9 / 21 (42.9)	2.8 [0.7; NE]	5 / 14 (35.7)	10.4 [4.8; NE]	1.8203 [0.6211; 5.9843] 0.2849	
ER >10%	117 / 364 (32.1)	9.7 [6.4; 13.1]	96 / 355 (27.0)	14.4 [9.7; NE]	1.3088 [1.0002; 1.7179] 0.0508	
Positive	26 / 51 (51.0)	3.0 [1.4; 9.7]	24 / 61 (39.3)	4.9 [2.2; NE]	1.5171 [0.8634; 2.6837] 0.1431	
Endocrine Resistance						0.8876
Primary	45 / 128 (35.2)	8.3 [2.2; NE]	39 / 140 (27.9)	14.4 [6.3; NE]	1.3729 [0.8941; 2.1174] 0.1502	
Secondary	107 / 308 (34.7)	8.3 [4.9; 12.4]	86 / 288 (29.9)	11.1 [7.7; 21.3]	1.3239 [0.9975; 1.7621] 0.0522	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.2578
Capecitabine	87 / 266 (32.7)	9.7 [5.0; 15.3]	73 / 257 (28.4)	13.8 [8.2; NE]	1.3109 [0.9609; 1.7932] 0.0877	
Nab-Paclitaxel	42 / 103 (40.8)	4.2 [2.1; 13.0]	33 / 105 (31.4)	14.4 [7.6; NE]	1.7711 [1.1234; 2.8157] 0.0135	
Paclitaxel	23 / 67 (34.3)	9.8 [4.9; 16.6]	19 / 68 (27.9)	10.3 [3.6; 15.2]	0.8437 [0.4536; 1.5831] 0.5865	
Prior anthracycline use						0.9148
Yes	65 / 199 (32.7)	9.1 [3.5; 13.9]	61 / 208 (29.3)	10.3 [6.9; NE]	1.3477 [0.9492; 1.9160] 0.0948	
No	87 / 237 (36.7)	7.7 [5.1; 12.4]	64 / 222 (28.8)	14.6 [9.6; 17.2]	1.3770 [0.9986; 1.9090] 0.0522	
Liver metastases						0.3274
Yes	94 / 296 (31.8)	9.7 [6.3; 13.9]	79 / 283 (27.9)	14.4 [8.3; NE]	1.2418 [0.9215; 1.6789] 0.1565	
No	58 / 140 (41.4)	4.9 [2.7; 9.8]	46 / 147 (31.3)	11.1 [6.3; NE]	1.5882 [1.0796; 2.3502] 0.0188	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.1101
0	94 / 252 (37.3)	6.9 [3.6; 11.7]	72 / 257 (28.0)	15.1 [10.3; NE]	1.5586 [1.1480; 2.1247] 0.0044	
>=1	58 / 179 (32.4)	9.7 [4.9; 17.3]	52 / 164 (31.7)	9.6 [4.9; 15.2]	1.0524 [0.7235; 1.5349] 0.8016	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Constipation						
Age at randomization						0.9959
<65 years of age	100 / 302 (33.1)	10.3 [4.9; 14.5]	65 / 297 (21.9)	22.2 [13.2; NE]	1.7554 [1.2879; 2.4093] 0.0004	
>=65 years of age	47 / 134 (35.1)	8.2 [3.5; 15.3]	31 / 133 (23.3)	19.4 [11.9; NE]	1.7604 [1.1202; 2.8041] 0.0140	
Race						0.9707
Asian	68 / 154 (44.2)	10.3 [3.5; NE]	41 / 151 (27.2)	22.0 [17.3; NE]	1.8835 [1.2836; 2.7980] 0.0012	
White	69 / 231 (29.9)	8.3 [3.5; 12.5]	50 / 230 (21.7)	18.0 [11.9; 26.2]	1.7541 [1.2192; 2.5430] 0.0023	
Other	10 / 51 (19.6)	10.3 [5.5; NE]	5 / 49 (10.2)	13.2 [4.9; NE]	1.6007 [0.5680; 5.1446] 0.3866	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7822
Asia	68 / 149 (45.6)	9.7 [3.5; 21.4]	40 / 147 (27.2)	22.0 [17.3; NE]	1.9526 [1.3274; 2.9105] 0.0007	
Europe	64 / 227 (28.2)	9.0 [4.5; 13.3]	41 / 213 (19.2)	19.4 [11.9; NE]	1.7321 [1.1721; 2.5908] 0.0058	
Rest of the World	15 / 60 (25.0)	9.2 [2.3; NE]	15 / 70 (21.4)	18.0 [7.5; NE]	1.4840 [0.7186; 3.0643] 0.2792	
HER2 IHC expression						0.7887
IHC 1+	79 / 239 (33.1)	11.9 [8.2; 21.4]	51 / 234 (21.8)	22.2 [13.2; NE]	1.6769 [1.1817; 2.4004] 0.0038	
IHC 2+/ISH-	41 / 117 (35.0)	6.2 [3.5; 11.8]	28 / 118 (23.7)	18.0 [9.0; NE]	1.7956 [1.1148; 2.9345] 0.0158	
IHC >0 <1+	27 / 76 (35.5)	3.4 [2.1; NE]	16 / 76 (21.1)	19.4 [7.0; NE]	2.1275 [1.1554; 4.0475] 0.0154	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3620
Yes	127 / 394 (32.2)	10.3 [6.3; 14.5]	85 / 389 (21.9)	19.4 [15.9; NE]	1.6729 [1.2730; 2.2094] 0.0002	
No	20 / 42 (47.6)	2.2 [1.5; 11.0]	11 / 41 (26.8)	NE [6.8; NE]	2.4435 [1.1888; 5.2939] 0.0143	
Prior Taxane Use In The Non-Metastatic Setting						0.5642
Yes	58 / 179 (32.4)	7.7 [2.8; 17.3]	39 / 177 (22.0)	18.0 [13.1; NE]	1.9219 [1.2845; 2.9067] 0.0014	
No	89 / 257 (34.6)	9.7 [4.9; 15.3]	57 / 253 (22.5)	22.0 [13.2; NE]	1.6346 [1.1742; 2.2936] 0.0037	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.7203
1	18 / 65 (27.7)	17.3 [4.1; NE]	15 / 82 (18.3)	NE [9.9; NE]	1.5151 [0.7614; 3.0571] 0.2347	
2	96 / 295 (32.5)	9.7 [4.8; 14.5]	66 / 288 (22.9)	19.4 [15.1; NE]	1.7439 [1.2778; 2.3959] 0.0004	
>=3	32 / 75 (42.7)	7.0 [3.4; 22.8]	14 / 58 (24.1)	18.0 [8.3; NE]	2.0448 [1.1080; 3.9704] 0.0239	
ER/PR status I						0.2348
ER+, PR+	82 / 253 (32.4)	10.3 [7.0; 23.4]	56 / 237 (23.6)	22.0 [13.2; NE]	1.5052 [1.0743; 2.1241] 0.0180	
ER+, PR-	64 / 167 (38.3)	5.5 [3.4; 12.5]	39 / 181 (21.5)	19.4 [13.1; NE]	2.0878 [1.4040; 3.1430] 0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9203
ER <=10%	5 / 21 (23.8)	NE [0.8; NE]	2 / 14 (14.3)	15.1 [6.3; NE]	1.8931 [0.4000; 13.3585] 0.4487	
ER >10%	125 / 364 (34.3)	8.9 [4.9; 11.9]	80 / 355 (22.5)	19.4 [15.9; 26.2]	1.7880 [1.3525; 2.3772] <.0001	
Positive	17 / 51 (33.3)	21.4 [3.0; NE]	14 / 61 (23.0)	NE [11.8; NE]	1.5214 [0.7502; 3.1362] 0.2421	
Endocrine Resistance						0.9497
Primary	46 / 128 (35.9)	8.3 [3.4; 17.3]	31 / 140 (22.1)	NE [11.8; NE]	1.7921 [1.1413; 2.8544] 0.0110	
Secondary	101 / 308 (32.8)	9.2 [4.9; 14.5]	64 / 288 (22.2)	19.4 [15.1; NE]	1.7609 [1.2906; 2.4201] 0.0004	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.8162
Capecitabine	88 / 266 (33.1)	10.3 [4.9; 17.3]	57 / 257 (22.2)	22.0 [15.9; NE]	1.7518 [1.2587; 2.4573] 0.0009	
Nab-Paclitaxel	36 / 103 (35.0)	8.2 [2.8; NE]	25 / 105 (23.8)	NE [15.1; NE]	1.9555 [1.1780; 3.2976] 0.0091	
Paclitaxel	23 / 67 (34.3)	9.2 [3.6; 12.5]	14 / 68 (20.6)	13.1 [3.6; NE]	1.3831 [0.7172; 2.7636] 0.3355	
Prior anthracycline use						0.9422
Yes	63 / 199 (31.7)	9.1 [4.2; 17.3]	46 / 208 (22.1)	NE [13.1; NE]	1.7476 [1.1972; 2.5702] 0.0036	
No	84 / 237 (35.4)	9.2 [4.5; 15.3]	50 / 222 (22.5)	19.4 [15.1; NE]	1.7547 [1.2395; 2.5093] 0.0016	
Liver metastases						0.5536
Yes	95 / 296 (32.1)	8.9 [5.5; 13.3]	56 / 283 (19.8)	NE [15.9; NE]	1.8732 [1.3505; 2.6225] 0.0002	
No	52 / 140 (37.1)	10.3 [3.4; 23.4]	40 / 147 (27.2)	19.4 [11.9; 26.2]	1.6202 [1.0747; 2.4606] 0.0211	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.2806
0	81 / 252 (32.1)	11.0 [6.3; 22.8]	60 / 257 (23.3)	19.4 [13.1; NE]	1.5728 [1.1266; 2.2073] 0.0078	
>=1	65 / 179 (36.3)	4.9 [3.4; 11.9]	33 / 164 (20.1)	NE [17.3; NE]	2.1303 [1.4119; 3.2769] 0.0003	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Diarrhea						
Age at randomization						0.0891
<65 years of age	75 / 302 (24.8)	19.9 [15.9; NE]	64 / 297 (21.5)	16.5 [14.5; 23.4]	0.9849 [0.7033; 1.3827] 0.9306	
>=65 years of age	26 / 134 (19.4)	NE [19.4; NE]	37 / 133 (27.8)	14.4 [9.0; NE]	0.6395 [0.3813; 1.0561] 0.0822	
Race						0.1191
Asian	43 / 154 (27.9)	NE [17.3; NE]	43 / 151 (28.5)	16.5 [13.9; NE]	0.8114 [0.5283; 1.2455] 0.3371	
White	54 / 231 (23.4)	19.4 [13.3; 33.1]	50 / 230 (21.7)	16.5 [13.1; 23.4]	1.0470 [0.7100; 1.5461] 0.8124	
Other	4 / 51 (7.8)	NE [10.3; NE]	8 / 49 (16.3)	13.9 [2.8; NE]	0.3191 [0.0829; 1.0418] 0.0569	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.6276
Asia	42 / 149 (28.2)	NE [17.2; NE]	43 / 147 (29.3)	16.5 [13.9; NE]	0.7725 [0.5012; 1.1892] 0.2389	
Europe	45 / 227 (19.8)	33.1 [13.9; NE]	45 / 213 (21.1)	15.2 [12.4; 23.4]	0.9028 [0.5939; 1.3715] 0.6355	
Rest of the World	14 / 60 (23.3)	13.8 [4.8; 29.0]	13 / 70 (18.6)	18.0 [8.9; NE]	1.0801 [0.4916; 2.3694] 0.8437	
HER2 IHC expression						0.0967
IHC 1+	61 / 239 (25.5)	22.1 [13.3; NE]	51 / 234 (21.8)	15.8 [13.9; NE]	1.1307 [0.7787; 1.6495] 0.5202	
IHC 2+/ISH-	22 / 117 (18.8)	29.0 [16.6; NE]	33 / 118 (28.0)	15.2 [6.3; 23.4]	0.5208 [0.2959; 0.8963] 0.0190	
IHC >0 <1+	18 / 76 (23.7)	17.2 [17.2; NE]	17 / 76 (22.4)	16.5 [6.9; NE]	0.8514 [0.4363; 1.6682] 0.6361	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.7677
Yes	90 / 394 (22.8)	29.0 [17.2; NE]	89 / 389 (22.9)	16.5 [14.4; 23.4]	0.8778 [0.6522; 1.1818] 0.3900	
No	11 / 42 (26.2)	22.1 [14.4; NE]	12 / 41 (29.3)	15.8 [9.7; NE]	0.7251 [0.3125; 1.6651] 0.4431	
Prior Taxane Use In The Non-Metastatic Setting						0.5674
Yes	38 / 179 (21.2)	33.1 [17.2; NE]	36 / 177 (20.3)	18.0 [12.4; NE]	0.9760 [0.6123; 1.5564] 0.9165	
No	63 / 257 (24.5)	19.9 [15.9; NE]	65 / 253 (25.7)	15.2 [13.8; 23.4]	0.8056 [0.5674; 1.1426] 0.2258	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3255
1	16 / 65 (24.6)	NE [2.9; NE]	13 / 82 (15.9)	NE [13.9; NE]	1.5573 [0.7491; 3.2984] 0.2339	
2	64 / 295 (21.7)	22.1 [17.2; NE]	72 / 288 (25.0)	14.6 [13.8; NE]	0.7514 [0.5340; 1.0549] 0.0976	
>=3	20 / 75 (26.7)	33.1 [10.3; NE]	16 / 58 (27.6)	18.0 [11.1; NE]	0.8520 [0.4350; 1.6882] 0.6404	
ER/PR status I						0.6284
ER+, PR+	61 / 253 (24.1)	22.1 [15.9; NE]	56 / 237 (23.6)	15.8 [13.8; NE]	0.8886 [0.6163; 1.2832] 0.5243	
ER+, PR-	37 / 167 (22.2)	29.0 [16.6; NE]	42 / 181 (23.2)	16.5 [13.8; NE]	0.7596 [0.4816; 1.1920] 0.2284	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6998
ER <=10%	5 / 21 (23.8)	17.3 [4.9; NE]	2 / 14 (14.3)	23.4 [NE; NE]	3.1982 [0.5120; 61.4350] 0.2635	
ER >10%	78 / 364 (21.4)	29.0 [19.4; NE]	79 / 355 (22.3)	16.5 [14.4; NE]	0.8340 [0.6072; 1.1450] 0.2587	
Positive	18 / 51 (35.3)	9.7 [2.1; NE]	20 / 61 (32.8)	13.9 [6.2; NE]	1.0444 [0.5451; 1.9855] 0.8943	
Endocrine Resistance						0.1146
Primary	30 / 128 (23.4)	NE [17.2; NE]	24 / 140 (17.1)	NE [13.9; NE]	1.2870 [0.7531; 2.2230] 0.3579	
Secondary	71 / 308 (23.1)	22.1 [16.6; NE]	76 / 288 (26.4)	15.8 [13.8; 23.4]	0.7396 [0.5317; 1.0271] 0.0714	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.7145
Capecitabine	69 / 266 (25.9)	19.4 [12.4; NE]	73 / 257 (28.4)	13.9 [9.7; 18.0]	0.8242 [0.5910; 1.1481] 0.2508	
Nab-Paclitaxel	19 / 103 (18.4)	NE [22.1; NE]	20 / 105 (19.0)	23.4 [15.2; NE]	0.8761 [0.4602; 1.6599] 0.7105	
Paclitaxel	13 / 67 (19.4)	33.1 [13.9; NE]	8 / 68 (11.8)	NE [14.6; NE]	1.1393 [0.4597; 2.9610] 0.7784	
Prior anthracycline use						0.7777
Yes	42 / 199 (21.1)	33.1 [17.3; NE]	44 / 208 (21.2)	18.0 [14.4; NE]	0.8855 [0.5737; 1.3633] 0.5789	
No	59 / 237 (24.9)	19.9 [13.8; NE]	57 / 222 (25.7)	15.8 [13.8; 23.4]	0.8318 [0.5760; 1.2015] 0.3229	
Liver metastases						0.2325
Yes	67 / 296 (22.6)	29.0 [14.4; NE]	61 / 283 (21.6)	21.3 [13.8; NE]	0.9652 [0.6799; 1.3720] 0.8445	
No	34 / 140 (24.3)	NE [15.9; NE]	40 / 147 (27.2)	15.8 [13.8; NE]	0.7191 [0.4503; 1.1412] 0.1623	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.2848
0	59 / 252 (23.4)	29.0 [16.6; NE]	64 / 257 (24.9)	18.0 [13.8; NE]	0.7845 [0.5473; 1.1222] 0.1861	
>=1	42 / 179 (23.5)	22.1 [13.3; NE]	34 / 164 (20.7)	15.8 [14.4; NE]	1.0643 [0.6742; 1.6907] 0.7954	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Financial Difficulties						
Age at randomization						0.8161
<65 years of age	66 / 302 (21.9)	28.2 [18.6; NE]	70 / 297 (23.6)	15.1 [9.9; NE]	0.7682 [0.5464; 1.0789] 0.1244	
>=65 years of age	17 / 134 (12.7)	NE [NE; NE]	23 / 133 (17.3)	NE [17.2; NE]	0.7232 [0.3799; 1.3496] 0.3111	
Race						0.3197
Asian	42 / 154 (27.3)	NE [26.3; NE]	47 / 151 (31.1)	20.0 [9.6; NE]	0.7192 [0.4713; 1.0938] 0.1203	
White	33 / 231 (14.3)	28.2 [28.2; NE]	42 / 230 (18.3)	20.1 [15.1; NE]	0.7090 [0.4437; 1.1219] 0.1414	
Other	8 / 51 (15.7)	NE [2.1; NE]	4 / 49 (8.2)	NE [9.6; NE]	1.7469 [0.5463; 6.5797] 0.3617	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.9024
Asia	43 / 149 (28.9)	NE [15.9; NE]	46 / 147 (31.3)	20.0 [9.6; NE]	0.7507 [0.4924; 1.1420] 0.1765	
Europe	31 / 227 (13.7)	28.2 [28.2; NE]	35 / 213 (16.4)	NE [15.1; NE]	0.7510 [0.4599; 1.2203] 0.2436	
Rest of the World	9 / 60 (15.0)	NE [4.2; NE]	12 / 70 (17.1)	17.2 [7.5; NE]	0.9765 [0.3961; 2.3198] 0.9615	
HER2 IHC expression						0.3047
IHC 1+	42 / 239 (17.6)	NE [26.3; NE]	59 / 234 (25.2)	17.2 [10.4; NE]	0.6310 [0.4214; 0.9366] 0.0220	
IHC 2+/ISH-	20 / 117 (17.1)	NE [28.2; NE]	19 / 118 (16.1)	NE [20.1; NE]	0.9055 [0.4755; 1.7247] 0.7600	
IHC >0 <1+	21 / 76 (27.6)	18.6 [9.7; NE]	15 / 76 (19.7)	16.5 [7.5; NE]	1.1117 [0.5757; 2.2001] 0.7563	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5077
Yes	73 / 394 (18.5)	NE [26.3; NE]	79 / 389 (20.3)	20.7 [15.1; NE]	0.7965 [0.5777; 1.0968] 0.1606	
No	10 / 42 (23.8)	28.2 [14.6; NE]	14 / 41 (34.1)	20.1 [3.5; NE]	0.6045 [0.2507; 1.3844] 0.2371	
Prior Taxane Use In The Non-Metastatic Setting						0.1472
Yes	27 / 179 (15.1)	NE [NE; NE]	42 / 177 (23.7)	20.1 [9.6; NE]	0.5775 [0.3504; 0.9359] 0.0259	
No	56 / 257 (21.8)	28.2 [16.7; NE]	51 / 253 (20.2)	NE [16.5; NE]	0.9146 [0.6246; 1.3427] 0.6448	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1958
1	11 / 65 (16.9)	NE [6.3; NE]	17 / 82 (20.7)	20.0 [7.5; NE]	0.6788 [0.3080; 1.4352] 0.3108	
2	53 / 295 (18.0)	28.2 [26.3; NE]	66 / 288 (22.9)	20.1 [10.4; NE]	0.6903 [0.4777; 0.9928] 0.0449	
>=3	19 / 75 (25.3)	NE [10.3; NE]	10 / 58 (17.2)	NE [12.5; NE]	1.5033 [0.7135; 3.3681] 0.2921	
ER/PR status I						0.1222
ER+, PR+	51 / 253 (20.2)	NE [NE; NE]	46 / 237 (19.4)	20.7 [15.1; NE]	0.9153 [0.6140; 1.3689] 0.6632	
ER+, PR-	30 / 167 (18.0)	28.2 [26.3; NE]	45 / 181 (24.9)	16.5 [9.0; NE]	0.5536 [0.3403; 0.8859] 0.0136	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7897
ER <=10%	4 / 21 (19.0)	NE [4.9; NE]	2 / 14 (14.3)	NE [4.8; NE]	0.7791 [0.1493; 5.6919] 0.7750	
ER >10%	68 / 364 (18.7)	NE [26.3; NE]	79 / 355 (22.3)	17.2 [12.5; NE]	0.7347 [0.5283; 1.0186] 0.0632	
Positive	11 / 51 (21.6)	NE [13.1; NE]	12 / 61 (19.7)	NE [20.0; NE]	0.9857 [0.4263; 2.2566] 0.9666	
Endocrine Resistance						0.6660
Primary	26 / 128 (20.3)	NE [13.1; NE]	34 / 140 (24.3)	20.0 [7.5; NE]	0.7065 [0.4193; 1.1767] 0.1814	
Secondary	57 / 308 (18.5)	NE [26.3; NE]	58 / 288 (20.1)	NE [16.5; NE]	0.8227 [0.5686; 1.1897] 0.2953	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.5226
Capecitabine	44 / 266 (16.5)	NE [26.3; NE]	58 / 257 (22.6)	20.1 [10.4; NE]	0.6452 [0.4331; 0.9552] 0.0278	
Nab-Paclitaxel	22 / 103 (21.4)	NE [12.4; NE]	22 / 105 (21.0)	NE [15.1; NE]	0.9932 [0.5469; 1.8036] 0.9813	
Paclitaxel	17 / 67 (25.4)	18.6 [6.3; NE]	13 / 68 (19.1)	14.6 [5.6; NE]	0.8759 [0.4192; 1.8632] 0.7179	
Prior anthracycline use						0.3581
Yes	31 / 199 (15.6)	NE [26.3; NE]	44 / 208 (21.2)	20.1 [10.4; NE]	0.6396 [0.3989; 1.0132] 0.0569	
No	52 / 237 (21.9)	NE [18.6; NE]	49 / 222 (22.1)	20.0 [14.6; NE]	0.8747 [0.5906; 1.2972] 0.4992	
Liver metastases						0.6735
Yes	55 / 296 (18.6)	NE [NE; NE]	59 / 283 (20.8)	20.1 [14.6; NE]	0.8179 [0.5643; 1.1836] 0.2813	
No	28 / 140 (20.0)	28.2 [26.3; NE]	34 / 147 (23.1)	NE [10.4; NE]	0.7002 [0.4207; 1.1560] 0.1616	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:58; Program name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.sas; Output name: T.2.11.2_EORTC_C30_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.2 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0453
0	39 / 252 (15.5)	NE [28.2; NE]	57 / 257 (22.2)	20.1 [16.5; NE]	0.5567 [0.3657; 0.8381] 0.0048	
>=1	43 / 179 (24.0)	NE [12.4; NE]	36 / 164 (22.0)	NE [9.6; NE]	1.0872 [0.6986; 1.7024] 0.7146	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Tabelle 2.11.3 EORTC-QLQ-C30 – Zeit bis zur bestätigten Verschlechterung – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.11.3 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Role Functioning						
ER/PR status I						0.0214
ER+, PR+	81 / 253 (32.0)	11.9 [7.7; NE]	101 / 237 (42.6)	4.2 [2.8; 6.9]	0.6085 [0.4514; 0.8175] 0.0009	
ER+, PR-	70 / 167 (41.9)	6.2 [3.5; 13.9]	65 / 181 (35.9)	7.7 [4.2; 12.4]	1.0161 [0.7224; 1.4308] 0.9371	
ECOG						0.0130
0	77 / 252 (30.6)	15.2 [9.8; NE]	108 / 257 (42.0)	5.6 [3.0; 7.7]	0.5859 [0.4343; 0.7860] 0.0003	
>=1	74 / 179 (41.3)	6.9 [2.2; 9.9]	63 / 164 (38.4)	4.8 [3.4; 6.9]	0.9924 [0.7072; 1.3962] 0.9428	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.3 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Cognitive Functioning						
Race						0.0462
Asian	59 / 154 (38.3)	23.5 [11.1; NE]	70 / 151 (46.4)	8.9 [4.9; 14.6]	0.6415 [0.4494; 0.9117] 0.0129	
White	73 / 231 (31.6)	8.3 [6.2; 11.7]	66 / 230 (28.7)	11.0 [7.6; 18.0]	1.1632 [0.8334; 1.6266] 0.3751	
Other	13 / 51 (25.5)	12.4 [2.8; NE]	7 / 49 (14.3)	13.2 [2.1; NE]	1.2539 [0.5086; 3.3617] 0.6321	
Region						0.0369
Asia	58 / 149 (38.9)	15.8 [11.1; NE]	67 / 147 (45.6)	9.6 [4.9; 14.6]	0.6643 [0.4632; 0.9490] 0.0239	
Europe	67 / 227 (29.5)	10.3 [7.4; 12.4]	59 / 213 (27.7)	10.3 [5.5; 22.0]	1.0110 [0.7118; 1.4399] 0.9462	
Rest of the World	20 / 60 (33.3)	6.2 [1.1; 21.5]	17 / 70 (24.3)	11.0 [7.1; NE]	1.4759 [0.7549; 2.8969] 0.2504	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.3 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Dyspnoea						
Prior anthracycline use						0.0445
Yes	43 / 199 (21.6)	20.0 [15.9; NE]	63 / 208 (30.3)	12.0 [4.9; NE]	0.5854 [0.3938; 0.8620] 0.0066	
No	55 / 237 (23.2)	19.4 [17.3; NE]	44 / 222 (19.8)	NE [15.9; NE]	1.0217 [0.6872; 1.5276] 0.9218	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.3 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Insomnia						
Prior Taxane Use In The Non-Metastatic Setting						0.0318
Yes	34 / 179 (19.0)	NE [17.3; NE]	51 / 177 (28.8)	13.8 [6.3; 16.8]	0.5130 [0.3273; 0.7939] 0.0025	
No	62 / 257 (24.1)	NE [12.4; NE]	57 / 253 (22.5)	21.3 [13.8; NE]	0.9820 [0.6852; 1.4100] 0.9167	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.3 EORTC QLQ-C30 - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Financial Difficulties						
ECOG						0.0453
0	39 / 252 (15.5)	NE [28.2; NE]	57 / 257 (22.2)	20.1 [16.5; NE]	0.5567 [0.3657; 0.8381] 0.0048	
>=1	43 / 179 (24.0)	NE [12.4; NE]	36 / 164 (22.0)	NE [9.6; NE]	1.0872 [0.6986; 1.7024] 0.7146	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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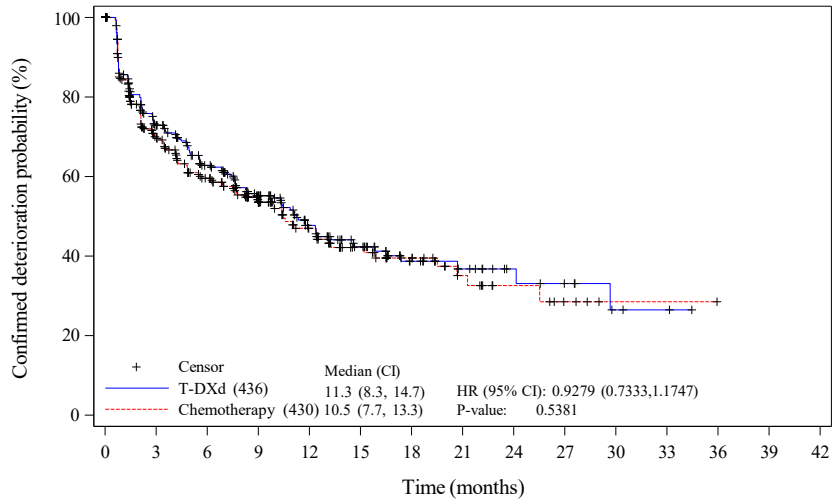
Abbildung 2.11.1 EORTC-QLQ-C30 – Zeit bis zur bestätigten Verschlechterung – Kaplan-Meier-Plot – FAS

Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Global Health Status



Patients still at risk:

T-DXd(436)	436	193	145	104	68	46	26	17	10	7	3	2	0
Chemotherapy (430)	430	170	122	84	51	33	23	14	8	4	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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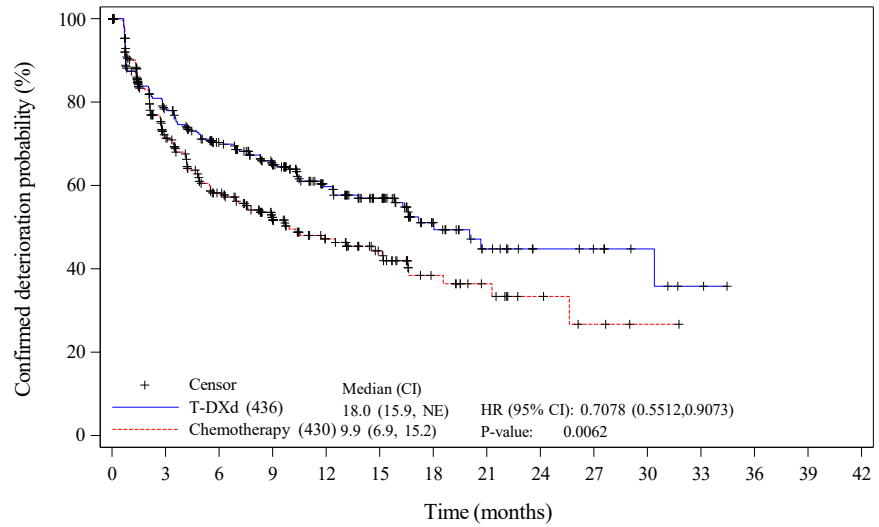
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Physical Functioning



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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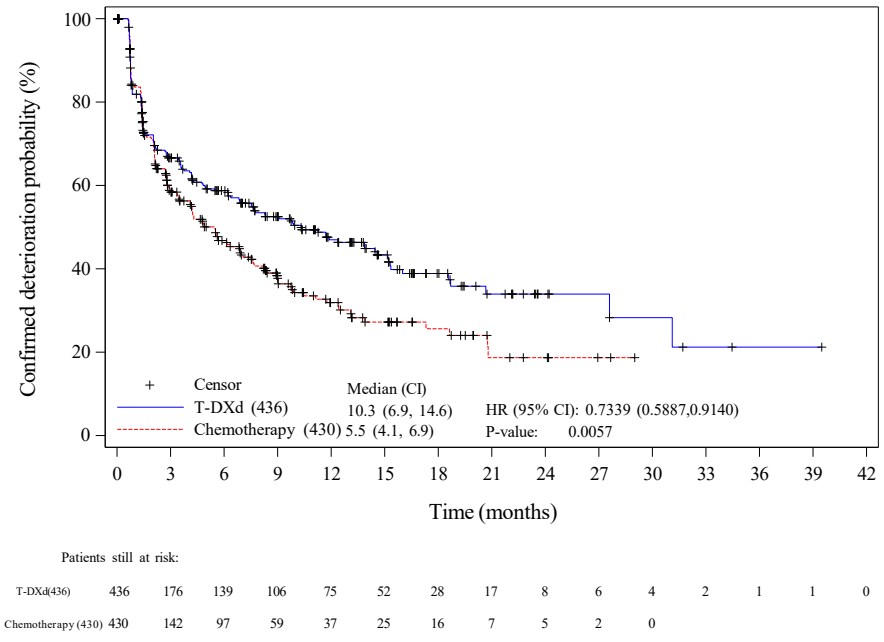
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Role Functioning



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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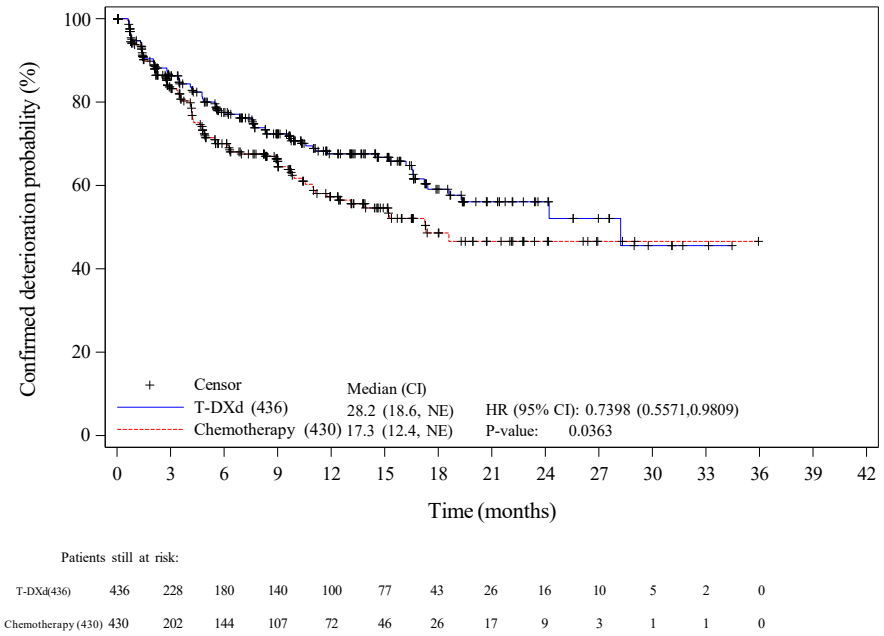
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Emotional Functioning



Patients still at risk:

T-DXd(436)	436	228	180	140	100	77	43	26	16	10	5	2	0
Chemotherapy (430)	430	202	144	107	72	46	26	17	9	3	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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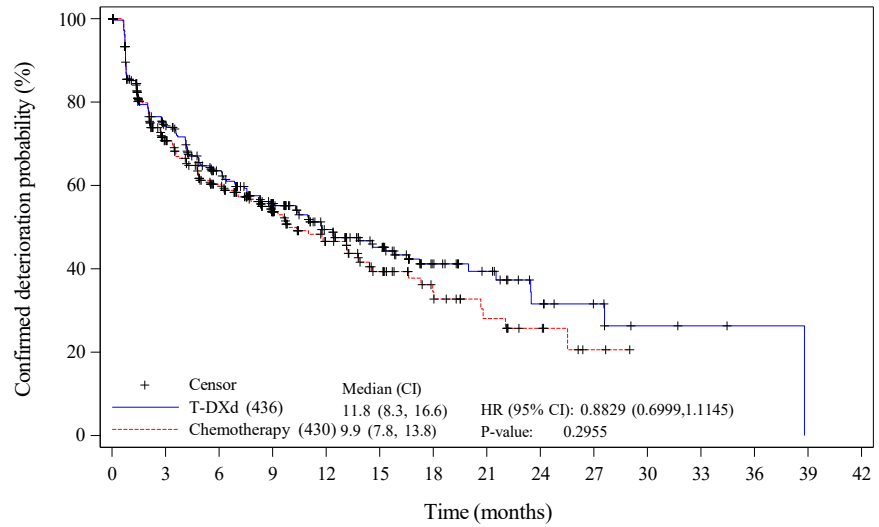
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Cognitive Functioning



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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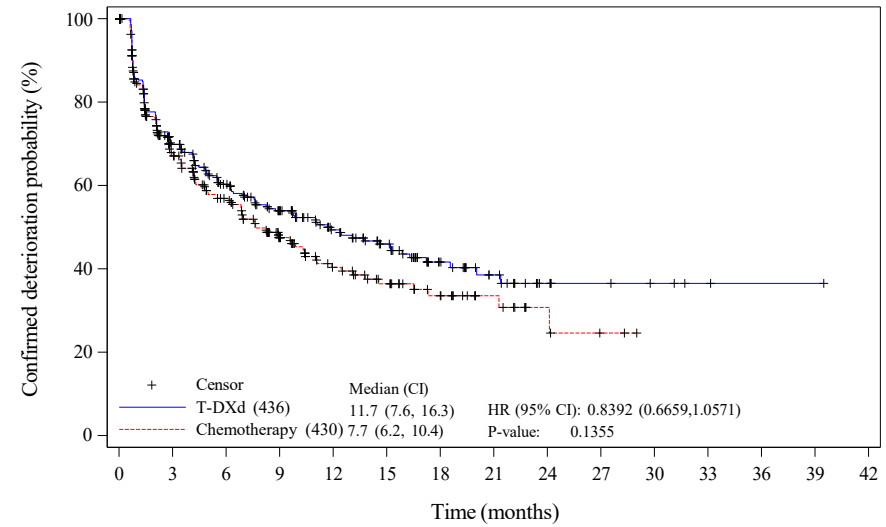
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Social Functioning



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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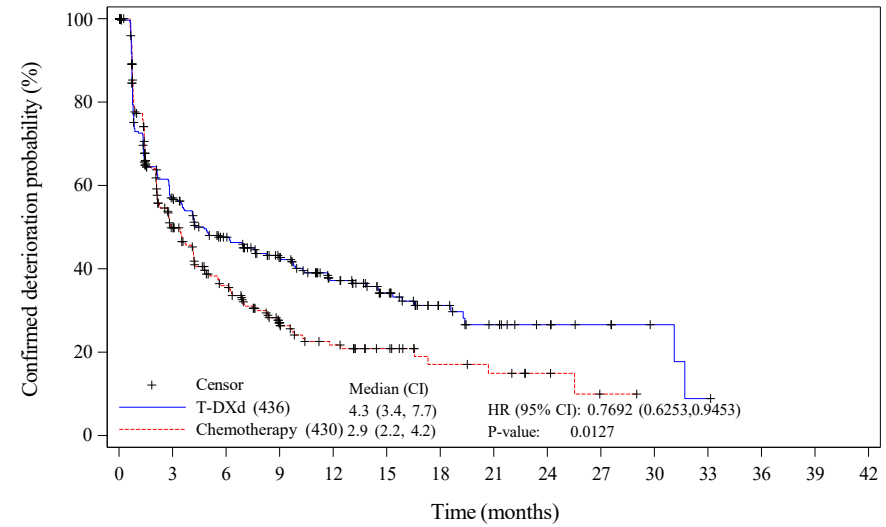
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Fatigue



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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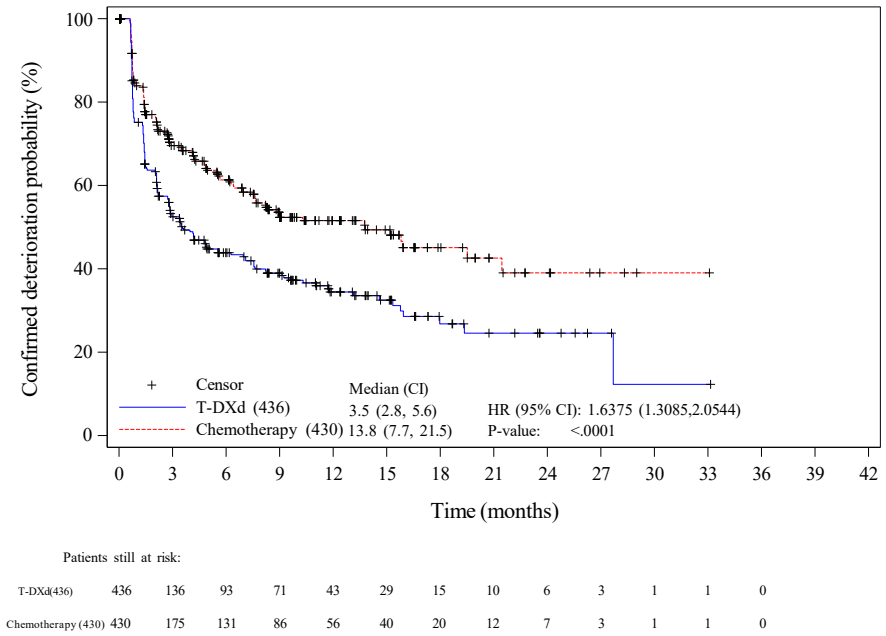
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Nausea and Vomiting



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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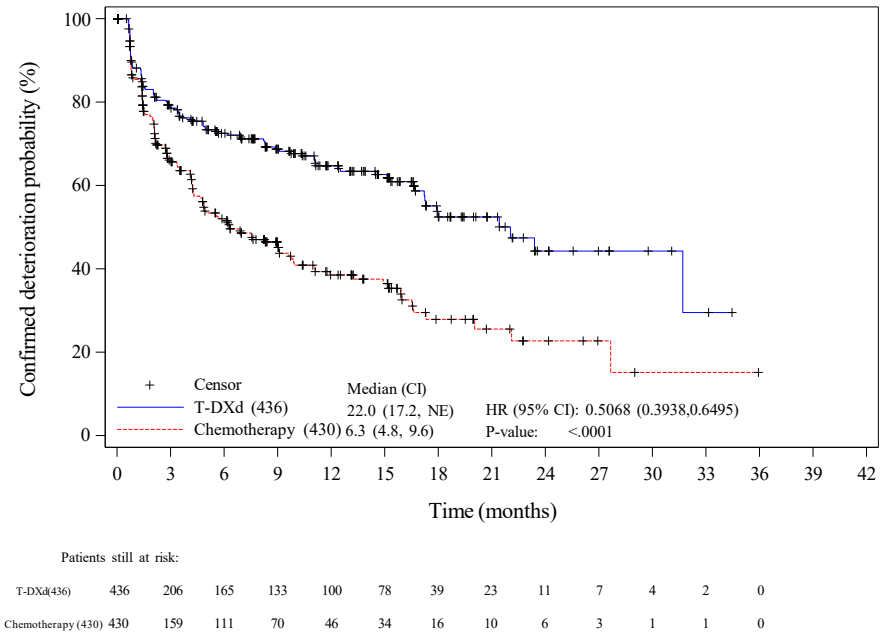
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Pain



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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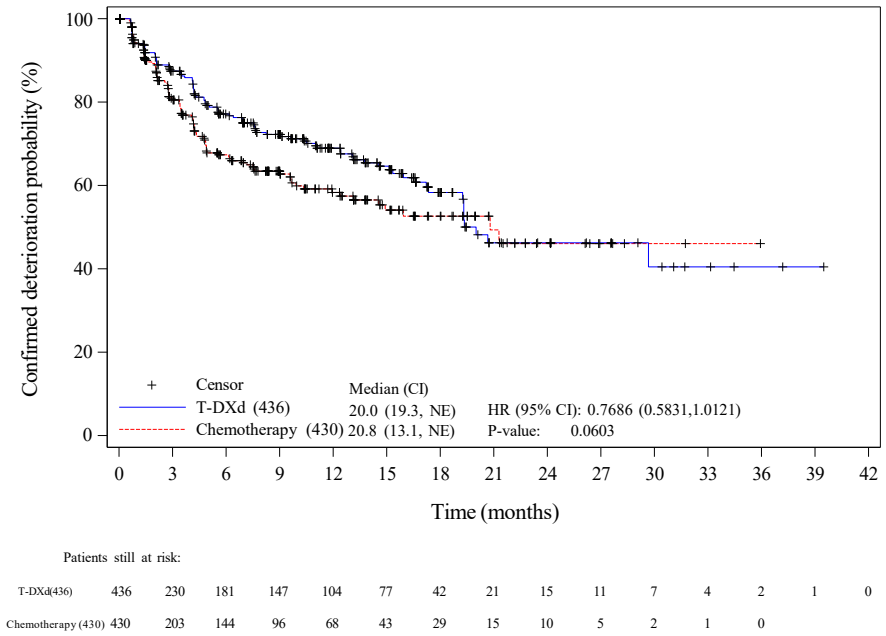
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Dyspnoea



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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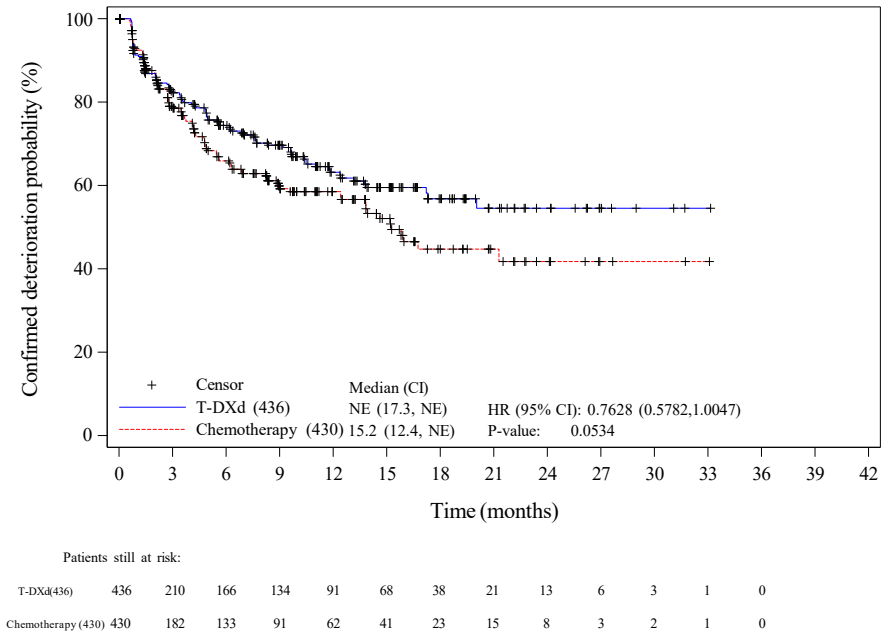
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Insomnia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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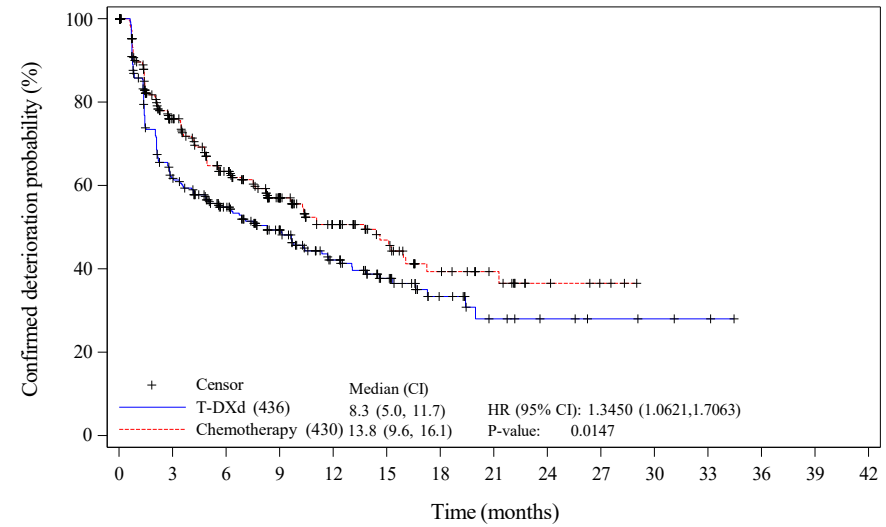
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Appetite Loss



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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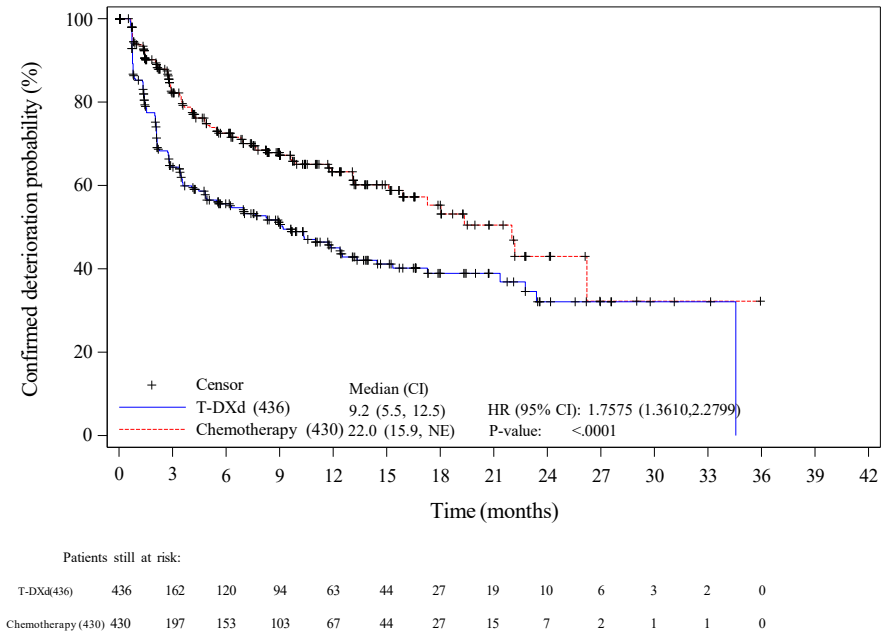
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Constipation



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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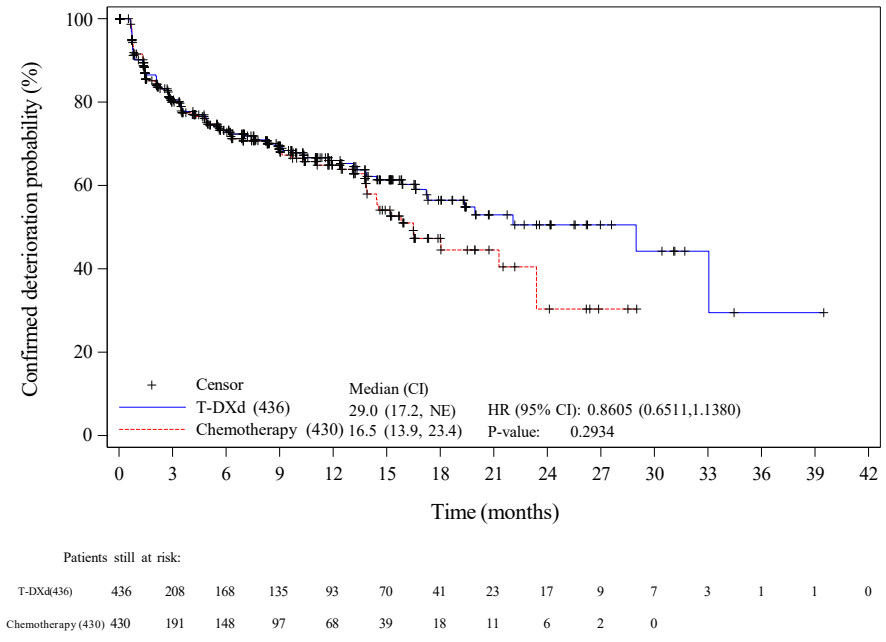
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Diarrhea



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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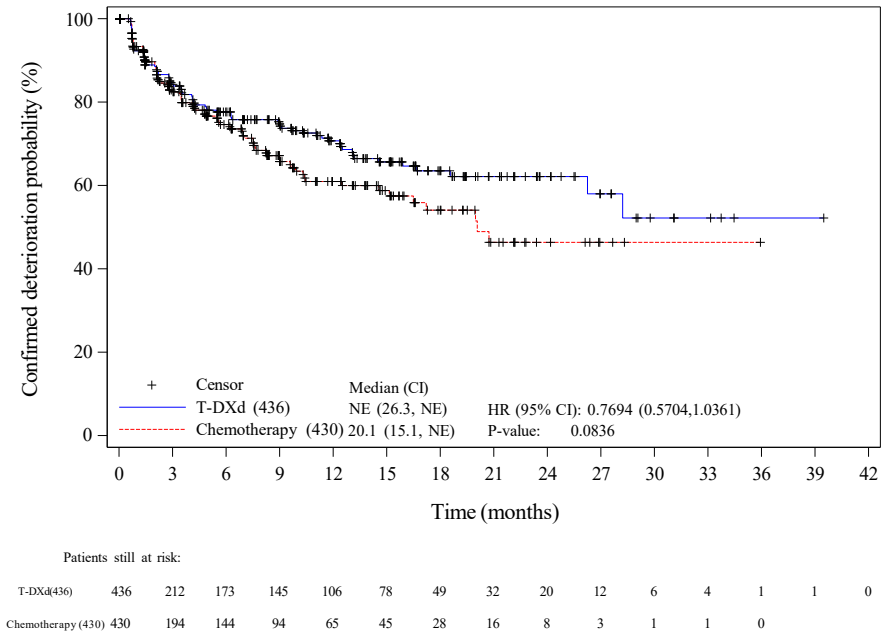
Figure 2.11.1 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Financial Difficulties



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Abbildung 2.11.2 EORTC-QLQ-C30 – Zeit bis zur bestätigten Verschlechterung – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

Daiichi Sankyo Europe GmbH
Data Intelligence – Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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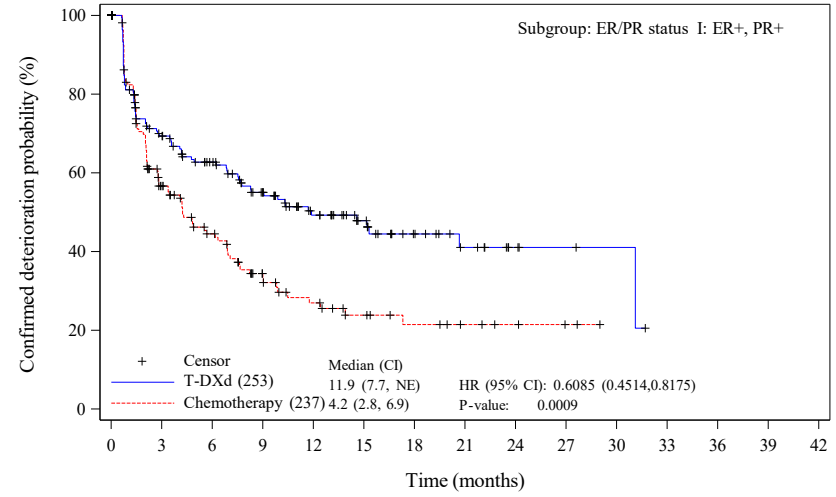
Final
Statistical analyses for AMNOG (HTA Germany)

Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Role Functioning



Patients still at risk:

T-DXd(253)	253	109	87	65	45	31	18	11	5	3	2	0
Chemotherapy (237)	237	76	51	30	20	13	9	6	4	2	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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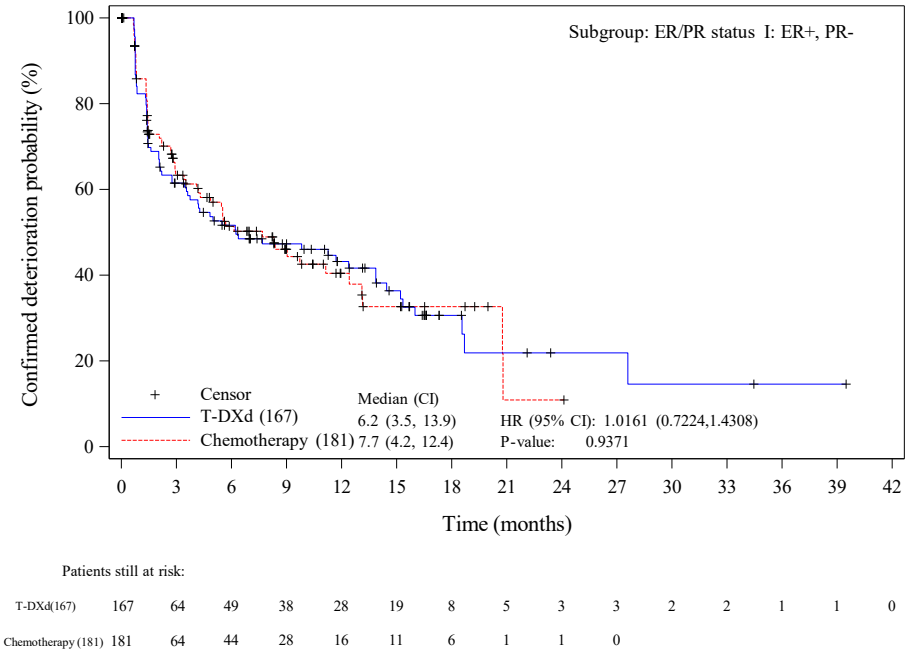
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Role Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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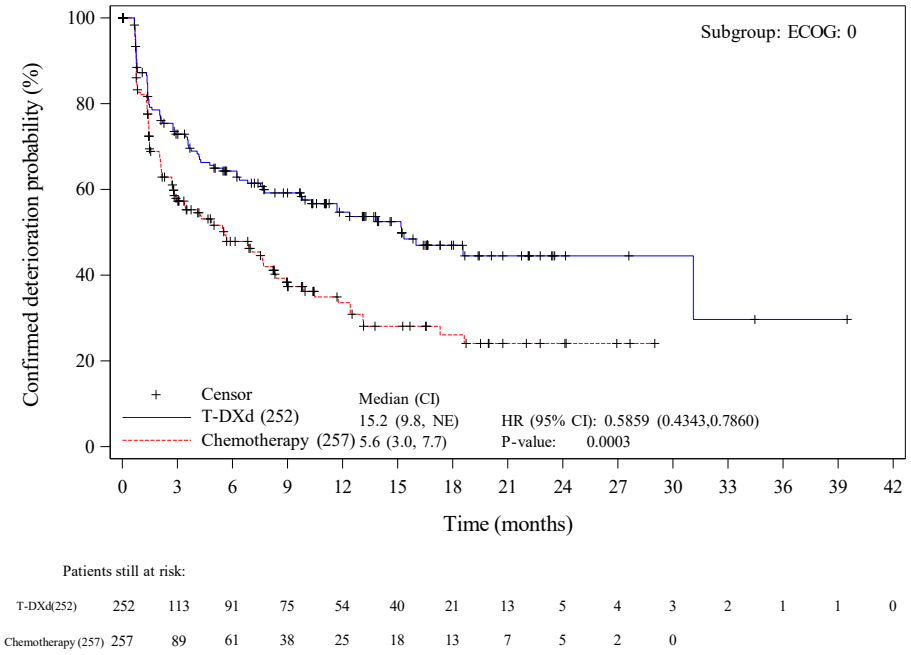
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Role Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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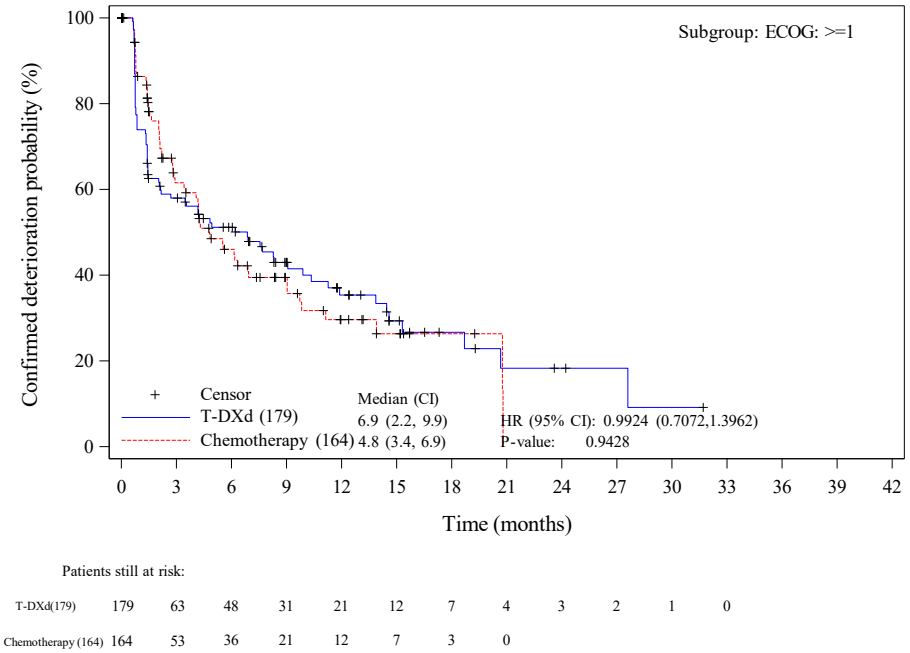
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Role Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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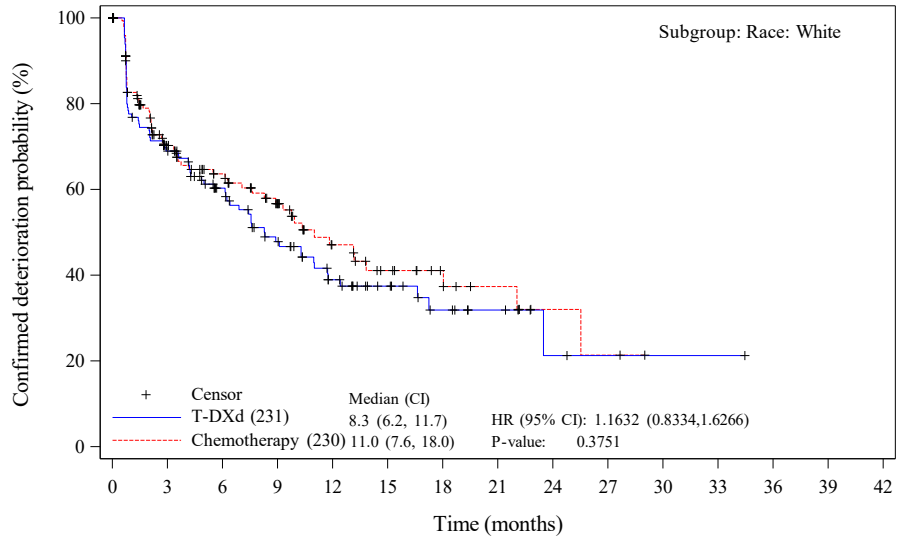
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Cognitive Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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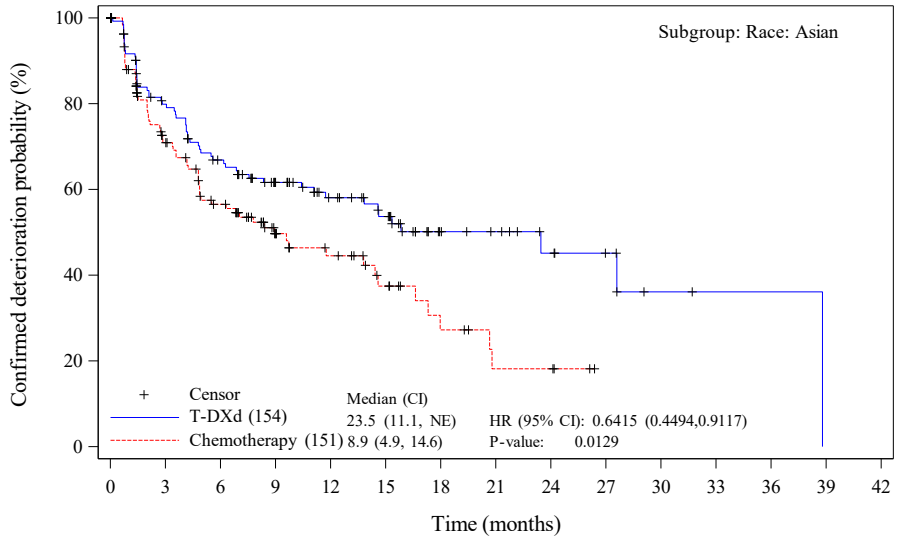
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Cognitive Functioning



Patients still at risk:

T-DXd(154)	154	99	79	60	45	36	17	14	9	6	2	1	1	0
Chemotherapy (151)	151	83	59	33	24	15	8	4	4	0				

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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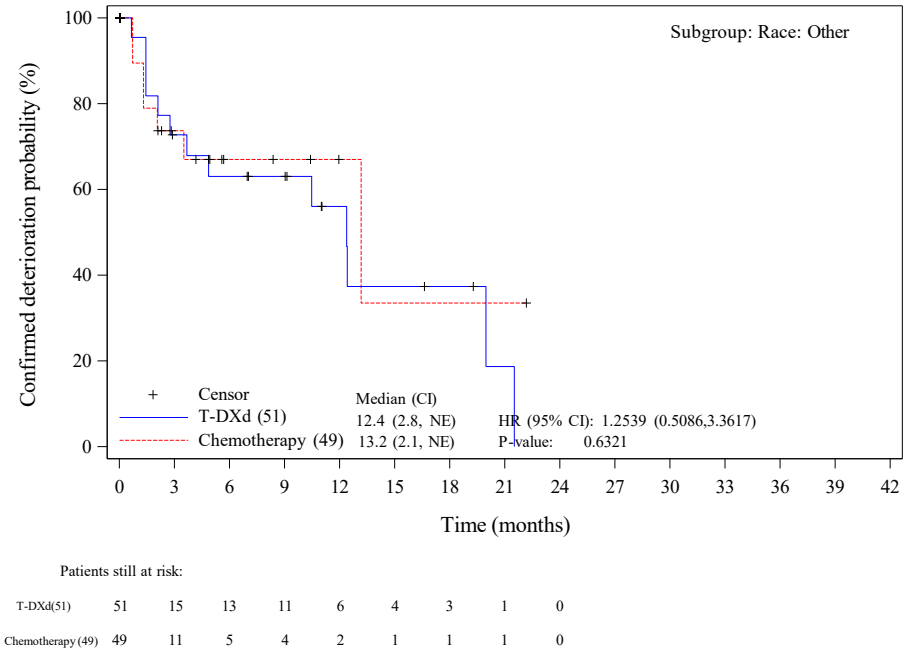
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Cognitive Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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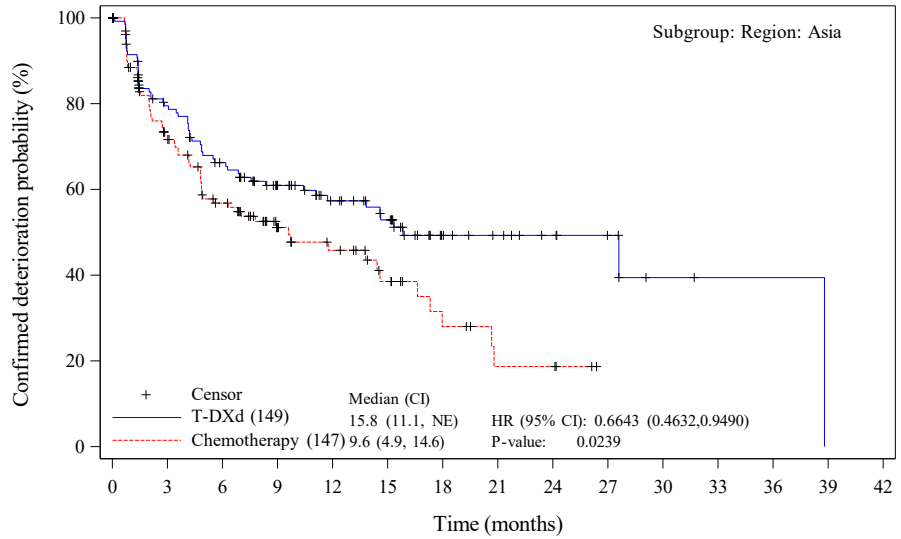
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Cognitive Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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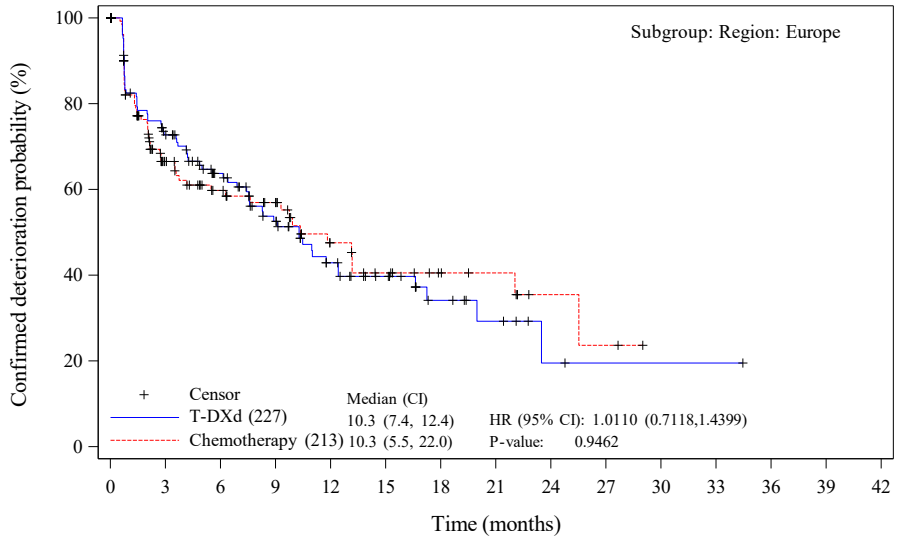
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Cognitive Functioning



Patients still at risk:

T-DXd(227)	227	87	62	44	28	19	10	6	2	1	1	1	0
Chemotherapy (213)	213	63	46	36	21	15	10	8	3	2	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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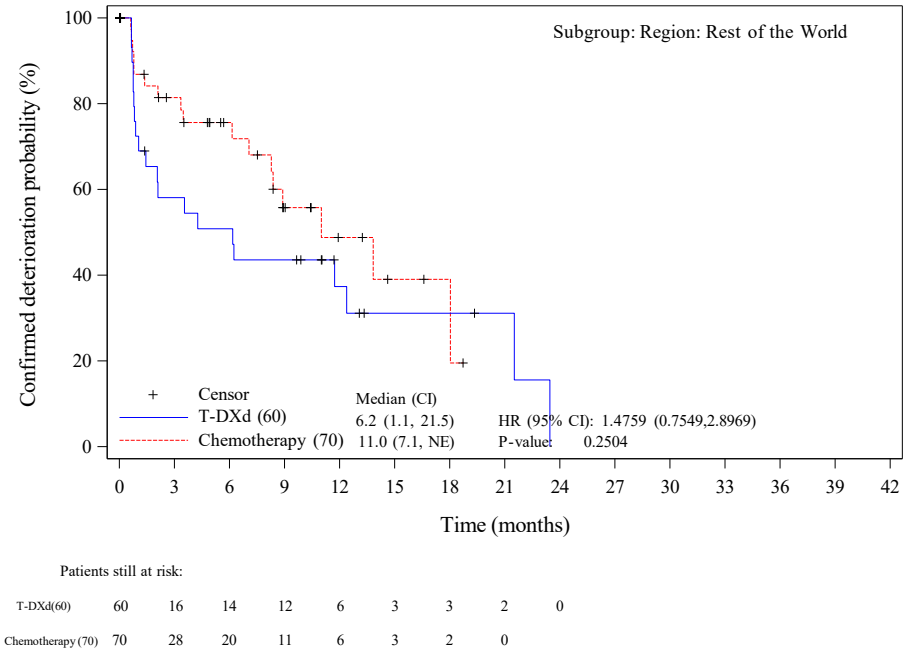
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Cognitive Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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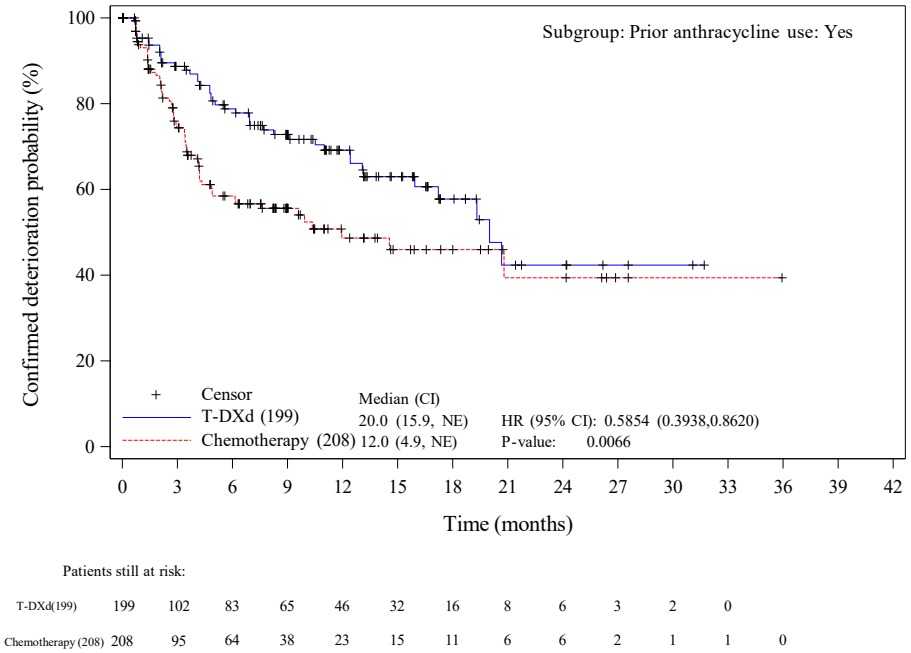
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Dyspnoea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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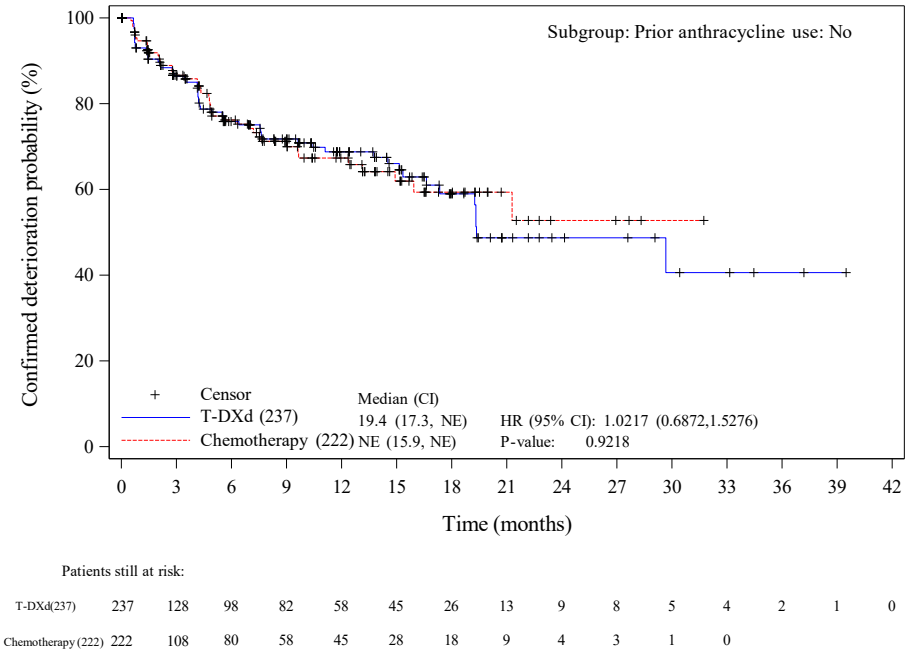
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Dyspnoea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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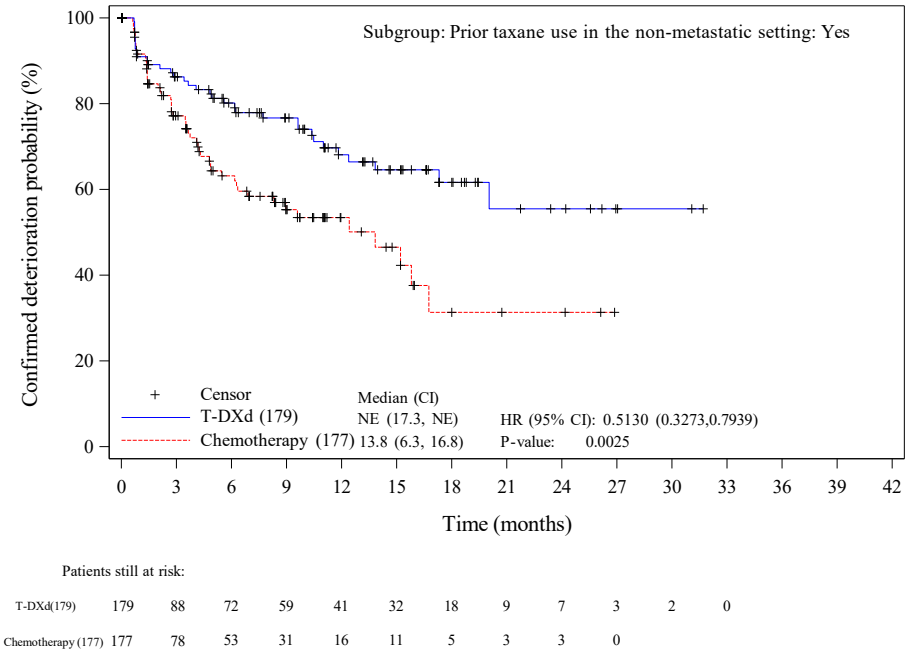
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Insomnia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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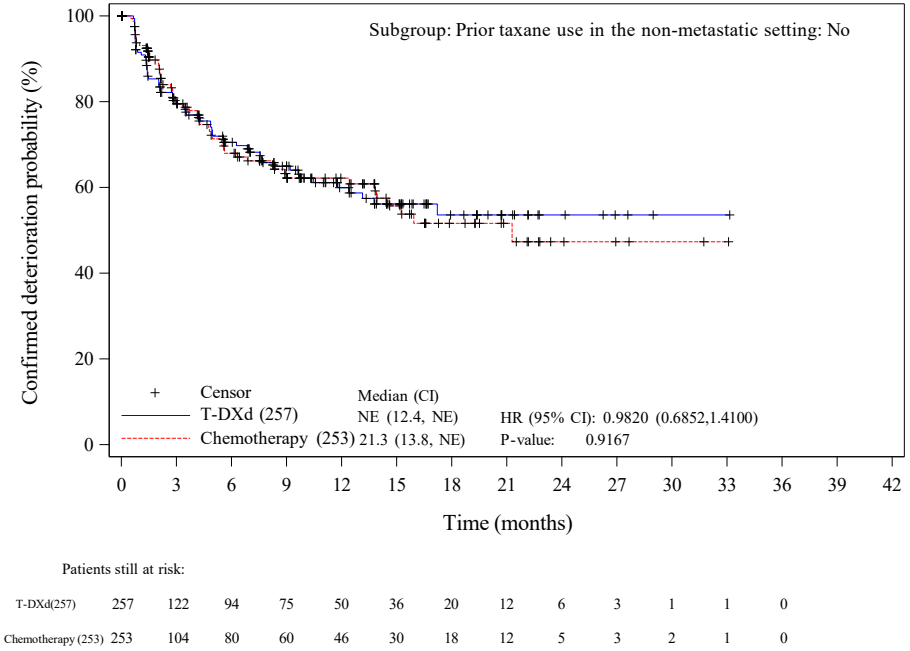
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Insomnia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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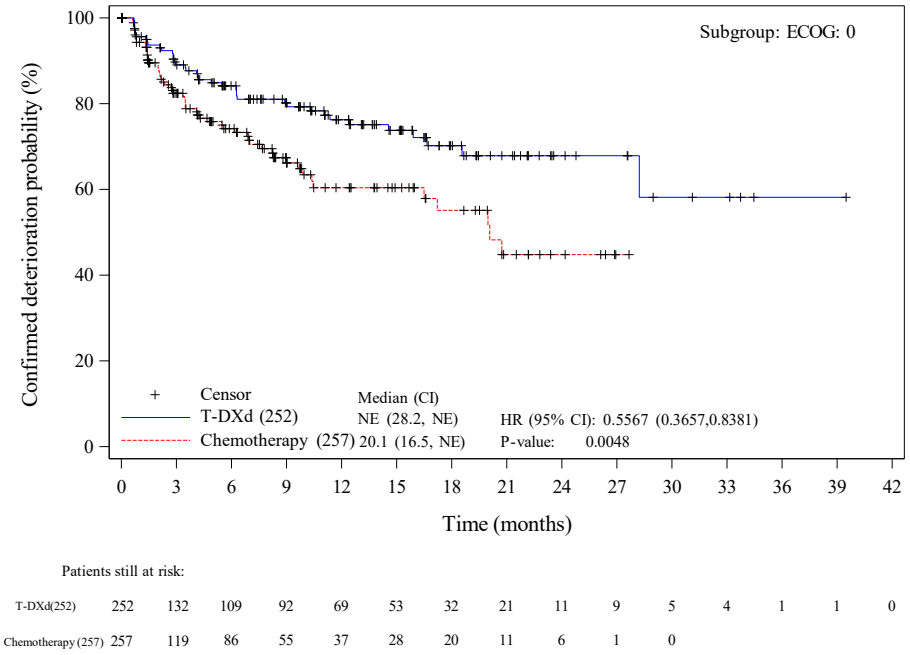
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Financial Difficulties



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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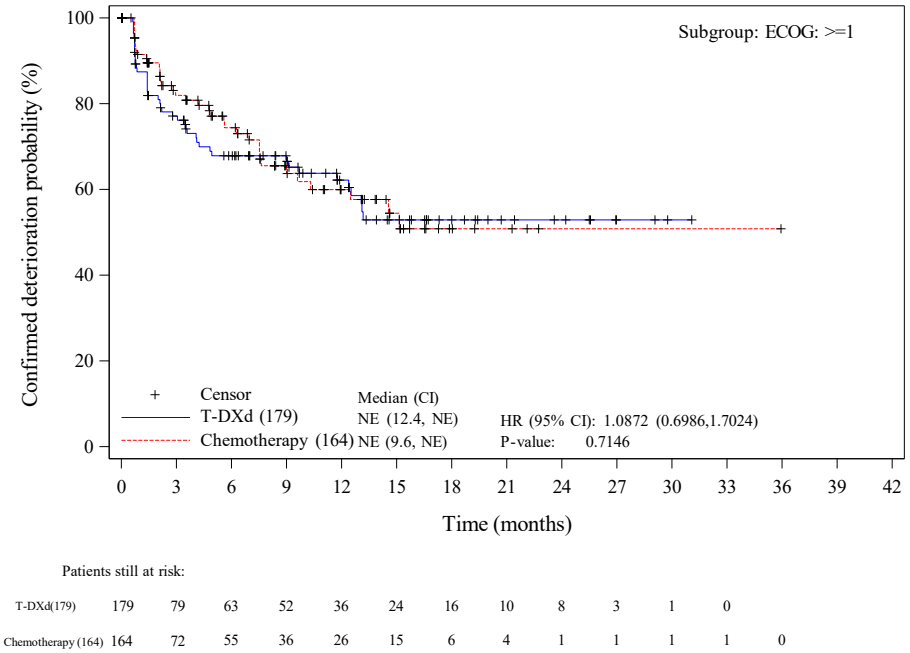
Figure 2.11.2 EORTC-QLQ-C30 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Financial Difficulties



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Tabelle 2.11.4 EORTC-QLQ-C30 – Zeit bis zur bestätigten Verschlechterung – Sensitivitätsanalyse – FAS

Table 2.11.4 EORTC-QLQ-C30 - Time to confirmed deterioration - Sensitivity analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Global Health Status	119 (27.3)	15.9 [11.1; NE]	113 (26.3)	15.9 [10.4; NE]	0.9543 [0.7372; 1.2361] 0.7222	0.7296
Functional Scales/Physical Functioning	99 (22.7)	30.4 [17.2; NE]	115 (26.7)	16.6 [9.7; NE]	0.7311 [0.5571; 0.9577] 0.0232	0.0226
Functional Scales/Role Functioning	136 (31.2)	13.9 [8.3; 18.6]	153 (35.6)	6.2 [4.2; 9.0]	0.7642 [0.6051; 0.9642] 0.0235	0.0231
Functional Scales/Emotional Functioning	77 (17.7)	NE [28.2; NE]	80 (18.6)	NE [18.6; NE]	0.8278 [0.6041; 1.1334] 0.2380	0.2393
Functional Scales/Cognitive Functioning	129 (29.6)	14.6 [11.0; 23.5]	125 (29.1)	13.2 [9.8; 18.0]	0.9060 [0.7074; 1.1612] 0.4346	0.4376
Functional Scales/Social Functioning	126 (28.9)	15.9 [9.8; NE]	128 (29.8)	9.9 [7.0; 16.5]	0.8750 [0.6835; 1.1206] 0.2890	0.2893
Symptom Scales/Fatigue	155 (35.6)	6.9 [4.1; 10.4]	175 (40.7)	3.6 [2.8; 5.1]	0.7907 [0.6354; 0.9837] 0.0350	0.0344
Symptom Scales/Nausea and Vomiting	166 (38.1)	4.2 [2.9; 7.1]	105 (24.4)	21.5 [15.2; NE]	1.9101 [1.4986; 2.4455] <.0001	<.0001
Symptom Scales/Pain	90 (20.6)	NE [22.0; NE]	134 (31.2)	9.1 [5.7; 15.9]	0.5288 [0.4027; 0.6911] <.0001	<.0001

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

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Table 2.11.4 EORTC-QLQ-C30 - Time to confirmed deterioration - Sensitivity analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Dyspnoea	86 (19.7)	29.7 [19.3; NE]	80 (18.6)	NE [20.8; NE]	0.9052 [0.6669; 1.2309] 0.5235	0.5242
Common Symptoms/Insomnia	84 (19.3)	NE [20.0; NE]	87 (20.2)	NE [15.2; NE]	0.8417 [0.6225; 1.1373] 0.2614	0.2601
Common Symptoms/Appetite Loss	138 (31.7)	9.7 [6.4; 14.6]	100 (23.3)	16.1 [11.1; NE]	1.5232 [1.1791; 1.9747] 0.0014	0.0014
Common Symptoms/Constipation	137 (31.4)	10.4 [6.3; 21.4]	77 (17.9)	26.2 [19.4; NE]	2.0451 [1.5514; 2.7158] <.0001	<.0001
Common Symptoms/Diarrhea	92 (21.1)	33.1 [19.9; NE]	78 (18.1)	NE [23.4; NE]	1.0603 [0.7830; 1.4393] 0.7058	0.7067
Common Symptoms/Financial Difficulties	74 (17.0)	NE [28.2; NE]	75 (17.4)	NE [20.1; NE]	0.8694 [0.6291; 1.2019] 0.3956	0.3950

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

Tabelle 2.11.9 EORTC-QLQ-C30 – Zeit bis zur erstmaligen Verschlechterung – FAS

Table 2.11.9 EORTC-QLQ-C30 - Time to first deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Global Health Status	189 (43.3)	4.2 [2.9; 5.6]	180 (41.9)	3.5 [2.3; 4.8]	0.9940 [0.8082; 1.2231] 0.9548	0.9579
Functional Scales/Physical Functioning	157 (36.0)	7.7 [4.9; 11.9]	171 (39.8)	4.8 [2.9; 6.9]	0.8188 [0.6586; 1.0181] 0.0717	0.0724
Functional Scales/Role Functioning	196 (45.0)	3.4 [2.1; 4.3]	204 (47.4)	2.1 [2.0; 2.8]	0.8431 [0.6907; 1.0290] 0.0932	0.0939
Functional Scales/Emotional Functioning	145 (33.3)	10.7 [8.3; 13.9]	159 (37.0)	8.3 [5.6; 9.9]	0.7924 [0.6304; 0.9951] 0.0454	0.0469
Functional Scales/Cognitive Functioning	205 (47.0)	3.5 [2.8; 4.8]	191 (44.4)	3.5 [2.8; 4.9]	0.9931 [0.8148; 1.2109] 0.9449	0.9502
Functional Scales/Social Functioning	198 (45.4)	3.5 [2.2; 4.3]	198 (46.0)	2.8 [2.1; 3.5]	0.8752 [0.7172; 1.0683] 0.1892	0.1924
Symptom Scales/Fatigue	221 (50.7)	1.4 [1.4; 2.8]	231 (53.7)	1.5 [1.4; 2.1]	0.8853 [0.7333; 1.0685] 0.2042	0.2093
Symptom Scales/Nausea and Vomiting	225 (51.6)	1.6 [1.4; 2.1]	185 (43.0)	3.6 [2.8; 5.5]	1.5312 [1.2607; 1.8620] <.0001	<.0001

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP*. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test*.
*: The following parameters were analysed using a stratified Cox proportional hazards model (hazard ratio) and a stratified log-rank test (two-sided p-value): Functional Scales/Emotional Functioning, Functional Scales/Role Functioning, Functional Scales/Social Functioning, Global Health Status, Symptom Scales/Fatigue. Otherwise unstratified analyses have been conducted.
CI: confidence interval; HR: hazard ratio; NE: not estimable.

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Table 2.11.9 EORTC-QLQ-C30 - Time to first deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Pain	158 (36.2)	7.6 [4.9; 11.0]	186 (43.3)	3.0 [2.1; 4.2]	0.6826 [0.5509; 0.8449] 0.0005	0.0005
Common Symptoms/Dyspnoea	151 (34.6)	9.7 [6.4; 15.2]	148 (34.4)	7.0 [4.8; 13.2]	0.9213 [0.7337; 1.1571] 0.4799	0.4803
Common Symptoms/Insomnia	148 (33.9)	8.9 [6.2; 13.8]	153 (35.6)	5.5 [4.1; 7.5]	0.8317 [0.6623; 1.0441] 0.1121	0.1124
Common Symptoms/Appetite Loss	201 (46.1)	2.2 [2.1; 2.9]	179 (41.6)	4.8 [3.5; 5.6]	1.2989 [1.0620; 1.5898] 0.0110	0.0120
Common Symptoms/Constipation	194 (44.5)	3.5 [2.7; 4.8]	154 (35.8)	6.9 [4.8; 10.3]	1.4300 [1.1570; 1.7688] 0.0009	0.0010
Common Symptoms/Diarrhea	172 (39.4)	6.2 [4.8; 8.4]	174 (40.5)	4.9 [3.5; 7.0]	0.8654 [0.6999; 1.0705] 0.1818	0.1845
Common Symptoms/Financial Difficulties	123 (28.2)	15.2 [11.0; NE]	132 (30.7)	9.6 [7.5; 14.6]	0.8059 [0.6290; 1.0319] 0.0872	0.0868

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP*. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test*.
*: The following parameters were analysed using a stratified Cox proportional hazards model (hazard ratio) and a stratified log-rank test (two-sided p-value): Functional Scales/Emotional Functioning, Functional Scales/Role Functioning, Functional Scales/Social Functioning, Global Health Status, Symptom Scales/Fatigue. Otherwise unstratified analyses have been conducted.
CI: confidence interval; HR: hazard ratio; NE: not estimable.

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Tabelle 2.11.10 EORTC-QLQ-C30 – Zeit bis zur erstmaligen Verschlechterung – Subgruppenanalyse – FAS

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Global Health Status						
Age at randomization						0.2420
<65 years of age	130 / 302 (43.0)	4.8 [2.8; 6.2]	116 / 297 (39.1)	4.8 [3.1; 7.6]	1.0388 [0.8084; 1.3364] 0.7676	
>=65 years of age	59 / 134 (44.0)	3.5 [2.2; 5.6]	64 / 133 (48.1)	2.1 [1.5; 2.8]	0.7816 [0.5461; 1.1164] 0.1766	
Race						0.2282
Asian	89 / 154 (57.8)	3.5 [2.2; 5.3]	80 / 151 (53.0)	3.4 [2.1; 5.6]	0.9982 [0.7369; 1.3540] 0.9979	
White	88 / 231 (38.1)	4.2 [2.2; 5.6]	86 / 230 (37.4)	3.5 [2.2; 6.2]	1.0409 [0.7720; 1.4043] 0.7932	
Other	12 / 51 (23.5)	10.3 [2.1; NE]	14 / 49 (28.6)	2.9 [1.5; 8.3]	0.4182 [0.1806; 0.9420] 0.0308	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.3776
Asia	87 / 149 (58.4)	3.5 [2.2; 4.9]	78 / 147 (53.1)	3.4 [2.1; 6.9]	1.0137 [0.7465; 1.3790] 0.9207	
Europe	85 / 227 (37.4)	4.8 [2.8; 5.6]	77 / 213 (36.2)	3.5 [2.3; 5.7]	1.0023 [0.7347; 1.3696] 0.9893	
Rest of the World	17 / 60 (28.3)	9.6 [1.4; NE]	25 / 70 (35.7)	2.7 [1.5; 7.7]	0.6532 [0.3394; 1.2210] 0.1857	
HER2 IHC expression						0.0771
IHC 1+	101 / 239 (42.3)	3.5 [2.2; 5.3]	106 / 234 (45.3)	2.9 [2.1; 4.2]	0.8915 [0.6775; 1.1725] 0.4133	
IHC 2+/ISH-	53 / 117 (45.3)	3.5 [1.5; 5.6]	41 / 118 (34.7)	7.8 [3.4; 21.3]	1.4661 [0.9743; 2.2236] 0.0674	
IHC >0 <1+	34 / 76 (44.7)	6.2 [3.5; 9.1]	32 / 76 (42.1)	2.7 [1.4; 6.9]	0.7427 [0.4572; 1.2092] 0.2339	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5586
Yes	167 / 394 (42.4)	4.8 [2.9; 5.6]	157 / 389 (40.4)	3.5 [2.3; 4.8]	0.9298 [0.7472; 1.1580] 0.5188	
No	22 / 42 (52.4)	1.8 [1.4; 5.6]	23 / 41 (56.1)	3.4 [1.4; 8.2]	1.1803 [0.6533; 2.1272] 0.5927	
Prior Taxane Use In The Non-Metastatic Setting						0.4131
Yes	77 / 179 (43.0)	4.9 [2.8; 6.2]	82 / 177 (46.3)	3.5 [2.1; 4.8]	0.8314 [0.6066; 1.1387] 0.2514	
No	112 / 257 (43.6)	3.5 [2.2; 5.6]	98 / 253 (38.7)	3.6 [2.2; 6.9]	1.0338 [0.7882; 1.3583] 0.8081	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.2981
1	24 / 65 (36.9)	6.2 [2.2; 16.6]	31 / 82 (37.8)	2.9 [1.5; 6.8]	0.6576 [0.3760; 1.1329] 0.1321	
2	129 / 295 (43.7)	3.4 [2.2; 4.9]	124 / 288 (43.1)	3.2 [2.1; 4.8]	1.0086 [0.7876; 1.2920] 0.9492	
>=3	36 / 75 (48.0)	4.8 [2.2; 9.0]	24 / 58 (41.4)	11.1 [2.1; 21.3]	1.2061 [0.7221; 2.0510] 0.4694	
ER/PR status I						0.1572
ER+, PR+	111 / 253 (43.9)	4.2 [2.8; 5.6]	108 / 237 (45.6)	2.7 [2.1; 4.2]	0.8491 [0.6506; 1.1083] 0.2284	
ER+, PR-	76 / 167 (45.5)	3.5 [2.2; 5.7]	67 / 181 (37.0)	5.6 [2.9; 9.9]	1.1539 [0.8303; 1.6075] 0.3915	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5644
ER <=10%	10 / 21 (47.6)	2.8 [0.7; 16.6]	5 / 14 (35.7)	4.2 [0.8; NE]	1.4681 [0.5039; 4.8031] 0.4969	
ER >10%	150 / 364 (41.2)	4.9 [2.9; 5.7]	149 / 355 (42.0)	3.6 [2.7; 5.6]	0.9036 [0.7197; 1.1348] 0.3826	
Positive	29 / 51 (56.9)	2.8 [1.3; 4.9]	26 / 61 (42.6)	2.1 [1.4; 21.3]	1.2265 [0.7208; 2.0967] 0.4226	
Endocrine Resistance						0.7730
Primary	54 / 128 (42.2)	4.8 [2.2; 6.2]	57 / 140 (40.7)	3.4 [2.1; 6.8]	0.9180 [0.6309; 1.3341] 0.6650	
Secondary	135 / 308 (43.8)	4.1 [2.8; 5.6]	122 / 288 (42.4)	3.5 [2.2; 5.5]	0.9720 [0.7605; 1.2435] 0.8193	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.2909
Capecitabine	115 / 266 (43.2)	4.2 [2.8; 5.5]	107 / 257 (41.6)	4.1 [2.3; 5.7]	0.9975 [0.7659; 1.3001] 0.9804	
Nab-Paclitaxel	47 / 103 (45.6)	4.8 [2.1; 7.7]	46 / 105 (43.8)	4.8 [2.1; 8.3]	1.0215 [0.6787; 1.5382] 0.9169	
Paclitaxel	27 / 67 (40.3)	4.1 [1.5; 9.1]	27 / 68 (39.7)	2.2 [0.8; 4.2]	0.6002 [0.3454; 1.0410] 0.0765	
Prior anthracycline use						0.6784
Yes	87 / 199 (43.7)	3.5 [2.2; 5.5]	92 / 208 (44.2)	3.5 [2.1; 5.6]	0.9868 [0.7345; 1.3246] 0.9382	
No	102 / 237 (43.0)	4.9 [2.9; 6.2]	88 / 222 (39.6)	3.2 [2.2; 5.7]	0.9225 [0.6934; 1.2305] 0.5855	
Liver metastases						0.2085
Yes	118 / 296 (39.9)	5.6 [3.5; 7.0]	115 / 283 (40.6)	3.5 [2.2; 6.2]	0.8602 [0.6633; 1.1156] 0.2550	
No	71 / 140 (50.7)	2.8 [1.5; 4.8]	65 / 147 (44.2)	2.9 [2.1; 5.5]	1.1178 [0.7979; 1.5686] 0.5149	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.9168
0	110 / 252 (43.7)	4.1 [2.8; 5.0]	112 / 257 (43.6)	3.5 [2.1; 6.9]	0.9576 [0.7350; 1.2474] 0.7454	
>=1	78 / 179 (43.6)	4.9 [2.2; 7.0]	66 / 164 (40.2)	3.4 [2.1; 4.8]	0.9340 [0.6729; 1.3009] 0.6952	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Physical Functioning						
Age at randomization						0.8685
<65 years of age	108 / 302 (35.8)	11.1 [5.6; 16.5]	113 / 297 (38.0)	6.9 [3.6; 10.5]	0.8345 [0.6397; 1.0881] 0.1761	
>=65 years of age	49 / 134 (36.6)	4.9 [2.9; 10.4]	58 / 133 (43.6)	2.8 [2.1; 4.8]	0.7933 [0.5399; 1.1603] 0.2328	
Race						0.2233
Asian	72 / 154 (46.8)	8.3 [4.9; 16.6]	72 / 151 (47.7)	7.5 [2.8; 15.2]	0.8638 [0.6216; 1.2003] 0.3754	
White	74 / 231 (32.0)	6.2 [3.6; 11.9]	84 / 230 (36.5)	3.6 [2.8; 6.9]	0.8637 [0.6301; 1.1812] 0.3555	
Other	11 / 51 (21.6)	11.7 [1.4; NE]	15 / 49 (30.6)	2.7 [0.8; 4.2]	0.3897 [0.1617; 0.8857] 0.0224	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5281
Asia	71 / 149 (47.7)	7.7 [4.3; 18.6]	70 / 147 (47.6)	7.5 [2.7; 15.2]	0.8732 [0.6264; 1.2176] 0.4172	
Europe	68 / 227 (30.0)	7.6 [3.6; 13.8]	80 / 213 (37.6)	2.9 [2.7; 4.8]	0.7263 [0.5236; 1.0046] 0.0527	
Rest of the World	18 / 60 (30.0)	10.3 [1.4; 15.9]	21 / 70 (30.0)	6.9 [2.1; NE]	1.0341 [0.5426; 1.9500] 0.9226	
HER2 IHC expression						0.7641
IHC 1+	86 / 239 (36.0)	7.6 [5.6; 14.5]	100 / 234 (42.7)	4.8 [2.8; 7.6]	0.7856 [0.5875; 1.0486] 0.1014	
IHC 2+/ISH-	42 / 117 (35.9)	4.9 [1.5; NE]	44 / 118 (37.3)	4.1 [2.2; 12.6]	0.9651 [0.6295; 1.4775] 0.8536	
IHC >0 <1+	28 / 76 (36.8)	11.0 [4.1; 16.6]	27 / 76 (35.5)	4.8 [2.1; NE]	0.7614 [0.4465; 1.3003] 0.3093	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.7382
Yes	143 / 394 (36.3)	7.6 [4.2; 11.7]	155 / 389 (39.8)	4.2 [2.8; 6.3]	0.8259 [0.6572; 1.0380] 0.0971	
No	14 / 42 (33.3)	NE [4.9; NE]	16 / 41 (39.0)	7.5 [2.1; NE]	0.7672 [0.3686; 1.5781] 0.4687	
Prior Taxane Use In The Non-Metastatic Setting						0.0187
Yes	63 / 179 (35.2)	9.6 [5.6; 16.0]	85 / 177 (48.0)	2.8 [2.1; 4.2]	0.5950 [0.4253; 0.8279] 0.0019	
No	94 / 257 (36.6)	6.2 [3.7; 11.9]	86 / 253 (34.0)	7.5 [4.2; 13.2]	1.0248 [0.7646; 1.3754] 0.8879	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.9761
1	22 / 65 (33.8)	11.7 [2.2; 16.5]	27 / 82 (32.9)	2.9 [2.1; NE]	0.7455 [0.4139; 1.3252] 0.3179	
2	104 / 295 (35.3)	7.0 [4.9; 13.8]	118 / 288 (41.0)	4.8 [3.0; 7.5]	0.8287 [0.6353; 1.0794] 0.1581	
>=3	30 / 75 (40.0)	8.3 [2.9; NE]	25 / 58 (43.1)	4.1 [1.5; NE]	0.8027 [0.4717; 1.3775] 0.4125	
ER/PR status I						0.8474
ER+, PR+	96 / 253 (37.9)	6.9 [4.2; 11.9]	98 / 237 (41.4)	4.2 [2.8; 7.5]	0.8021 [0.6043; 1.0644] 0.1222	
ER+, PR-	59 / 167 (35.3)	8.3 [3.6; 16.6]	66 / 181 (36.5)	4.8 [2.3; NE]	0.8838 [0.6196; 1.2573] 0.4887	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6296
ER <=10%	8 / 21 (38.1)	5.6 [1.3; NE]	6 / 14 (42.9)	2.2 [1.4; NE]	0.6562 [0.2259; 2.0129] 0.4359	
ER >10%	132 / 364 (36.3)	6.9 [4.2; 11.1]	138 / 355 (38.9)	4.8 [2.9; 7.5]	0.8538 [0.6718; 1.0853] 0.1910	
Positive	17 / 51 (33.3)	16.0 [4.3; NE]	27 / 61 (44.3)	2.9 [2.1; 9.7]	0.6538 [0.3480; 1.1946] 0.1677	
Endocrine Resistance						0.8603
Primary	46 / 128 (35.9)	9.6 [3.4; 16.5]	54 / 140 (38.6)	3.6 [2.1; 13.1]	0.8019 [0.5385; 1.1886] 0.2718	
Secondary	111 / 308 (36.0)	7.6 [4.9; 13.8]	117 / 288 (40.6)	4.8 [2.9; 7.5]	0.8196 [0.6309; 1.0641] 0.1300	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1475
Capecitabine	97 / 266 (36.5)	6.9 [3.7; 11.7]	97 / 257 (37.7)	4.9 [2.9; 10.5]	0.9513 [0.7170; 1.2621] 0.7174	
Nab-Paclitaxel	34 / 103 (33.0)	13.8 [5.6; NE]	40 / 105 (38.1)	7.6 [2.8; NE]	0.7567 [0.4759; 1.1972] 0.2292	
Paclitaxel	26 / 67 (38.8)	5.6 [2.2; 11.9]	34 / 68 (50.0)	2.2 [1.8; 4.1]	0.4464 [0.2574; 0.7617] 0.0028	
Prior anthracycline use						0.1258
Yes	74 / 199 (37.2)	7.6 [4.3; 11.7]	95 / 208 (45.7)	2.8 [2.1; 4.2]	0.6863 [0.5038; 0.9308] 0.0158	
No	83 / 237 (35.0)	10.4 [4.2; 18.6]	76 / 222 (34.2)	6.9 [4.8; 13.2]	0.9765 [0.7147; 1.3360] 0.8620	
Liver metastases						0.3916
Yes	100 / 296 (33.8)	8.3 [4.9; 13.8]	114 / 283 (40.3)	3.0 [2.3; 6.3]	0.7680 [0.5854; 1.0059] 0.0526	
No	57 / 140 (40.7)	6.9 [3.6; 16.5]	57 / 147 (38.8)	4.9 [4.1; 10.3]	0.9130 [0.6310; 1.3213] 0.6214	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0242
0	81 / 252 (32.1)	11.7 [5.6; NE]	106 / 257 (41.2)	4.1 [2.2; 5.5]	0.6761 [0.5041; 0.9035] 0.0079	
>=1	75 / 179 (41.9)	5.7 [2.9; 8.3]	62 / 164 (37.8)	6.9 [2.9; 12.6]	1.1145 [0.7969; 1.5652] 0.5336	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Role Functioning						
Age at randomization						0.8488
<65 years of age	135 / 302 (44.7)	3.6 [2.1; 6.2]	136 / 297 (45.8)	2.8 [2.1; 4.1]	0.8445 [0.6635; 1.0745] 0.1664	
>=65 years of age	61 / 134 (45.5)	2.1 [1.4; 4.3]	68 / 133 (51.1)	2.1 [1.5; 2.1]	0.8215 [0.5784; 1.1646] 0.2599	
Race						0.1138
Asian	98 / 154 (63.6)	2.9 [2.0; 4.2]	88 / 151 (58.3)	2.8 [2.0; 4.2]	1.0137 [0.7587; 1.3563] 0.9273	
White	85 / 231 (36.8)	2.9 [1.5; 6.2]	101 / 230 (43.9)	2.1 [1.5; 2.8]	0.7523 [0.5608; 1.0068] 0.0528	
Other	13 / 51 (25.5)	8.3 [1.4; NE]	15 / 49 (30.6)	2.1 [0.8; 4.9]	0.4025 [0.1712; 0.9048] 0.0244	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1378
Asia	95 / 149 (63.8)	2.9 [2.0; 4.2]	86 / 147 (58.5)	2.8 [2.0; 4.2]	1.0185 [0.7599; 1.3669] 0.9030	
Europe	79 / 227 (34.8)	4.3 [2.1; 7.6]	91 / 213 (42.7)	2.1 [1.5; 2.8]	0.6533 [0.4796; 0.8878] 0.0059	
Rest of the World	22 / 60 (36.7)	1.6 [0.8; 9.6]	27 / 70 (38.6)	2.1 [1.3; 5.7]	0.9214 [0.5115; 1.6356] 0.7817	
HER2 IHC expression						0.9567
IHC 1+	107 / 239 (44.8)	2.1 [1.5; 4.2]	115 / 234 (49.1)	2.1 [1.5; 2.8]	0.8815 [0.6751; 1.1499] 0.3508	
IHC 2+/ISH-	51 / 117 (43.6)	4.2 [2.1; 7.5]	54 / 118 (45.8)	2.3 [1.5; 4.2]	0.8000 [0.5416; 1.1799] 0.2537	
IHC >0 <1+	37 / 76 (48.7)	4.8 [1.4; 8.3]	34 / 76 (44.7)	2.1 [1.4; 4.9]	0.7557 [0.4723; 1.2126] 0.2391	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6595
Yes	173 / 394 (43.9)	3.5 [2.1; 4.8]	180 / 389 (46.3)	2.1 [2.0; 2.8]	0.8197 [0.6637; 1.0119] 0.0628	
No	23 / 42 (54.8)	1.4 [1.3; 9.7]	24 / 41 (58.5)	2.8 [1.3; 4.8]	0.9827 [0.5464; 1.7613] 0.9193	
Prior Taxane Use In The Non-Metastatic Setting						0.2763
Yes	80 / 179 (44.7)	4.1 [2.1; 6.2]	91 / 177 (51.4)	2.1 [1.5; 2.8]	0.7174 [0.5278; 0.9731] 0.0321	
No	116 / 257 (45.1)	2.9 [1.5; 4.8]	113 / 253 (44.7)	2.3 [2.1; 3.5]	0.9275 [0.7141; 1.2051] 0.5563	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1575
1	26 / 65 (40.0)	3.4 [1.4; 7.6]	31 / 82 (37.8)	2.8 [1.5; 4.1]	0.9099 [0.5349; 1.5346] 0.7201	
2	126 / 295 (42.7)	3.6 [2.1; 6.2]	145 / 288 (50.3)	2.1 [1.5; 2.8]	0.7327 [0.5744; 0.9333] 0.0112	
>=3	43 / 75 (57.3)	1.5 [0.8; 4.8]	27 / 58 (46.6)	2.8 [1.4; 5.7]	1.2875 [0.7998; 2.1094] 0.3098	
ER/PR status I						0.1102
ER+, PR+	112 / 253 (44.3)	4.2 [2.8; 6.3]	116 / 237 (48.9)	2.1 [1.5; 2.9]	0.7370 [0.5657; 0.9595] 0.0227	
ER+, PR-	82 / 167 (49.1)	2.1 [1.4; 3.5]	80 / 181 (44.2)	2.3 [1.5; 4.2]	1.0600 [0.7778; 1.4452] 0.7241	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3139
ER <=10%	9 / 21 (42.9)	3.4 [0.7; NE]	6 / 14 (42.9)	2.2 [0.6; 4.2]	0.8608 [0.3028; 2.6192] 0.7474	
ER >10%	166 / 364 (45.6)	2.8 [2.0; 4.2]	169 / 355 (47.6)	2.1 [2.1; 3.2]	0.8848 [0.7125; 1.0988] 0.2573	
Positive	21 / 51 (41.2)	10.3 [2.2; NE]	29 / 61 (47.5)	1.5 [1.4; 2.8]	0.5992 [0.3353; 1.0538] 0.0783	
Endocrine Resistance						0.2759
Primary	58 / 128 (45.3)	2.2 [1.4; 4.8]	60 / 140 (42.9)	2.8 [2.0; 4.2]	1.0044 [0.6981; 1.4439] 0.9832	
Secondary	138 / 308 (44.8)	3.5 [2.1; 5.5]	143 / 288 (49.7)	2.1 [1.5; 2.7]	0.7682 [0.6058; 0.9737] 0.0276	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:27; Program name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1021
Capecitabine	111 / 266 (41.7)	3.5 [2.1; 6.2]	127 / 257 (49.4)	2.1 [1.5; 2.2]	0.7080 [0.5462; 0.9161] 0.0080	
Nab-Paclitaxel	55 / 103 (53.4)	2.8 [1.4; 4.8]	51 / 105 (48.6)	3.5 [2.1; 5.7]	1.1531 [0.7857; 1.6945] 0.4786	
Paclitaxel	30 / 67 (44.8)	2.2 [1.4; 7.5]	26 / 68 (38.2)	2.1 [1.0; 3.0]	0.8379 [0.4902; 1.4397] 0.5348	
Prior anthracycline use						0.8620
Yes	93 / 199 (46.7)	2.2 [1.5; 4.2]	104 / 208 (50.0)	2.1 [1.5; 2.8]	0.8579 [0.6460; 1.1371] 0.2857	
No	103 / 237 (43.5)	3.6 [2.1; 7.4]	100 / 222 (45.0)	2.2 [2.0; 4.2]	0.8293 [0.6278; 1.0958] 0.1829	
Liver metastases						0.7145
Yes	127 / 296 (42.9)	3.5 [2.1; 6.2]	134 / 283 (47.3)	2.1 [2.0; 2.8]	0.8097 [0.6328; 1.0354] 0.0890	
No	69 / 140 (49.3)	2.8 [1.6; 4.9]	70 / 147 (47.6)	2.7 [1.5; 3.5]	0.8707 [0.6223; 1.2186] 0.4156	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0232
0	107 / 252 (42.5)	4.2 [2.9; 6.2]	127 / 257 (49.4)	2.1 [1.5; 2.8]	0.6977 [0.5371; 0.9046] 0.0065	
>=1	88 / 179 (49.2)	2.0 [1.3; 3.5]	74 / 164 (45.1)	2.3 [2.0; 4.2]	1.0962 [0.8038; 1.4996] 0.5938	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Emotional Functioning						
Age at randomization						0.8547
<65 years of age	101 / 302 (33.4)	11.1 [9.5; 16.6]	102 / 297 (34.3)	9.0 [6.2; 11.1]	0.8082 [0.6123; 1.0665] 0.1317	
>=65 years of age	44 / 134 (32.8)	7.6 [3.5; 13.9]	57 / 133 (42.9)	6.2 [3.4; 9.7]	0.7997 [0.5368; 1.1834] 0.2664	
Race						0.5222
Asian	68 / 154 (44.2)	11.1 [8.3; 20.1]	79 / 151 (52.3)	8.3 [4.8; 9.7]	0.7044 [0.5067; 0.9765] 0.0347	
White	69 / 231 (29.9)	8.4 [6.1; 12.0]	73 / 230 (31.7)	9.8 [5.5; 10.5]	0.9137 [0.6562; 1.2709] 0.5961	
Other	8 / 51 (15.7)	NE [4.2; NE]	7 / 49 (14.3)	4.9 [2.2; NE]	0.7423 [0.2641; 2.1338] 0.5679	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.3714
Asia	69 / 149 (46.3)	10.3 [7.7; 17.3]	76 / 147 (51.7)	8.3 [4.8; 9.7]	0.7441 [0.5344; 1.0338] 0.0769	
Europe	63 / 227 (27.8)	10.6 [6.9; 13.8]	60 / 213 (28.2)	9.8 [4.9; 14.0]	0.9300 [0.6520; 1.3284] 0.6910	
Rest of the World	13 / 60 (21.7)	11.8 [5.7; NE]	23 / 70 (32.9)	6.4 [2.2; 10.5]	0.5813 [0.2845; 1.1378] 0.1188	
HER2 IHC expression						0.4182
IHC 1+	79 / 239 (33.1)	10.6 [7.6; 17.3]	90 / 234 (38.5)	8.2 [4.9; 10.5]	0.7802 [0.5748; 1.0574] 0.1096	
IHC 2+/ISH-	38 / 117 (32.5)	10.7 [7.1; 20.1]	44 / 118 (37.3)	6.2 [3.6; 10.5]	0.6825 [0.4375; 1.0604] 0.0875	
IHC >0 <1+	27 / 76 (35.5)	9.7 [4.8; NE]	24 / 76 (31.6)	9.7 [4.9; 20.8]	1.0725 [0.6172; 1.8756] 0.8011	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.7048
Yes	125 / 394 (31.7)	10.6 [7.7; 14.6]	137 / 389 (35.2)	8.3 [6.2; 10.4]	0.8072 [0.6326; 1.0292] 0.0841	
No	20 / 42 (47.6)	11.1 [2.1; 20.7]	22 / 41 (53.7)	6.8 [2.1; 13.8]	0.7336 [0.3923; 1.3591] 0.3214	
Prior Taxane Use In The Non-Metastatic Setting						0.8655
Yes	63 / 179 (35.2)	9.7 [6.9; 14.6]	70 / 177 (39.5)	6.8 [4.2; 9.6]	0.7710 [0.5449; 1.0883] 0.1399	
No	82 / 257 (31.9)	11.1 [7.7; 17.3]	89 / 253 (35.2)	9.7 [6.2; 11.1]	0.8218 [0.6081; 1.1104] 0.2017	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6908
1	18 / 65 (27.7)	20.1 [4.2; NE]	24 / 82 (29.3)	8.9 [4.1; 13.1]	0.6600 [0.3459; 1.2306] 0.1922	
2	95 / 295 (32.2)	11.1 [8.3; 16.6]	109 / 288 (37.8)	8.3 [4.9; 10.4]	0.7874 [0.5968; 1.0377] 0.0904	
>=3	31 / 75 (41.3)	7.6 [4.8; 13.8]	25 / 58 (43.1)	9.7 [4.2; 11.1]	0.9913 [0.5861; 1.6934] 0.9764	
ER/PR status I						0.2732
ER+, PR+	82 / 253 (32.4)	10.3 [7.7; 20.7]	90 / 237 (38.0)	7.7 [4.9; 10.4]	0.7115 [0.5259; 0.9611] 0.0262	
ER+, PR-	62 / 167 (37.1)	10.7 [5.7; 13.9]	64 / 181 (35.4)	9.0 [4.9; 11.8]	0.9192 [0.6457; 1.3075] 0.6366	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1547
ER <=10%	7 / 21 (33.3)	7.6 [1.4; NE]	6 / 14 (42.9)	4.2 [1.4; NE]	0.5231 [0.1676; 1.6735] 0.2515	
ER >10%	118 / 364 (32.4)	11.0 [8.3; 13.9]	134 / 355 (37.7)	7.7 [5.5; 9.8]	0.7324 [0.5704; 0.9391] 0.0138	
Positive	20 / 51 (39.2)	10.3 [2.8; NE]	19 / 61 (31.1)	11.8 [5.0; NE]	1.3264 [0.7041; 2.5077] 0.3723	
Endocrine Resistance						0.0860
Primary	49 / 128 (38.3)	7.7 [4.2; 10.7]	48 / 140 (34.3)	9.6 [5.0; 13.1]	1.0437 [0.6983; 1.5600] 0.8332	
Secondary	96 / 308 (31.2)	11.8 [9.7; 18.6]	111 / 288 (38.5)	7.7 [4.9; 10.3]	0.7042 [0.5346; 0.9261] 0.0118	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.2927
Capecitabine	82 / 266 (30.8)	13.8 [7.7; 18.6]	88 / 257 (34.2)	9.8 [6.4; 13.8]	0.8560 [0.6326; 1.1575] 0.3115	
Nab-Paclitaxel	43 / 103 (41.7)	8.4 [3.5; 11.1]	48 / 105 (45.7)	6.9 [4.1; 9.9]	0.8529 [0.5612; 1.2908] 0.4475	
Paclitaxel	20 / 67 (29.9)	11.7 [7.5; NE]	23 / 68 (33.8)	4.2 [2.2; 10.5]	0.4267 [0.2269; 0.7955] 0.0063	
Prior anthracycline use						0.8576
Yes	69 / 199 (34.7)	9.7 [6.9; 16.6]	78 / 208 (37.5)	7.5 [4.2; 9.9]	0.8167 [0.5876; 1.1324] 0.2263	
No	76 / 237 (32.1)	11.1 [8.3; NE]	81 / 222 (36.5)	9.6 [6.2; 11.1]	0.7895 [0.5763; 1.0804] 0.1386	
Liver metastases						0.1272
Yes	89 / 296 (30.1)	11.0 [7.7; 20.1]	103 / 283 (36.4)	8.2 [4.9; 9.8]	0.7050 [0.5289; 0.9376] 0.0162	
No	56 / 140 (40.0)	10.3 [5.7; 13.9]	56 / 147 (38.1)	9.8 [4.9; 13.8]	1.0216 [0.7030; 1.4853] 0.9078	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.6801
0	85 / 252 (33.7)	9.8 [6.9; 13.9]	95 / 257 (37.0)	9.8 [7.5; 10.5]	0.8137 [0.6060; 1.0913] 0.1686	
>=1	59 / 179 (33.0)	10.7 [7.7; 18.6]	62 / 164 (37.8)	5.5 [3.6; 8.3]	0.7546 [0.5260; 1.0808] 0.1234	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 15:27; Program name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Cognitive Functioning						
Age at randomization						0.0782
<65 years of age	149 / 302 (49.3)	3.5 [2.1; 4.9]	126 / 297 (42.4)	4.2 [3.4; 6.3]	1.1158 [0.8800; 1.4176] 0.3675	
>=65 years of age	56 / 134 (41.8)	4.2 [2.8; 6.3]	65 / 133 (48.9)	2.8 [2.0; 4.2]	0.7484 [0.5208; 1.0719] 0.1144	
Race						0.2220
Asian	90 / 154 (58.4)	3.5 [2.7; 5.6]	86 / 151 (57.0)	4.2 [2.8; 6.3]	0.9043 [0.6702; 1.2209] 0.5119	
White	99 / 231 (42.9)	3.0 [2.0; 4.3]	92 / 230 (40.0)	3.4 [2.2; 5.0]	1.1719 [0.8819; 1.5581] 0.2671	
Other	16 / 51 (31.4)	5.0 [2.1; 13.2]	13 / 49 (26.5)	2.1 [0.8; 4.9]	0.4989 [0.2151; 1.1317] 0.0880	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.6757
Asia	88 / 149 (59.1)	4.1 [2.8; 6.2]	82 / 147 (55.8)	4.2 [2.9; 6.9]	0.9072 [0.6687; 1.2321] 0.5340	
Europe	92 / 227 (40.5)	3.5 [2.1; 5.0]	81 / 213 (38.0)	3.1 [2.1; 4.9]	1.0647 [0.7898; 1.4381] 0.6738	
Rest of the World	25 / 60 (41.7)	2.1 [0.9; 6.1]	28 / 70 (40.0)	2.8 [1.4; 5.0]	1.1492 [0.6656; 1.9733] 0.6124	
HER2 IHC expression						0.3978
IHC 1+	110 / 239 (46.0)	3.4 [2.8; 5.5]	114 / 234 (48.7)	3.4 [2.0; 4.9]	0.8958 [0.6875; 1.1667] 0.4140	
IHC 2+/ISH-	53 / 117 (45.3)	3.5 [2.0; 5.5]	45 / 118 (38.1)	4.2 [2.3; 14.6]	1.1602 [0.7797; 1.7349] 0.4697	
IHC >0 <1+	41 / 76 (53.9)	3.5 [2.0; 6.2]	31 / 76 (40.8)	3.5 [2.2; 11.0]	1.1498 [0.7216; 1.8508] 0.5400	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9950
Yes	183 / 394 (46.4)	3.5 [2.8; 4.9]	170 / 389 (43.7)	3.5 [2.8; 4.9]	0.9923 [0.8046; 1.2244] 0.9486	
No	22 / 42 (52.4)	3.2 [2.1; 11.1]	21 / 41 (51.2)	3.4 [1.5; 5.0]	0.9990 [0.5464; 1.8315] 0.9899	
Prior Taxane Use In The Non-Metastatic Setting						0.1701
Yes	80 / 179 (44.7)	3.7 [2.7; 6.2]	87 / 177 (49.2)	3.4 [2.1; 4.2]	0.8324 [0.6109; 1.1326] 0.2439	
No	125 / 257 (48.6)	3.5 [2.2; 4.9]	104 / 253 (41.1)	4.8 [2.8; 6.3]	1.1201 [0.8640; 1.4562] 0.3917	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6925
1	30 / 65 (46.2)	2.1 [1.4; 12.4]	37 / 82 (45.1)	3.5 [2.1; 4.9]	0.8381 [0.5061; 1.3728] 0.4658	
2	137 / 295 (46.4)	3.5 [2.8; 5.0]	128 / 288 (44.4)	3.4 [2.2; 4.9]	0.9966 [0.7823; 1.2703] 0.9855	
>=3	37 / 75 (49.3)	4.3 [2.1; 8.3]	25 / 58 (43.1)	13.2 [2.1; 18.0]	1.2016 [0.7259; 2.0220] 0.4742	
ER/PR status I						0.1605
ER+, PR+	118 / 253 (46.6)	4.2 [2.9; 6.2]	109 / 237 (46.0)	3.4 [2.2; 4.9]	0.8612 [0.6624; 1.1205] 0.2640	
ER+, PR-	82 / 167 (49.1)	2.8 [1.5; 5.0]	76 / 181 (42.0)	4.2 [2.8; 8.3]	1.1453 [0.8369; 1.5688] 0.4005	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.8148
ER <=10%	9 / 21 (42.9)	3.5 [1.4; NE]	6 / 14 (42.9)	2.1 [1.4; NE]	0.7371 [0.2600; 2.2394] 0.5756	
ER >10%	168 / 364 (46.2)	3.5 [2.7; 4.9]	155 / 355 (43.7)	3.5 [2.8; 4.9]	1.0108 [0.8117; 1.2595] 0.9213	
Positive	28 / 51 (54.9)	4.2 [2.2; 8.3]	30 / 61 (49.2)	3.5 [1.4; 14.6]	0.9965 [0.5916; 1.6736] 0.9902	
Endocrine Resistance						0.9167
Primary	63 / 128 (49.2)	2.4 [2.0; 3.7]	66 / 140 (47.1)	3.5 [2.3; 4.9]	1.0150 [0.7166; 1.4364] 0.9247	
Secondary	142 / 308 (46.1)	4.2 [2.9; 6.2]	125 / 288 (43.4)	3.5 [2.2; 6.2]	0.9913 [0.7786; 1.2637] 0.9455	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.4155
Capecitabine	122 / 266 (45.9)	3.5 [2.7; 5.0]	113 / 257 (44.0)	3.4 [2.2; 4.9]	1.0259 [0.7936; 1.3273] 0.8434	
Nab-Paclitaxel	52 / 103 (50.5)	2.8 [2.0; 4.9]	50 / 105 (47.6)	4.9 [2.8; 8.9]	1.0951 [0.7395; 1.6226] 0.6491	
Paclitaxel	31 / 67 (46.3)	6.2 [2.1; 8.9]	28 / 68 (41.2)	2.8 [0.8; 4.9]	0.6689 [0.3956; 1.1343] 0.1366	
Prior anthracycline use						0.7550
Yes	89 / 199 (44.7)	2.9 [2.1; 5.6]	95 / 208 (45.7)	3.5 [2.7; 4.9]	0.9719 [0.7258; 1.3003] 0.8578	
No	116 / 237 (48.9)	3.5 [2.8; 4.9]	96 / 222 (43.2)	3.4 [2.2; 5.5]	1.0206 [0.7788; 1.3406] 0.8828	
Liver metastases						0.5536
Yes	134 / 296 (45.3)	3.5 [2.7; 4.3]	127 / 283 (44.9)	3.5 [2.1; 4.9]	0.9450 [0.7403; 1.2070] 0.6605	
No	71 / 140 (50.7)	3.5 [2.1; 6.2]	64 / 147 (43.5)	3.5 [2.8; 6.9]	1.0859 [0.7736; 1.5276] 0.6416	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.2379
0	118 / 252 (46.8)	3.5 [2.8; 5.5]	119 / 257 (46.3)	2.8 [2.1; 4.9]	0.9119 [0.7054; 1.1789] 0.4853	
>=1	86 / 179 (48.0)	3.5 [2.1; 4.9]	69 / 164 (42.1)	4.2 [3.1; 6.9]	1.1596 [0.8453; 1.5965] 0.3493	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Social Functioning						
Age at randomization						0.4903
<65 years of age	136 / 302 (45.0)	3.6 [2.6; 6.2]	131 / 297 (44.1)	3.4 [2.1; 4.1]	0.8564 [0.6728; 1.0904] 0.2095	
>=65 years of age	62 / 134 (46.3)	2.3 [1.4; 4.2]	67 / 133 (50.4)	2.7 [1.5; 3.4]	0.9789 [0.6906; 1.3853] 0.8874	
Race						0.9925
Asian	91 / 154 (59.1)	2.9 [2.1; 5.5]	89 / 151 (58.9)	3.4 [2.1; 4.2]	0.9103 [0.6781; 1.2224] 0.5247	
White	93 / 231 (40.3)	3.5 [2.1; 5.1]	97 / 230 (42.2)	2.8 [1.5; 3.5]	0.8587 [0.6449; 1.1433] 0.2931	
Other	14 / 51 (27.5)	7.0 [0.8; 13.1]	12 / 49 (24.5)	2.7 [1.4; NE]	0.8515 [0.3899; 1.8870] 0.6954	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.8112
Asia	90 / 149 (60.4)	2.9 [2.1; 5.6]	85 / 147 (57.8)	3.4 [2.1; 4.9]	0.9403 [0.6978; 1.2682] 0.6812	
Europe	88 / 227 (38.8)	3.5 [2.1; 5.6]	86 / 213 (40.4)	2.8 [1.5; 3.5]	0.8590 [0.6367; 1.1591] 0.3185	
Rest of the World	20 / 60 (33.3)	5.1 [1.4; 9.7]	27 / 70 (38.6)	2.1 [1.5; 7.6]	0.7197 [0.3955; 1.2877] 0.2680	
HER2 IHC expression						0.3029
IHC 1+	104 / 239 (43.5)	3.6 [2.1; 5.6]	120 / 234 (51.3)	2.1 [1.5; 3.5]	0.7868 [0.6036; 1.0241] 0.0735	
IHC 2+/ISH-	55 / 117 (47.0)	2.8 [2.0; 5.6]	49 / 118 (41.5)	3.0 [2.1; 6.3]	1.0022 [0.6806; 1.4797] 0.9998	
IHC >0 <1+	38 / 76 (50.0)	3.4 [2.1; 6.9]	28 / 76 (36.8)	3.5 [2.1; 7.6]	1.0677 [0.6561; 1.7591] 0.7909	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4371
Yes	179 / 394 (45.4)	3.4 [2.2; 4.2]	176 / 389 (45.2)	2.8 [2.1; 3.5]	0.9044 [0.7340; 1.1149] 0.3411	
No	19 / 42 (45.2)	9.7 [1.7; 18.0]	22 / 41 (53.7)	2.8 [1.4; 5.6]	0.6628 [0.3465; 1.2507] 0.2045	
Prior Taxane Use In The Non-Metastatic Setting						0.5585
Yes	79 / 179 (44.1)	3.4 [2.1; 7.0]	86 / 177 (48.6)	2.8 [2.0; 3.5]	0.8233 [0.6039; 1.1214] 0.2150	
No	119 / 257 (46.3)	3.5 [2.2; 4.9]	112 / 253 (44.3)	2.8 [2.1; 4.9]	0.9273 [0.7161; 1.2020] 0.5597	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0847
1	28 / 65 (43.1)	3.6 [2.1; 9.1]	28 / 82 (34.1)	2.8 [2.1; NE]	1.0282 [0.6063; 1.7436] 0.9126	
2	124 / 295 (42.0)	3.5 [2.8; 5.6]	141 / 288 (49.0)	2.8 [2.0; 3.5]	0.7582 [0.5938; 0.9669] 0.0243	
>=3	45 / 75 (60.0)	1.6 [1.4; 2.2]	28 / 58 (48.3)	3.6 [1.4; 7.7]	1.3670 [0.8578; 2.2168] 0.1873	
ER/PR status I						0.6544
ER+, PR+	118 / 253 (46.6)	2.9 [2.1; 4.2]	107 / 237 (45.1)	2.9 [2.1; 3.5]	0.9434 [0.7256; 1.2281] 0.6584	
ER+, PR-	78 / 167 (46.7)	4.1 [2.1; 6.2]	84 / 181 (46.4)	2.8 [2.1; 4.2]	0.8268 [0.6056; 1.1282] 0.2271	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1529
ER <=10%	8 / 21 (38.1)	4.2 [1.4; NE]	7 / 14 (50.0)	2.0 [0.6; NE]	0.3307 [0.1023; 1.0354] 0.0428	
ER >10%	164 / 364 (45.1)	3.5 [2.1; 4.8]	161 / 355 (45.4)	2.9 [2.1; 3.5]	0.9003 [0.7234; 1.1212] 0.3399	
Positive	26 / 51 (51.0)	2.8 [2.1; 9.1]	30 / 61 (49.2)	2.0 [1.4; 7.7]	0.9525 [0.5572; 1.6196] 0.8888	
Endocrine Resistance						0.0343
Primary	66 / 128 (51.6)	2.3 [1.5; 3.5]	59 / 140 (42.1)	2.9 [2.1; 4.2]	1.2191 [0.8578; 1.7357] 0.2648	
Secondary	132 / 308 (42.9)	4.1 [2.6; 6.2]	139 / 288 (48.3)	2.8 [2.0; 3.5]	0.7578 [0.5956; 0.9637] 0.0218	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3725
Capecitabine	116 / 266 (43.6)	3.5 [2.3; 5.5]	116 / 257 (45.1)	2.8 [2.0; 3.5]	0.9111 [0.7037; 1.1798] 0.4782	
Nab-Paclitaxel	52 / 103 (50.5)	2.2 [1.4; 6.2]	52 / 105 (49.5)	3.5 [2.1; 4.9]	0.9716 [0.6578; 1.4342] 0.8696	
Paclitaxel	30 / 67 (44.8)	4.3 [1.4; 8.3]	30 / 68 (44.1)	2.1 [1.0; 2.9]	0.5139 [0.2962; 0.8851] 0.0150	
Prior anthracycline use						0.9685
Yes	88 / 199 (44.2)	2.9 [2.1; 6.2]	96 / 208 (46.2)	2.8 [2.1; 3.5]	0.8890 [0.6639; 1.1888] 0.4310	
No	110 / 237 (46.4)	3.5 [2.1; 5.1]	102 / 222 (45.9)	2.8 [2.1; 4.1]	0.8724 [0.6655; 1.1445] 0.3132	
Liver metastases						0.0234
Yes	127 / 296 (42.9)	3.5 [2.6; 5.6]	137 / 283 (48.4)	2.1 [1.5; 2.9]	0.7390 [0.5789; 0.9426] 0.0141	
No	71 / 140 (50.7)	2.8 [2.0; 4.3]	61 / 147 (41.5)	3.6 [2.8; 7.0]	1.2157 [0.8634; 1.7173] 0.2663	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.3848
0	108 / 252 (42.9)	3.6 [2.8; 6.9]	117 / 257 (45.5)	2.8 [2.1; 4.8]	0.8164 [0.6269; 1.0622] 0.1278	
>=1	89 / 179 (49.7)	2.3 [1.4; 4.1]	79 / 164 (48.2)	2.9 [1.5; 3.5]	0.9625 [0.7105; 1.3063] 0.8025	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Fatigue						
Age at randomization						0.5605
<65 years of age	153 / 302 (50.7)	1.5 [1.4; 2.9]	153 / 297 (51.5)	1.5 [1.4; 2.2]	0.9148 [0.7296; 1.1471] 0.4264	
>=65 years of age	68 / 134 (50.7)	1.4 [0.9; 2.8]	78 / 133 (58.6)	1.4 [1.4; 2.1]	0.7725 [0.5537; 1.0748] 0.1185	
Race						0.3631
Asian	96 / 154 (62.3)	2.1 [1.4; 5.0]	97 / 151 (64.2)	1.5 [1.4; 2.2]	0.8586 [0.6445; 1.1438] 0.2875	
White	108 / 231 (46.8)	1.4 [1.3; 2.8]	115 / 230 (50.0)	1.5 [1.3; 2.1]	0.9687 [0.7428; 1.2627] 0.8072	
Other	17 / 51 (33.3)	1.5 [0.7; 11.0]	19 / 49 (38.8)	1.4 [0.8; 2.3]	0.5916 [0.2936; 1.1697] 0.1207	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2791
Asia	92 / 149 (61.7)	2.2 [1.4; 5.0]	94 / 147 (63.9)	1.5 [1.4; 2.2]	0.8508 [0.6358; 1.1388] 0.2697	
Europe	102 / 227 (44.9)	1.4 [1.3; 2.8]	107 / 213 (50.2)	1.4 [0.9; 2.1]	0.8297 [0.6296; 1.0929] 0.1788	
Rest of the World	27 / 60 (45.0)	0.9 [0.8; 1.4]	30 / 70 (42.9)	1.5 [1.3; 2.1]	1.3346 [0.7821; 2.2625] 0.2791	
HER2 IHC expression						0.0301
IHC 1+	117 / 239 (49.0)	1.6 [1.4; 4.2]	132 / 234 (56.4)	1.4 [1.3; 1.5]	0.7421 [0.5758; 0.9550] 0.0199	
IHC 2+/ISH-	60 / 117 (51.3)	1.4 [0.9; 2.8]	64 / 118 (54.2)	1.5 [1.4; 2.7]	0.9969 [0.6966; 1.4255] 0.9653	
IHC >0 <1+	43 / 76 (56.6)	1.4 [0.8; 2.8]	33 / 76 (43.4)	2.2 [1.5; 4.8]	1.4162 [0.9006; 2.2470] 0.1329	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1405
Yes	196 / 394 (49.7)	1.4 [1.4; 2.8]	204 / 389 (52.4)	1.5 [1.4; 2.1]	0.9092 [0.7459; 1.1078] 0.3297	
No	25 / 42 (59.5)	1.4 [0.8; 6.2]	27 / 41 (65.9)	0.9 [0.8; 2.1]	0.6011 [0.3396; 1.0549] 0.0696	
Prior Taxane Use In The Non-Metastatic Setting						0.1090
Yes	85 / 179 (47.5)	2.0 [1.3; 3.0]	104 / 177 (58.8)	1.5 [1.3; 2.1]	0.7336 [0.5473; 0.9803] 0.0334	
No	136 / 257 (52.9)	1.4 [1.3; 2.8]	127 / 253 (50.2)	1.5 [1.4; 2.1]	0.9987 [0.7829; 1.2746] 0.9852	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.2731
1	31 / 65 (47.7)	1.4 [0.8; 7.6]	37 / 82 (45.1)	1.4 [0.8; 2.7]	0.8330 [0.5055; 1.3599] 0.4479	
2	144 / 295 (48.8)	1.5 [1.4; 2.8]	159 / 288 (55.2)	1.5 [1.4; 2.1]	0.8201 [0.6522; 1.0304] 0.0820	
>=3	46 / 75 (61.3)	1.4 [0.8; 2.8]	34 / 58 (58.6)	1.4 [0.9; 2.3]	1.2014 [0.7676; 1.9013] 0.4175	
ER/PR status I						0.8413
ER+, PR+	133 / 253 (52.6)	1.5 [1.4; 3.0]	126 / 237 (53.2)	2.0 [1.4; 2.2]	0.8749 [0.6840; 1.1195] 0.2852	
ER+, PR-	84 / 167 (50.3)	1.4 [0.9; 2.8]	97 / 181 (53.6)	1.4 [1.3; 1.5]	0.8839 [0.6573; 1.1854] 0.3964	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4514
ER <=10%	9 / 21 (42.9)	3.0 [0.7; NE]	5 / 14 (35.7)	4.1 [1.4; NE]	1.3068 [0.4456; 4.2924] 0.6489	
ER >10%	183 / 364 (50.3)	1.4 [1.3; 2.1]	191 / 355 (53.8)	1.5 [1.4; 2.1]	0.9104 [0.7418; 1.1168] 0.3463	
Positive	29 / 51 (56.9)	3.5 [1.4; 7.0]	35 / 61 (57.4)	1.4 [0.8; 2.1]	0.6520 [0.3932; 1.0728] 0.1021	
Endocrine Resistance						0.8609
Primary	65 / 128 (50.8)	1.4 [0.9; 2.9]	72 / 140 (51.4)	2.1 [1.4; 2.7]	0.9177 [0.6522; 1.2879] 0.5947	
Secondary	156 / 308 (50.6)	1.6 [1.4; 2.8]	158 / 288 (54.9)	1.5 [1.4; 2.0]	0.8596 [0.6877; 1.0752] 0.1783	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 15:27; Program name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.2643
Capecitabine	129 / 266 (48.5)	2.0 [1.4; 2.8]	139 / 257 (54.1)	1.4 [1.4; 2.1]	0.8036 [0.6302; 1.0237] 0.0726	
Nab-Paclitaxel	58 / 103 (56.3)	1.3 [0.8; 2.8]	57 / 105 (54.3)	2.1 [1.4; 4.8]	1.1206 [0.7735; 1.6225] 0.5927	
Paclitaxel	34 / 67 (50.7)	1.5 [1.4; 4.9]	35 / 68 (51.5)	1.4 [0.8; 2.2]	0.6056 [0.3646; 0.9986] 0.0459	
Prior anthracycline use						0.4229
Yes	100 / 199 (50.3)	1.4 [1.3; 2.8]	113 / 208 (54.3)	2.0 [1.4; 2.2]	0.9499 [0.7234; 1.2452] 0.7094	
No	121 / 237 (51.1)	1.5 [1.4; 2.8]	118 / 222 (53.2)	1.4 [1.4; 2.0]	0.8073 [0.6242; 1.0442] 0.0961	
Liver metastases						0.2314
Yes	142 / 296 (48.0)	1.4 [1.3; 2.9]	153 / 283 (54.1)	1.5 [1.4; 2.1]	0.8041 [0.6375; 1.0135] 0.0589	
No	79 / 140 (56.4)	1.4 [1.4; 2.2]	78 / 147 (53.1)	1.5 [1.3; 2.3]	1.0214 [0.7458; 1.3991] 0.8977	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:27; Program name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.2064
0	128 / 252 (50.8)	1.4 [1.4; 3.0]	147 / 257 (57.2)	1.4 [1.4; 2.0]	0.7870 [0.6186; 0.9999] 0.0461	
>=1	91 / 179 (50.8)	1.4 [1.3; 2.8]	81 / 164 (49.4)	1.5 [1.4; 2.2]	1.0225 [0.7563; 1.3843] 0.8997	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Nausea and Vomiting						
Age at randomization						0.1875
<65 years of age	169 / 302 (56.0)	1.5 [1.3; 2.1]	131 / 297 (44.1)	3.6 [2.7; 5.7]	1.6574 [1.3195; 2.0863] <.0001	
>=65 years of age	56 / 134 (41.8)	2.2 [1.4; 4.9]	54 / 133 (40.6)	4.1 [2.7; 5.7]	1.2445 [0.8555; 1.8121] 0.2480	
Race						0.7260
Asian	108 / 154 (70.1)	1.5 [1.4; 2.1]	84 / 151 (55.6)	4.2 [2.8; 5.5]	1.6435 [1.2365; 2.1917] 0.0006	
White	101 / 231 (43.7)	1.6 [1.4; 2.6]	89 / 230 (38.7)	3.5 [2.2; 6.1]	1.4918 [1.1215; 1.9878] 0.0058	
Other	16 / 51 (31.4)	2.1 [0.8; 4.2]	12 / 49 (24.5)	4.9 [0.8; 6.2]	1.1446 [0.5360; 2.4975] 0.7289	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.6213
Asia	106 / 149 (71.1)	1.7 [1.4; 2.1]	83 / 147 (56.5)	3.6 [2.7; 5.5]	1.6289 [1.2229; 2.1771] 0.0008	
Europe	97 / 227 (42.7)	2.0 [1.4; 2.2]	76 / 213 (35.7)	4.8 [2.8; 6.2]	1.5420 [1.1425; 2.0887] 0.0045	
Rest of the World	22 / 60 (36.7)	1.5 [0.8; 5.1]	26 / 70 (37.1)	2.7 [1.5; 6.4]	1.1589 [0.6453; 2.0570] 0.6272	
HER2 IHC expression						0.7367
IHC 1+	127 / 239 (53.1)	1.5 [1.4; 2.1]	104 / 234 (44.4)	4.2 [2.8; 5.7]	1.6703 [1.2889; 2.1694] 0.0001	
IHC 2+/ISH-	58 / 117 (49.6)	1.5 [0.9; 2.2]	50 / 118 (42.4)	3.5 [1.5; 6.3]	1.3924 [0.9530; 2.0413] 0.0906	
IHC >0 <1+	40 / 76 (52.6)	2.1 [1.3; 3.5]	29 / 76 (38.2)	3.5 [2.2; 12.4]	1.4660 [0.9097; 2.3914] 0.1165	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8666
Yes	199 / 394 (50.5)	2.0 [1.4; 2.1]	164 / 389 (42.2)	4.2 [2.9; 5.7]	1.5194 [1.2359; 1.8706] 0.0001	
No	26 / 42 (61.9)	1.4 [1.3; 2.2]	21 / 41 (51.2)	2.7 [1.5; 13.8]	1.6363 [0.9179; 2.9530] 0.0947	
Prior Taxane Use In The Non-Metastatic Setting						0.4448
Yes	85 / 179 (47.5)	2.1 [1.4; 2.2]	78 / 177 (44.1)	4.2 [2.9; 6.2]	1.3779 [1.0117; 1.8789] 0.0430	
No	140 / 257 (54.5)	1.5 [1.4; 2.1]	107 / 253 (42.3)	3.5 [2.1; 5.7]	1.6164 [1.2563; 2.0855] 0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.2181
1	29 / 65 (44.6)	1.6 [0.8; 2.7]	32 / 82 (39.0)	2.9 [1.4; 6.9]	1.2627 [0.7595; 2.0904] 0.3672	
2	151 / 295 (51.2)	1.5 [1.4; 2.1]	118 / 288 (41.0)	4.8 [3.4; 6.1]	1.7314 [1.3609; 2.2079] <.0001	
>=3	44 / 75 (58.7)	2.1 [0.8; 3.5]	34 / 58 (58.6)	2.1 [1.4; 4.8]	1.1872 [0.7591; 1.8728] 0.4602	
ER/PR status I						0.1473
ER+, PR+	129 / 253 (51.0)	2.1 [1.5; 2.2]	107 / 237 (45.1)	3.5 [2.7; 5.5]	1.3440 [1.0397; 1.7395] 0.0246	
ER+, PR-	92 / 167 (55.1)	1.4 [1.3; 2.1]	74 / 181 (40.9)	4.2 [2.7; 7.6]	1.7955 [1.3217; 2.4475] 0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6903
ER <=10%	12 / 21 (57.1)	1.4 [0.7; 3.5]	8 / 14 (57.1)	3.6 [0.7; 6.2]	1.3577 [0.5574; 3.4895] 0.5081	
ER >10%	184 / 364 (50.5)	1.7 [1.4; 2.1]	147 / 355 (41.4)	4.2 [2.8; 5.7]	1.5874 [1.2782; 1.9749] <.0001	
Positive	29 / 51 (56.9)	2.1 [1.4; 2.2]	30 / 61 (49.2)	2.9 [1.4; 7.0]	1.2741 [0.7613; 2.1289] 0.3577	
Endocrine Resistance						0.2067
Primary	62 / 128 (48.4)	1.5 [1.3; 2.2]	61 / 140 (43.6)	2.8 [2.0; 5.7]	1.2776 [0.8961; 1.8221] 0.1773	
Secondary	163 / 308 (52.9)	2.0 [1.4; 2.1]	123 / 288 (42.7)	4.3 [2.9; 5.7]	1.6786 [1.3286; 2.1262] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1437
Capecitabine	136 / 266 (51.1)	2.0 [1.4; 2.2]	122 / 257 (47.5)	2.8 [2.1; 4.1]	1.3496 [1.0564; 1.7258] 0.0163	
Nab-Paclitaxel	58 / 103 (56.3)	1.4 [1.3; 2.1]	40 / 105 (38.1)	8.3 [4.8; 13.8]	2.0493 [1.3712; 3.0933] 0.0004	
Paclitaxel	31 / 67 (46.3)	2.1 [1.4; 2.7]	23 / 68 (33.8)	4.2 [2.1; 7.0]	1.4399 [0.8396; 2.5041] 0.1910	
Prior anthracycline use						0.7849
Yes	99 / 199 (49.7)	1.5 [1.4; 2.2]	89 / 208 (42.8)	4.8 [2.9; 6.3]	1.5563 [1.1685; 2.0759] 0.0024	
No	126 / 237 (53.2)	2.1 [1.4; 2.1]	96 / 222 (43.2)	3.4 [2.1; 5.5]	1.4910 [1.1431; 1.9508] 0.0031	
Liver metastases						0.9046
Yes	146 / 296 (49.3)	1.6 [1.4; 2.1]	118 / 283 (41.7)	4.2 [2.8; 6.2]	1.5120 [1.1866; 1.9307] 0.0008	
No	79 / 140 (56.4)	2.0 [1.4; 2.1]	67 / 147 (45.6)	3.6 [2.2; 5.5]	1.5870 [1.1453; 2.2054] 0.0053	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.7478
0	134 / 252 (53.2)	1.5 [1.4; 2.1]	114 / 257 (44.4)	3.5 [2.2; 5.6]	1.5029 [1.1704; 1.9328] 0.0014	
>=1	90 / 179 (50.3)	2.1 [1.4; 2.8]	67 / 164 (40.9)	4.8 [2.8; 6.4]	1.6040 [1.1696; 2.2105] 0.0033	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 15:27; Program name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Pain						
Age at randomization						0.1844
<65 years of age	110 / 302 (36.4)	8.3 [4.9; 15.1]	125 / 297 (42.1)	4.2 [2.8; 6.2]	0.7428 [0.5735; 0.9608] 0.0228	
>=65 years of age	48 / 134 (35.8)	7.6 [3.5; 11.0]	61 / 133 (45.9)	2.1 [1.4; 3.0]	0.5563 [0.3773; 0.8155] 0.0025	
Race						0.6711
Asian	72 / 154 (46.8)	11.0 [4.9; 23.5]	85 / 151 (56.3)	4.1 [2.1; 4.9]	0.6375 [0.4629; 0.8755] 0.0050	
White	76 / 231 (32.9)	6.9 [4.1; 9.6]	89 / 230 (38.7)	2.9 [1.8; 4.3]	0.7568 [0.5556; 1.0285] 0.0755	
Other	10 / 51 (19.6)	5.0 [1.5; NE]	12 / 49 (24.5)	2.1 [1.3; NE]	0.6367 [0.2670; 1.4844] 0.2851	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.8430
Asia	69 / 149 (46.3)	11.0 [4.9; 23.5]	81 / 147 (55.1)	4.1 [2.2; 5.6]	0.6436 [0.4639; 0.8902] 0.0073	
Europe	69 / 227 (30.4)	7.6 [4.1; 10.4]	75 / 213 (35.2)	2.7 [1.5; 4.2]	0.7512 [0.5403; 1.0428] 0.0901	
Rest of the World	20 / 60 (33.3)	4.8 [1.4; 15.9]	30 / 70 (42.9)	2.1 [1.5; 5.6]	0.7403 [0.4127; 1.2999] 0.2853	
HER2 IHC expression						0.5221
IHC 1+	88 / 239 (36.8)	8.2 [4.2; 15.1]	107 / 234 (45.7)	3.4 [2.1; 4.9]	0.7031 [0.5277; 0.9342] 0.0150	
IHC 2+/ISH-	43 / 117 (36.8)	5.6 [2.2; 9.7]	53 / 118 (44.9)	2.0 [1.4; 3.4]	0.5670 [0.3753; 0.8516] 0.0059	
IHC >0 <1+	26 / 76 (34.2)	11.6 [4.8; NE]	25 / 76 (32.9)	10.4 [2.1; 13.9]	0.7991 [0.4593; 1.3928] 0.4264	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.7392
Yes	140 / 394 (35.5)	7.6 [4.9; 10.4]	163 / 389 (41.9)	3.0 [2.2; 4.3]	0.6902 [0.5493; 0.8659] 0.0013	
No	18 / 42 (42.9)	11.8 [1.4; 26.8]	23 / 41 (56.1)	2.1 [1.4; 6.2]	0.6475 [0.3415; 1.2082] 0.1651	
Prior Taxane Use In The Non-Metastatic Setting						0.5977
Yes	61 / 179 (34.1)	11.0 [4.2; 22.0]	79 / 177 (44.6)	2.9 [2.1; 4.3]	0.6499 [0.4621; 0.9096] 0.0119	
No	97 / 257 (37.7)	6.9 [4.8; 9.7]	107 / 253 (42.3)	3.1 [2.1; 5.6]	0.7183 [0.5444; 0.9466] 0.0181	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6194
1	20 / 65 (30.8)	15.9 [2.2; 26.8]	27 / 82 (32.9)	4.2 [2.1; 9.9]	0.6515 [0.3513; 1.1793] 0.1575	
2	107 / 295 (36.3)	7.6 [3.6; 11.1]	136 / 288 (47.2)	2.2 [2.0; 4.1]	0.6529 [0.5047; 0.8424] 0.0010	
>=3	30 / 75 (40.0)	8.3 [4.2; 15.1]	23 / 58 (39.7)	4.9 [2.1; 17.3]	0.8331 [0.4839; 1.4528] 0.5172	
ER/PR status I						0.3219
ER+, PR+	87 / 253 (34.4)	9.0 [6.2; 15.3]	107 / 237 (45.1)	2.8 [2.1; 4.2]	0.6052 [0.4544; 0.8039] 0.0005	
ER+, PR-	68 / 167 (40.7)	5.6 [2.6; 11.8]	74 / 181 (40.9)	3.4 [2.1; 5.6]	0.7697 [0.5494; 1.0758] 0.1244	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7748
ER <=10%	7 / 21 (33.3)	8.9 [2.9; NE]	5 / 14 (35.7)	4.1 [0.6; NE]	0.5865 [0.1853; 2.0008] 0.3615	
ER >10%	133 / 364 (36.5)	6.9 [4.2; 11.0]	156 / 355 (43.9)	3.4 [2.1; 4.9]	0.7007 [0.5544; 0.8843] 0.0026	
Positive	18 / 51 (35.3)	11.0 [3.5; NE]	25 / 61 (41.0)	2.8 [1.5; 4.3]	0.6060 [0.3218; 1.1185] 0.1098	
Endocrine Resistance						0.2211
Primary	47 / 128 (36.7)	6.9 [2.2; 23.5]	52 / 140 (37.1)	4.2 [2.1; 9.9]	0.8475 [0.5693; 1.2586] 0.4130	
Secondary	111 / 308 (36.0)	8.2 [4.9; 11.0]	133 / 288 (46.2)	2.8 [2.1; 4.1]	0.6228 [0.4821; 0.8029] 0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0445
Capecitabine	92 / 266 (34.6)	8.2 [4.8; 11.8]	114 / 257 (44.4)	2.2 [1.5; 4.1]	0.6167 [0.4668; 0.8125] 0.0005	
Nab-Paclitaxel	45 / 103 (43.7)	7.6 [2.0; 20.7]	44 / 105 (41.9)	6.9 [3.4; 10.3]	1.0020 [0.6525; 1.5362] 0.9974	
Paclitaxel	21 / 67 (31.3)	6.9 [3.6; NE]	28 / 68 (41.2)	2.1 [0.8; 4.2]	0.4438 [0.2467; 0.7864] 0.0049	
Prior anthracycline use						0.6157
Yes	72 / 199 (36.2)	8.9 [4.2; 15.3]	88 / 208 (42.3)	3.4 [2.1; 5.6]	0.7217 [0.5261; 0.9870] 0.0417	
No	86 / 237 (36.3)	6.9 [4.8; 11.1]	98 / 222 (44.1)	2.8 [2.1; 4.3]	0.6518 [0.4861; 0.8724] 0.0037	
Liver metastases						0.0706
Yes	97 / 296 (32.8)	7.6 [4.9; 22.1]	124 / 283 (43.8)	2.7 [2.1; 3.5]	0.5928 [0.4521; 0.7747] 0.0001	
No	61 / 140 (43.6)	7.6 [2.1; 11.6]	62 / 147 (42.2)	4.9 [2.2; 9.7]	0.8675 [0.6074; 1.2394] 0.4265	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0490
0	90 / 252 (35.7)	8.4 [4.2; 15.9]	124 / 257 (48.2)	2.1 [2.0; 3.4]	0.5909 [0.4481; 0.7763] 0.0001	
>=1	67 / 179 (37.4)	6.9 [4.2; 11.6]	59 / 164 (36.0)	5.6 [2.8; 10.3]	0.8839 [0.6221; 1.2588] 0.4981	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Dyspnoea						
Age at randomization						0.1256
<65 years of age	104 / 302 (34.4)	14.4 [7.6; 17.2]	105 / 297 (35.4)	7.5 [4.2; 15.9]	0.8147 [0.6193; 1.0713] 0.1403	
>=65 years of age	47 / 134 (35.1)	5.1 [3.5; 15.3]	43 / 133 (32.3)	5.7 [4.2; NE]	1.2148 [0.8021; 1.8430] 0.3584	
Race						0.0521
Asian	67 / 154 (43.5)	15.3 [7.6; 19.4]	61 / 151 (40.4)	15.9 [5.6; NE]	1.0212 [0.7211; 1.4488] 0.9049	
White	74 / 231 (32.0)	7.6 [5.5; 14.4]	72 / 230 (31.3)	6.3 [4.2; 13.2]	0.9524 [0.6875; 1.3201] 0.7619	
Other	10 / 51 (19.6)	5.7 [2.8; NE]	15 / 49 (30.6)	2.2 [1.6; 4.1]	0.3945 [0.1694; 0.8794] 0.0196	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.3716
Asia	65 / 149 (43.6)	15.2 [7.6; 19.4]	59 / 147 (40.1)	15.9 [5.6; NE]	1.0156 [0.7133; 1.4488] 0.9300	
Europe	67 / 227 (29.5)	7.6 [5.0; 15.2]	73 / 213 (34.3)	4.2 [2.8; 7.2]	0.7702 [0.5512; 1.0745] 0.1214	
Rest of the World	19 / 60 (31.7)	6.4 [3.7; 19.3]	16 / 70 (22.9)	16.6 [3.4; NE]	1.1923 [0.6028; 2.3764] 0.6149	
HER2 IHC expression						0.9645
IHC 1+	80 / 239 (33.5)	13.2 [7.5; 19.3]	81 / 234 (34.6)	8.9 [4.9; NE]	0.9057 [0.6633; 1.2365] 0.5335	
IHC 2+/ISH-	43 / 117 (36.8)	5.1 [3.5; 15.3]	42 / 118 (35.6)	4.3 [3.4; 16.6]	0.9549 [0.6230; 1.4649] 0.8246	
IHC >0 <1+	27 / 76 (35.5)	11.0 [4.1; 19.3]	23 / 76 (30.3)	5.5 [3.4; NE]	0.9722 [0.5561; 1.7132] 0.9164	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:27; Program name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3750
Yes	131 / 394 (33.2)	11.0 [6.3; 15.2]	133 / 389 (34.2)	6.3 [4.8; 13.2]	0.8878 [0.6969; 1.1313] 0.3358	
No	20 / 42 (47.6)	8.4 [2.1; 19.3]	15 / 41 (36.6)	8.9 [3.4; NE]	1.1941 [0.6055; 2.3964] 0.6182	
Prior Taxane Use In The Non-Metastatic Setting						0.3676
Yes	59 / 179 (33.0)	8.3 [4.9; 19.4]	67 / 177 (37.9)	4.3 [3.4; 16.6]	0.8280 [0.5815; 1.1760] 0.2966	
No	92 / 257 (35.8)	11.0 [6.4; 15.3]	81 / 253 (32.0)	8.3 [5.5; 15.9]	0.9897 [0.7333; 1.3383] 0.9353	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6134
1	20 / 65 (30.8)	7.5 [4.3; NE]	19 / 82 (23.2)	NE [3.7; NE]	1.2789 [0.6795; 2.4152] 0.4406	
2	101 / 295 (34.2)	13.2 [6.2; 15.9]	104 / 288 (36.1)	5.6 [4.2; 9.7]	0.8636 [0.6556; 1.1380] 0.2925	
>=3	30 / 75 (40.0)	11.0 [4.8; 24.2]	24 / 58 (41.4)	8.3 [2.8; NE]	0.9809 [0.5703; 1.7023] 0.9456	
ER/PR status I						0.4965
ER+, PR+	86 / 253 (34.0)	11.0 [7.6; 17.2]	80 / 237 (33.8)	7.6 [4.2; 16.6]	0.8957 [0.6602; 1.2175] 0.4784	
ER+, PR-	64 / 167 (38.3)	6.9 [4.8; 15.3]	62 / 181 (34.3)	7.0 [4.2; 21.3]	1.0487 [0.7377; 1.4914] 0.7914	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5926
ER <=10%	6 / 21 (28.6)	8.3 [2.0; NE]	6 / 14 (42.9)	4.8 [0.7; NE]	0.6173 [0.1923; 1.9819] 0.4073	
ER >10%	126 / 364 (34.6)	9.6 [6.3; 15.2]	122 / 355 (34.4)	6.3 [4.3; 13.2]	0.9088 [0.7076; 1.1680] 0.4509	
Positive	19 / 51 (37.3)	15.1 [3.4; NE]	20 / 61 (32.8)	21.3 [2.8; NE]	1.0977 [0.5811; 2.0653] 0.7695	
Endocrine Resistance						0.1975
Primary	44 / 128 (34.4)	6.9 [4.9; 15.2]	41 / 140 (29.3)	9.9 [4.2; NE]	1.1497 [0.7505; 1.7646] 0.5185	
Secondary	107 / 308 (34.7)	11.0 [7.6; 17.2]	106 / 288 (36.8)	5.6 [4.2; 13.2]	0.8412 [0.6418; 1.1025] 0.2069	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.7755
Capecitabine	90 / 266 (33.8)	11.0 [6.3; 15.2]	88 / 257 (34.2)	7.0 [4.3; 16.6]	0.9584 [0.7135; 1.2878] 0.7726	
Nab-Paclitaxel	36 / 103 (35.0)	17.2 [5.0; 29.6]	36 / 105 (34.3)	9.0 [5.7; 15.9]	0.8864 [0.5528; 1.4196] 0.6080	
Paclitaxel	25 / 67 (37.3)	6.3 [2.9; 19.3]	24 / 68 (35.3)	3.6 [1.6; 5.6]	0.6827 [0.3814; 1.2187] 0.1997	
Prior anthracycline use						0.3597
Yes	72 / 199 (36.2)	6.2 [4.8; 11.0]	83 / 208 (39.9)	4.2 [3.0; 8.3]	0.8334 [0.6060; 1.1430] 0.2639	
No	79 / 237 (33.3)	15.2 [7.8; 19.3]	65 / 222 (29.3)	13.2 [6.3; NE]	1.0176 [0.7319; 1.4195] 0.9266	
Liver metastases						0.4025
Yes	96 / 296 (32.4)	9.6 [5.6; 19.3]	90 / 283 (31.8)	8.3 [4.8; NE]	0.9902 [0.7407; 1.3244] 0.9418	
No	55 / 140 (39.3)	11.0 [6.2; 15.9]	58 / 147 (39.5)	5.5 [3.6; 9.7]	0.7974 [0.5497; 1.1553] 0.2318	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.4385
0	89 / 252 (35.3)	13.1 [6.9; 19.3]	91 / 257 (35.4)	7.0 [4.8; 15.9]	0.8517 [0.6348; 1.1425] 0.2846	
>=1	61 / 179 (34.1)	9.7 [3.5; 17.2]	54 / 164 (32.9)	8.3 [4.2; 21.3]	1.0495 [0.7268; 1.5194] 0.8087	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Insomnia						
Age at randomization						0.8054
<65 years of age	102 / 302 (33.8)	9.7 [6.3; 15.9]	105 / 297 (35.4)	5.5 [4.1; 10.3]	0.8181 [0.6212; 1.0767] 0.1487	
>=65 years of age	46 / 134 (34.3)	6.9 [4.3; 11.9]	48 / 133 (36.1)	5.0 [2.7; 8.3]	0.8765 [0.5832; 1.3163] 0.5276	
Race						0.8950
Asian	68 / 154 (44.2)	13.0 [7.5; 17.4]	67 / 151 (44.4)	5.5 [4.3; 14.0]	0.8227 [0.5840; 1.1590] 0.2566	
White	70 / 231 (30.3)	5.6 [4.1; 11.1]	76 / 230 (33.0)	4.8 [2.8; 8.3]	0.8567 [0.6180; 1.1862] 0.3510	
Other	10 / 51 (19.6)	9.7 [1.5; NE]	10 / 49 (20.4)	7.5 [1.3; NE]	0.6692 [0.2648; 1.6667] 0.3800	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5259
Asia	67 / 149 (45.0)	13.0 [7.5; 17.4]	65 / 147 (44.2)	5.5 [4.2; 15.2]	0.8188 [0.5791; 1.1581] 0.2519	
Europe	63 / 227 (27.8)	8.3 [4.2; 13.8]	67 / 213 (31.5)	4.8 [2.8; 7.5]	0.7694 [0.5441; 1.0868] 0.1364	
Rest of the World	18 / 60 (30.0)	4.9 [1.3; NE]	21 / 70 (30.0)	5.5 [2.2; 13.8]	1.1559 [0.6087; 2.1727] 0.6586	
HER2 IHC expression						0.3759
IHC 1+	87 / 239 (36.4)	7.7 [4.9; 14.5]	87 / 234 (37.2)	5.5 [3.6; 7.7]	0.8759 [0.6485; 1.1834] 0.3851	
IHC 2+/ISH-	36 / 117 (30.8)	9.7 [3.5; NE]	39 / 118 (33.1)	6.2 [3.5; 16.6]	0.9099 [0.5760; 1.4333] 0.6779	
IHC >0 <1+	24 / 76 (31.6)	13.0 [6.2; NE]	27 / 76 (35.5)	3.4 [2.1; 10.4]	0.5801 [0.3317; 1.0087] 0.0533	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3114
Yes	131 / 394 (33.2)	8.9 [6.2; 13.8]	131 / 389 (33.7)	5.5 [4.3; 9.0]	0.8636 [0.6771; 1.1023] 0.2373	
No	17 / 42 (40.5)	8.7 [0.8; NE]	22 / 41 (53.7)	3.6 [2.1; 7.7]	0.6305 [0.3210; 1.2092] 0.1616	
Prior Taxane Use In The Non-Metastatic Setting						0.0414
Yes	53 / 179 (29.6)	14.5 [6.2; 30.4]	70 / 177 (39.5)	4.8 [2.8; 7.5]	0.6305 [0.4364; 0.9050] 0.0117	
No	95 / 257 (37.0)	7.7 [4.9; 11.8]	83 / 253 (32.8)	5.5 [4.1; 10.4]	1.0107 [0.7529; 1.3595] 0.9429	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.2394
1	17 / 65 (26.2)	18.6 [3.5; NE]	25 / 82 (30.5)	5.0 [2.2; 14.0]	0.6164 [0.3210; 1.1488] 0.1262	
2	98 / 295 (33.2)	11.1 [5.6; 14.5]	106 / 288 (36.8)	5.5 [3.6; 6.3]	0.8079 [0.6119; 1.0655] 0.1286	
>=3	33 / 75 (44.0)	6.2 [4.1; 8.9]	21 / 58 (36.2)	16.6 [2.1; NE]	1.2301 [0.7162; 2.1601] 0.4589	
ER/PR status I						0.0332
ER+, PR+	82 / 253 (32.4)	9.6 [6.2; 15.9]	93 / 237 (39.2)	4.8 [3.2; 6.3]	0.6646 [0.4924; 0.8953] 0.0069	
ER+, PR-	65 / 167 (38.9)	7.8 [3.5; 12.4]	57 / 181 (31.5)	8.3 [3.5; NE]	1.1105 [0.7760; 1.5933] 0.5685	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4455
ER <=10%	7 / 21 (33.3)	7.5 [1.4; NE]	3 / 14 (21.4)	NE [0.7; NE]	1.7374 [0.4822; 8.0740] 0.4148	
ER >10%	122 / 364 (33.5)	8.3 [5.5; 13.0]	126 / 355 (35.5)	5.5 [3.7; 7.5]	0.8308 [0.6466; 1.0671] 0.1429	
Positive	19 / 51 (37.3)	13.9 [2.9; NE]	24 / 61 (39.3)	5.0 [2.1; 21.3]	0.7124 [0.3801; 1.3114] 0.2754	
Endocrine Resistance						0.4774
Primary	39 / 128 (30.5)	14.5 [5.5; NE]	48 / 140 (34.3)	5.6 [3.7; 10.4]	0.7279 [0.4718; 1.1155] 0.1425	
Secondary	109 / 308 (35.4)	7.8 [5.0; 11.9]	104 / 288 (36.1)	5.5 [3.5; 7.7]	0.8779 [0.6700; 1.1509] 0.3423	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:27; Program name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.8743
Capecitabine	92 / 266 (34.6)	7.7 [5.0; 11.9]	97 / 257 (37.7)	4.8 [3.5; 6.3]	0.8016 [0.6010; 1.0682] 0.1286	
Nab-Paclitaxel	38 / 103 (36.9)	13.0 [4.1; NE]	39 / 105 (37.1)	6.3 [3.5; NE]	0.9469 [0.6008; 1.4895] 0.8088	
Paclitaxel	18 / 67 (26.9)	18.6 [7.6; NE]	17 / 68 (25.0)	10.4 [2.2; NE]	0.7722 [0.3944; 1.5177] 0.4451	
Prior anthracycline use						0.1789
Yes	56 / 199 (28.1)	16.0 [7.5; NE]	73 / 208 (35.1)	5.6 [3.6; 10.3]	0.7126 [0.4986; 1.0124] 0.0569	
No	92 / 237 (38.8)	7.6 [4.3; 11.7]	80 / 222 (36.0)	5.0 [3.5; 9.0]	0.9387 [0.6957; 1.2698] 0.6807	
Liver metastases						0.4343
Yes	98 / 296 (33.1)	7.7 [5.6; 13.0]	97 / 283 (34.3)	5.6 [4.2; 9.0]	0.8860 [0.6684; 1.1754] 0.3962	
No	50 / 140 (35.7)	11.9 [4.3; NE]	56 / 147 (38.1)	4.8 [2.8; 10.3]	0.7478 [0.5071; 1.0991] 0.1348	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.6642
0	86 / 252 (34.1)	8.3 [4.9; NE]	94 / 257 (36.6)	5.5 [3.5; 8.3]	0.8187 [0.6098; 1.0986] 0.1782	
>=1	61 / 179 (34.1)	11.1 [5.6; 15.9]	56 / 164 (34.1)	5.5 [4.1; 15.2]	0.8784 [0.6093; 1.2684] 0.4842	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Appetite Loss						
Age at randomization						0.0307
<65 years of age	143 / 302 (47.4)	2.1 [1.5; 2.9]	113 / 297 (38.0)	5.6 [4.8; 9.6]	1.5002 [1.1729; 1.9234] 0.0012	
>=65 years of age	58 / 134 (43.3)	2.2 [1.5; 4.2]	66 / 133 (49.6)	2.2 [1.5; 3.7]	0.9486 [0.6645; 1.3503] 0.7736	
Race						0.3271
Asian	102 / 154 (66.2)	2.1 [1.4; 2.2]	83 / 151 (55.0)	4.8 [2.8; 6.4]	1.5338 [1.1485; 2.0543] 0.0036	
White	84 / 231 (36.4)	2.9 [2.1; 5.0]	83 / 230 (36.1)	4.8 [2.8; 7.6]	1.1528 [0.8500; 1.5625] 0.3551	
Other	15 / 51 (29.4)	2.2 [0.9; 11.7]	13 / 49 (26.5)	3.5 [1.3; 10.4]	0.9919 [0.4695; 2.1230] 0.9791	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2520
Asia	100 / 149 (67.1)	2.1 [1.4; 2.2]	81 / 147 (55.1)	4.8 [2.8; 6.9]	1.5700 [1.1717; 2.1099] 0.0024	
Europe	81 / 227 (35.7)	2.9 [2.1; 6.3]	73 / 213 (34.3)	4.3 [2.9; 9.6]	1.1672 [0.8501; 1.6057] 0.3316	
Rest of the World	20 / 60 (33.3)	2.1 [1.4; 9.9]	25 / 70 (35.7)	3.5 [1.5; 7.5]	0.9821 [0.5351; 1.7779] 0.9445	
HER2 IHC expression						0.6738
IHC 1+	104 / 239 (43.5)	2.2 [1.5; 4.2]	101 / 234 (43.2)	4.9 [3.6; 7.5]	1.2021 [0.9138; 1.5819] 0.1905	
IHC 2+/ISH-	59 / 117 (50.4)	2.1 [1.5; 3.1]	46 / 118 (39.0)	3.6 [2.2; 10.5]	1.5189 [1.0335; 2.2463] 0.0324	
IHC >0 <1+	37 / 76 (48.7)	2.5 [1.4; 4.9]	30 / 76 (39.5)	4.9 [2.1; 12.4]	1.3535 [0.8366; 2.2085] 0.2183	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6430
Yes	177 / 394 (44.9)	2.6 [2.1; 3.5]	157 / 389 (40.4)	4.8 [3.5; 6.2]	1.2856 [1.0372; 1.5949] 0.0215	
No	24 / 42 (57.1)	1.4 [0.8; 2.1]	22 / 41 (53.7)	2.8 [1.3; 8.2]	1.4256 [0.7929; 2.5764] 0.2468	
Prior Taxane Use In The Non-Metastatic Setting						0.3530
Yes	80 / 179 (44.7)	2.2 [2.0; 3.5]	80 / 177 (45.2)	3.6 [2.2; 5.5]	1.1658 [0.8541; 1.5915] 0.3289	
No	121 / 257 (47.1)	2.1 [1.5; 3.4]	99 / 253 (39.1)	4.9 [3.5; 7.5]	1.4147 [1.0852; 1.8485] 0.0106	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.9798
1	28 / 65 (43.1)	2.2 [1.4; 4.2]	30 / 82 (36.6)	3.7 [2.2; 8.9]	1.2513 [0.7436; 2.0992] 0.3995	
2	136 / 295 (46.1)	2.1 [1.5; 2.8]	123 / 288 (42.7)	4.8 [3.4; 6.2]	1.3268 [1.0397; 1.6950] 0.0233	
>=3	36 / 75 (48.0)	4.9 [2.0; 7.5]	25 / 58 (43.1)	4.9 [2.1; 15.9]	1.3210 [0.7939; 2.2334] 0.2857	
ER/PR status I						0.9448
ER+, PR+	112 / 253 (44.3)	2.8 [2.1; 4.8]	93 / 237 (39.2)	5.5 [3.5; 10.3]	1.3201 [1.0033; 1.7412] 0.0480	
ER+, PR-	85 / 167 (50.9)	2.1 [1.4; 2.8]	79 / 181 (43.6)	3.6 [2.1; 4.9]	1.3199 [0.9712; 1.7959] 0.0747	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5620
ER <=10%	11 / 21 (52.4)	2.1 [0.7; 2.9]	7 / 14 (50.0)	4.2 [0.6; 9.7]	1.6152 [0.6212; 4.4907] 0.3326	
ER >10%	160 / 364 (44.0)	2.6 [2.1; 3.5]	144 / 355 (40.6)	4.9 [3.5; 6.4]	1.2380 [0.9881; 1.5511] 0.0634	
Positive	30 / 51 (58.8)	1.4 [0.9; 2.2]	28 / 61 (45.9)	3.6 [2.1; 16.1]	1.8004 [1.0616; 3.0745] 0.0279	
Endocrine Resistance						0.8350
Primary	59 / 128 (46.1)	2.0 [1.4; 2.9]	57 / 140 (40.7)	4.8 [2.7; 8.2]	1.3326 [0.9248; 1.9218] 0.1230	
Secondary	142 / 308 (46.1)	2.2 [2.1; 3.6]	122 / 288 (42.4)	4.3 [3.4; 6.2]	1.2805 [1.0055; 1.6327] 0.0450	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.4618
Capecitabine	122 / 266 (45.9)	2.2 [1.5; 3.5]	107 / 257 (41.6)	4.3 [2.9; 5.5]	1.3145 [1.0140; 1.7066] 0.0389	
Nab-Paclitaxel	50 / 103 (48.5)	2.0 [1.4; 2.8]	46 / 105 (43.8)	5.6 [2.8; 9.6]	1.4359 [0.9600; 2.1522] 0.0782	
Paclitaxel	29 / 67 (43.3)	3.6 [2.1; 8.3]	26 / 68 (38.2)	3.6 [2.1; 10.3]	0.9659 [0.5672; 1.6529] 0.8992	
Prior anthracycline use						0.3368
Yes	90 / 199 (45.2)	2.1 [1.4; 2.8]	87 / 208 (41.8)	4.8 [3.5; 7.6]	1.4523 [1.0804; 1.9532] 0.0126	
No	111 / 237 (46.8)	2.6 [2.1; 4.1]	92 / 222 (41.4)	4.2 [2.2; 6.4]	1.1937 [0.9061; 1.5764] 0.2127	
Liver metastases						0.0108
Yes	125 / 296 (42.2)	2.8 [2.1; 4.4]	118 / 283 (41.7)	4.2 [2.2; 6.9]	1.0804 [0.8399; 1.3907] 0.5477	
No	76 / 140 (54.3)	1.5 [1.4; 2.2]	61 / 147 (41.5)	4.9 [3.5; 7.5]	1.8824 [1.3427; 2.6506] 0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.2221
0	119 / 252 (47.2)	2.1 [1.5; 3.5]	107 / 257 (41.6)	4.9 [3.5; 7.5]	1.4240 [1.0965; 1.8514] 0.0082	
>=1	80 / 179 (44.7)	2.8 [2.1; 4.1]	69 / 164 (42.1)	3.5 [2.1; 6.4]	1.1061 [0.8020; 1.5299] 0.5297	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 04SEP2024 15:27; Program name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Constipation						
Age at randomization						0.1280
<65 years of age	138 / 302 (45.7)	3.5 [2.2; 4.8]	101 / 297 (34.0)	8.2 [4.8; 11.8]	1.5938 [1.2344; 2.0651] 0.0003	
>=65 years of age	56 / 134 (41.8)	3.5 [2.1; 6.2]	53 / 133 (39.8)	4.2 [2.8; 7.7]	1.1186 [0.7646; 1.6366] 0.5622	
Race						0.7244
Asian	89 / 154 (57.8)	3.4 [2.1; 5.5]	73 / 151 (48.3)	6.9 [4.2; 11.7]	1.3705 [1.0051; 1.8743] 0.0468	
White	90 / 231 (39.0)	3.5 [2.1; 4.9]	70 / 230 (30.4)	8.3 [4.1; 12.5]	1.5397 [1.1266; 2.1125] 0.0065	
Other	15 / 51 (29.4)	5.3 [1.3; 7.0]	11 / 49 (22.4)	4.2 [2.2; NE]	1.0646 [0.4872; 2.3984] 0.8787	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.9717
Asia	89 / 149 (59.7)	3.5 [2.1; 5.5]	70 / 147 (47.6)	7.0 [4.2; 11.8]	1.4327 [1.0472; 1.9661] 0.0246	
Europe	85 / 227 (37.4)	3.6 [2.2; 5.5]	61 / 213 (28.6)	6.3 [3.5; 13.2]	1.4499 [1.0445; 2.0243] 0.0266	
Rest of the World	20 / 60 (33.3)	3.5 [2.0; 6.2]	23 / 70 (32.9)	7.5 [2.9; 12.5]	1.3977 [0.7594; 2.5510] 0.2718	
HER2 IHC expression						0.9464
IHC 1+	110 / 239 (46.0)	4.2 [2.2; 6.2]	87 / 234 (37.2)	6.9 [4.2; 10.5]	1.4099 [1.0638; 1.8732] 0.0168	
IHC 2+/ISH-	49 / 117 (41.9)	2.8 [2.0; 5.5]	39 / 118 (33.1)	6.3 [2.8; NE]	1.6102 [1.0533; 2.4827] 0.0280	
IHC >0 <1+	35 / 76 (46.1)	3.4 [2.1; 5.5]	27 / 76 (35.5)	7.6 [4.1; 12.5]	1.4580 [0.8812; 2.4389] 0.1418	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9513
Yes	170 / 394 (43.1)	3.6 [2.8; 5.3]	134 / 389 (34.4)	7.0 [4.8; 10.5]	1.4268 [1.1378; 1.7923] 0.0021	
No	24 / 42 (57.1)	2.1 [1.4; 4.2]	20 / 41 (48.8)	4.1 [2.7; NE]	1.5138 [0.8348; 2.7749] 0.1709	
Prior Taxane Use In The Non-Metastatic Setting						0.5049
Yes	83 / 179 (46.4)	2.8 [2.0; 4.8]	69 / 177 (39.0)	6.3 [4.1; 9.9]	1.5741 [1.1439; 2.1726] 0.0050	
No	111 / 257 (43.2)	3.6 [2.8; 7.0]	85 / 253 (33.6)	7.7 [4.2; 11.8]	1.3659 [1.0300; 1.8174] 0.0310	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6614
1	29 / 65 (44.6)	4.1 [2.1; 5.5]	25 / 82 (30.5)	8.2 [2.9; NE]	1.6650 [0.9720; 2.8730] 0.0605	
2	125 / 295 (42.4)	3.5 [2.1; 5.3]	106 / 288 (36.8)	5.6 [4.1; 10.3]	1.3566 [1.0474; 1.7604] 0.0212	
>=3	39 / 75 (52.0)	3.5 [1.5; 7.8]	22 / 58 (37.9)	11.8 [4.1; 18.0]	1.6677 [0.9943; 2.8670] 0.0551	
ER/PR status I						0.9802
ER+, PR+	113 / 253 (44.7)	4.1 [2.8; 6.2]	83 / 237 (35.0)	6.3 [4.1; 10.3]	1.4034 [1.0584; 1.8685] 0.0190	
ER+, PR-	78 / 167 (46.7)	2.8 [2.1; 4.8]	69 / 181 (38.1)	7.0 [4.1; 11.8]	1.3665 [0.9859; 1.8974] 0.0602	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5716
ER <=10%	9 / 21 (42.9)	8.9 [0.7; 15.9]	3 / 14 (21.4)	NE [0.6; NE]	2.0276 [0.5851; 9.2710] 0.2903	
ER >10%	162 / 364 (44.5)	3.5 [2.2; 4.5]	126 / 355 (35.5)	5.6 [4.2; 9.9]	1.4718 [1.1663; 1.8613] 0.0011	
Positive	23 / 51 (45.1)	5.5 [2.0; 14.6]	25 / 61 (41.0)	9.0 [3.5; 12.5]	1.1279 [0.6356; 1.9925] 0.6656	
Endocrine Resistance						0.3010
Primary	63 / 128 (49.2)	2.3 [1.5; 4.1]	51 / 140 (36.4)	5.6 [3.5; 9.9]	1.6836 [1.1636; 2.4478] 0.0053	
Secondary	131 / 308 (42.5)	4.2 [2.8; 6.9]	102 / 288 (35.4)	7.5 [4.3; 11.8]	1.3398 [1.0343; 1.7402] 0.0274	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.9494
Capecitabine	116 / 266 (43.6)	3.5 [2.2; 5.5]	92 / 257 (35.8)	7.7 [4.8; 11.7]	1.4150 [1.0760; 1.8649] 0.0131	
Nab-Paclitaxel	49 / 103 (47.6)	2.8 [2.0; 4.8]	42 / 105 (40.0)	6.9 [3.5; 11.8]	1.4941 [0.9891; 2.2668] 0.0564	
Paclitaxel	29 / 67 (43.3)	4.3 [2.0; 7.8]	20 / 68 (29.4)	4.2 [3.5; NE]	1.3240 [0.7517; 2.3784] 0.3368	
Prior anthracycline use						0.4047
Yes	92 / 199 (46.2)	3.5 [2.1; 4.8]	76 / 208 (36.5)	6.3 [4.1; 11.8]	1.5817 [1.1678; 2.1486] 0.0028	
No	102 / 237 (43.0)	3.6 [2.2; 7.5]	78 / 222 (35.1)	7.5 [4.2; 11.7]	1.3316 [0.9918; 1.7945] 0.0590	
Liver metastases						0.4795
Yes	128 / 296 (43.2)	3.6 [2.7; 5.5]	95 / 283 (33.6)	8.2 [4.8; 11.8]	1.5136 [1.1618; 1.9788] 0.0021	
No	66 / 140 (47.1)	2.8 [2.1; 5.3]	59 / 147 (40.1)	6.3 [4.1; 10.3]	1.2896 [0.9058; 1.8395] 0.1572	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.8891
0	109 / 252 (43.3)	4.1 [2.8; 5.5]	91 / 257 (35.4)	9.0 [4.8; 11.8]	1.4046 [1.0629; 1.8602] 0.0170	
>=1	84 / 179 (46.9)	2.8 [2.1; 4.8]	60 / 164 (36.6)	5.6 [4.1; 7.7]	1.4826 [1.0667; 2.0732] 0.0190	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Diarrhea						
Age at randomization						0.6067
<65 years of age	120 / 302 (39.7)	7.0 [4.8; 9.7]	118 / 297 (39.7)	5.0 [3.4; 8.9]	0.8338 [0.6448; 1.0783] 0.1634	
>=65 years of age	52 / 134 (38.8)	4.9 [2.1; 8.4]	56 / 133 (42.1)	4.8 [2.8; 8.3]	0.9502 [0.6497; 1.3871] 0.7860	
Race						0.5083
Asian	78 / 154 (50.6)	8.4 [4.2; 13.8]	70 / 151 (46.4)	8.4 [4.9; 13.1]	0.9735 [0.7030; 1.3501] 0.8761	
White	82 / 231 (35.5)	5.6 [3.5; 8.3]	91 / 230 (39.6)	3.4 [2.8; 4.9]	0.8018 [0.5931; 1.0823] 0.1464	
Other	12 / 51 (23.5)	5.7 [2.1; NE]	13 / 49 (26.5)	2.8 [1.3; 7.7]	0.6858 [0.3073; 1.5177] 0.3382	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.6405
Asia	76 / 149 (51.0)	8.4 [4.2; 13.8]	69 / 147 (46.9)	8.4 [4.9; 13.1]	0.9438 [0.6792; 1.3136] 0.7363	
Europe	77 / 227 (33.9)	5.6 [3.5; 8.2]	78 / 213 (36.6)	3.5 [2.9; 5.6]	0.8394 [0.6112; 1.1525] 0.2762	
Rest of the World	19 / 60 (31.7)	4.8 [1.3; 15.2]	27 / 70 (38.6)	2.2 [1.4; 7.7]	0.7059 [0.3805; 1.2787] 0.2413	
HER2 IHC expression						0.5704
IHC 1+	99 / 239 (41.4)	5.7 [3.5; 9.1]	98 / 234 (41.9)	6.8 [3.5; 8.4]	0.9448 [0.7123; 1.2532] 0.6897	
IHC 2+/ISH-	43 / 117 (36.8)	7.6 [3.5; 15.2]	45 / 118 (38.1)	5.6 [2.9; 9.6]	0.8967 [0.5859; 1.3730] 0.6222	
IHC >0 <1+	30 / 76 (39.5)	4.8 [2.8; NE]	31 / 76 (40.8)	2.9 [2.1; 6.9]	0.6976 [0.4201; 1.1568] 0.1603	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6968
Yes	151 / 394 (38.3)	6.2 [4.4; 9.1]	152 / 389 (39.1)	4.9 [3.4; 6.9]	0.8536 [0.6797; 1.0717] 0.1710	
No	21 / 42 (50.0)	7.1 [1.4; 13.9]	22 / 41 (53.7)	7.0 [2.0; 13.8]	0.9682 [0.5281; 1.7699] 0.9177	
Prior Taxane Use In The Non-Metastatic Setting						0.0259
Yes	73 / 179 (40.8)	4.4 [2.8; 9.7]	66 / 177 (37.3)	7.7 [4.1; 11.1]	1.1626 [0.8309; 1.6287] 0.3827	
No	99 / 257 (38.5)	8.2 [4.9; 11.0]	108 / 253 (42.7)	4.1 [2.8; 6.8]	0.7052 [0.5353; 0.9281] 0.0121	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4681
1	26 / 65 (40.0)	2.1 [1.3; 16.6]	27 / 82 (32.9)	4.2 [2.2; 13.9]	1.2780 [0.7419; 2.1972] 0.3739	
2	108 / 295 (36.6)	8.2 [5.5; 11.8]	117 / 288 (40.6)	4.9 [3.4; 8.9]	0.7989 [0.6130; 1.0399] 0.0933	
>=3	37 / 75 (49.3)	7.1 [2.9; 9.2]	30 / 58 (51.7)	6.2 [1.5; 7.6]	0.8623 [0.5319; 1.4087] 0.5568	
ER/PR status I						0.6579
ER+, PR+	104 / 253 (41.1)	6.2 [4.1; 9.0]	98 / 237 (41.4)	4.2 [2.8; 6.2]	0.8263 [0.6258; 1.0918] 0.1783	
ER+, PR-	65 / 167 (38.9)	7.6 [4.2; 11.9]	71 / 181 (39.2)	7.7 [3.4; 11.1]	0.8910 [0.6323; 1.2523] 0.5014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2028
ER <=10%	11 / 21 (52.4)	4.8 [1.4; 5.7]	4 / 14 (28.6)	8.9 [4.8; NE]	2.6405 [0.8611; 9.8175] 0.0962	
ER >10%	137 / 364 (37.6)	7.0 [4.8; 9.7]	140 / 355 (39.4)	4.9 [3.5; 7.7]	0.8560 [0.6756; 1.0852] 0.1969	
Positive	24 / 51 (47.1)	4.9 [1.4; 13.9]	30 / 61 (49.2)	2.2 [1.5; 8.4]	0.7847 [0.4479; 1.3566] 0.3895	
Endocrine Resistance						0.5240
Primary	48 / 128 (37.5)	4.8 [2.8; NE]	50 / 140 (35.7)	6.2 [3.4; 11.1]	0.9929 [0.6661; 1.4784] 0.9665	
Secondary	124 / 308 (40.3)	7.0 [4.8; 9.2]	123 / 288 (42.7)	4.9 [2.9; 7.7]	0.8123 [0.6310; 1.0457] 0.1056	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3579
Capecitabine	109 / 266 (41.0)	5.7 [3.5; 8.3]	115 / 257 (44.7)	3.4 [2.3; 5.0]	0.8013 [0.6149; 1.0435] 0.0990	
Nab-Paclitaxel	36 / 103 (35.0)	9.7 [4.8; NE]	41 / 105 (39.0)	7.7 [4.8; 13.8]	0.8363 [0.5303; 1.3124] 0.4325	
Paclitaxel	27 / 67 (40.3)	4.2 [2.1; 11.0]	18 / 68 (26.5)	6.9 [2.1; NE]	1.3306 [0.7371; 2.4596] 0.3465	
Prior anthracycline use						0.1631
Yes	81 / 199 (40.7)	5.0 [2.9; 8.4]	81 / 208 (38.9)	5.6 [3.5; 9.0]	1.0199 [0.7472; 1.3916] 0.8994	
No	91 / 237 (38.4)	8.2 [4.8; 12.4]	93 / 222 (41.9)	4.3 [2.9; 7.0]	0.7534 [0.5628; 1.0083] 0.0548	
Liver metastases						0.0638
Yes	115 / 296 (38.9)	5.7 [4.2; 8.2]	107 / 283 (37.8)	5.6 [3.5; 8.9]	1.0039 [0.7711; 1.3080] 0.9791	
No	57 / 140 (40.7)	8.4 [3.3; 13.9]	67 / 147 (45.6)	4.2 [2.2; 6.9]	0.6748 [0.4694; 0.9662] 0.0313	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.1639
0	97 / 252 (38.5)	8.2 [4.8; 9.7]	109 / 257 (42.4)	4.9 [3.4; 7.0]	0.7743 [0.5870; 1.0197] 0.0685	
>=1	74 / 179 (41.3)	4.9 [2.8; 8.2]	61 / 164 (37.2)	4.8 [2.8; 10.3]	1.0560 [0.7515; 1.4891] 0.7625	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Financial Difficulties						
Age at randomization						0.1234
<65 years of age	96 / 302 (31.8)	11.4 [9.0; 16.6]	90 / 297 (30.3)	10.3 [6.2; 16.6]	0.9049 [0.6774; 1.2106] 0.4949	
>=65 years of age	27 / 134 (20.1)	NE [11.8; NE]	42 / 133 (31.6)	9.0 [5.7; NE]	0.5887 [0.3583; 0.9508] 0.0307	
Race						0.7853
Asian	59 / 154 (38.3)	15.9 [9.7; NE]	63 / 151 (41.7)	8.9 [4.2; 20.0]	0.7490 [0.5222; 1.0725] 0.1117	
White	55 / 231 (23.8)	12.4 [9.7; NE]	61 / 230 (26.5)	11.0 [7.5; 20.1]	0.8688 [0.6016; 1.2517] 0.4443	
Other	9 / 51 (17.6)	NE [2.1; NE]	8 / 49 (16.3)	13.9 [2.1; NE]	0.8630 [0.3256; 2.3256] 0.7650	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.9068
Asia	60 / 149 (40.3)	13.8 [8.3; NE]	62 / 147 (42.2)	7.6 [4.2; 20.0]	0.7731 [0.5393; 1.1073] 0.1569	
Europe	50 / 227 (22.0)	15.2 [9.8; NE]	52 / 213 (24.4)	13.1 [7.6; NE]	0.8353 [0.5650; 1.2338] 0.3580	
Rest of the World	13 / 60 (21.7)	NE [2.8; NE]	18 / 70 (25.7)	11.0 [2.8; NE]	0.9174 [0.4385; 1.8667] 0.8103	
HER2 IHC expression						0.3096
IHC 1+	67 / 239 (28.0)	15.2 [11.0; NE]	82 / 234 (35.0)	9.0 [4.8; 13.9]	0.6839 [0.4926; 0.9463] 0.0216	
IHC 2+/ISH-	33 / 117 (28.2)	15.9 [8.3; NE]	28 / 118 (23.7)	20.1 [6.2; NE]	1.1554 [0.6978; 1.9277] 0.5860	
IHC >0 <1+	23 / 76 (30.3)	12.5 [2.8; NE]	22 / 76 (28.9)	9.6 [4.3; 13.8]	0.8573 [0.4757; 1.5490] 0.6050	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3918
Yes	109 / 394 (27.7)	13.8 [11.0; NE]	114 / 389 (29.3)	9.6 [7.0; 16.6]	0.8322 [0.6387; 1.0838] 0.1696	
No	14 / 42 (33.3)	16.6 [2.2; NE]	18 / 41 (43.9)	8.3 [1.3; NE]	0.5968 [0.2820; 1.2260] 0.1573	
Prior Taxane Use In The Non-Metastatic Setting						0.0966
Yes	46 / 179 (25.7)	NE [9.8; NE]	64 / 177 (36.2)	7.5 [4.2; 10.3]	0.6207 [0.4194; 0.9111] 0.0145	
No	77 / 257 (30.0)	13.8 [9.7; NE]	68 / 253 (26.9)	13.9 [8.3; NE]	0.9691 [0.6991; 1.3465] 0.8474	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5160
1	19 / 65 (29.2)	11.0 [2.1; NE]	23 / 82 (28.0)	7.6 [2.2; NE]	0.8531 [0.4582; 1.5694] 0.5985	
2	77 / 295 (26.1)	16.6 [11.0; NE]	92 / 288 (31.9)	9.6 [6.2; 14.6]	0.7354 [0.5410; 0.9976] 0.0476	
>=3	26 / 75 (34.7)	11.8 [6.3; NE]	17 / 58 (29.3)	16.6 [4.2; NE]	1.1281 [0.6167; 2.1185] 0.7021	
ER/PR status I						0.1845
ER+, PR+	74 / 253 (29.2)	13.8 [9.7; NE]	68 / 237 (28.7)	11.0 [7.6; 16.6]	0.8861 [0.6365; 1.2354] 0.4702	
ER+, PR-	47 / 167 (28.1)	15.9 [9.8; NE]	62 / 181 (34.3)	7.6 [3.5; 20.0]	0.6658 [0.4512; 0.9756] 0.0367	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 15:27; Program name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: T.2.11.10_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9750
ER <=10%	6 / 21 (28.6)	12.1 [4.9; NE]	3 / 14 (21.4)	NE [2.2; NE]	0.6057 [0.1561; 2.9228] 0.4814	
ER >10%	102 / 364 (28.0)	13.8 [9.8; NE]	109 / 355 (30.7)	9.0 [6.2; 14.6]	0.8139 [0.6197; 1.0681] 0.1353	
Positive	15 / 51 (29.4)	NE [4.2; NE]	20 / 61 (32.8)	13.9 [4.2; NE]	0.8051 [0.4041; 1.5698] 0.5199	
Endocrine Resistance						0.7625
Primary	42 / 128 (32.8)	9.8 [4.9; 16.6]	46 / 140 (32.9)	6.2 [4.2; 14.6]	0.8520 [0.5573; 1.2989] 0.4524	
Secondary	81 / 308 (26.3)	21.3 [11.8; NE]	85 / 288 (29.5)	13.1 [7.6; 20.7]	0.7998 [0.5882; 1.0866] 0.1493	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.8348
Capecitabine	68 / 266 (25.6)	16.6 [11.3; NE]	79 / 257 (30.7)	10.3 [7.6; 20.0]	0.7498 [0.5402; 1.0381] 0.0810	
Nab-Paclitaxel	33 / 103 (32.0)	11.0 [4.9; NE]	35 / 105 (33.3)	9.0 [3.4; NE]	0.8710 [0.5382; 1.4066] 0.5720	
Paclitaxel	22 / 67 (32.8)	9.8 [2.8; NE]	18 / 68 (26.5)	6.9 [2.8; NE]	0.9062 [0.4791; 1.7300] 0.7489	
Prior anthracycline use						0.2402
Yes	48 / 199 (24.1)	15.9 [11.0; NE]	64 / 208 (30.8)	9.0 [5.6; 20.1]	0.6683 [0.4556; 0.9736] 0.0353	
No	75 / 237 (31.6)	11.8 [8.3; NE]	68 / 222 (30.6)	9.6 [7.0; 20.0]	0.9256 [0.6661; 1.2889] 0.6407	
Liver metastases						0.4881
Yes	83 / 296 (28.0)	11.8 [9.7; NE]	84 / 283 (29.7)	9.0 [6.2; 20.0]	0.8524 [0.6275; 1.1576] 0.3026	
No	40 / 140 (28.6)	16.6 [11.0; NE]	48 / 147 (32.7)	10.3 [4.9; 16.6]	0.7193 [0.4695; 1.0960] 0.1224	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.10 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0702
0	59 / 252 (23.4)	NE [15.2; NE]	76 / 257 (29.6)	11.0 [8.3; 20.1]	0.6474 [0.4577; 0.9113] 0.0123	
>=1	63 / 179 (35.2)	8.3 [3.6; 11.8]	53 / 164 (32.3)	7.5 [4.2; 15.1]	1.0747 [0.7464; 1.5540] 0.7002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Tabelle 2.11.11 EORTC-QLQ-C30 – Zeit bis zur erstmaligen Verschlechterung – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.11.11 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Physical Functioning						
Prior Taxane Use In The Non-Metastatic Setting						0.0187
Yes	63 / 179 (35.2)	9.6 [5.6; 16.0]	85 / 177 (48.0)	2.8 [2.1; 4.2]	0.5950 [0.4253; 0.8279] 0.0019	
No	94 / 257 (36.6)	6.2 [3.7; 11.9]	86 / 253 (34.0)	7.5 [4.2; 13.2]	1.0248 [0.7646; 1.3754] 0.8879	
ECOG						0.0242
0	81 / 252 (32.1)	11.7 [5.6; NE]	106 / 257 (41.2)	4.1 [2.2; 5.5]	0.6761 [0.5041; 0.9035] 0.0079	
>=1	75 / 179 (41.9)	5.7 [2.9; 8.3]	62 / 164 (37.8)	6.9 [2.9; 12.6]	1.1145 [0.7969; 1.5652] 0.5336	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.11 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Role Functioning						
ECOG						0.0232
0	107 / 252 (42.5)	4.2 [2.9; 6.2]	127 / 257 (49.4)	2.1 [1.5; 2.8]	0.6977 [0.5371; 0.9046] 0.0065	
>=1	88 / 179 (49.2)	2.0 [1.3; 3.5]	74 / 164 (45.1)	2.3 [2.0; 4.2]	1.0962 [0.8038; 1.4996] 0.5938	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.11 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Social Functioning						
Endocrine Resistance						0.0343
Primary	66 / 128 (51.6)	2.3 [1.5; 3.5]	59 / 140 (42.1)	2.9 [2.1; 4.2]	1.2191 [0.8578; 1.7357] 0.2648	
Secondary	132 / 308 (42.9)	4.1 [2.6; 6.2]	139 / 288 (48.3)	2.8 [2.0; 3.5]	0.7578 [0.5956; 0.9637] 0.0218	
Liver metastases						0.0234
Yes	127 / 296 (42.9)	3.5 [2.6; 5.6]	137 / 283 (48.4)	2.1 [1.5; 2.9]	0.7390 [0.5789; 0.9426] 0.0141	
No	71 / 140 (50.7)	2.8 [2.0; 4.3]	61 / 147 (41.5)	3.6 [2.8; 7.0]	1.2157 [0.8634; 1.7173] 0.2663	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.11 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Fatigue						
HER2 IHC expression						0.0301
IHC 1+	117 / 239 (49.0)	1.6 [1.4; 4.2]	132 / 234 (56.4)	1.4 [1.3; 1.5]	0.7421 [0.5758; 0.9550] 0.0199	
IHC 2+/ISH-	60 / 117 (51.3)	1.4 [0.9; 2.8]	64 / 118 (54.2)	1.5 [1.4; 2.7]	0.9969 [0.6966; 1.4255] 0.9653	
IHC >0 <1+	43 / 76 (56.6)	1.4 [0.8; 2.8]	33 / 76 (43.4)	2.2 [1.5; 4.8]	1.4162 [0.9006; 2.2470] 0.1329	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.11 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Pain						
T-DXd vs. each Investigator's choice chemotherapy						0.0445
Capecitabine	92 / 266 (34.6)	8.2 [4.8; 11.8]	114 / 257 (44.4)	2.2 [1.5; 4.1]	0.6167 [0.4668; 0.8125] 0.0005	
Nab-Paclitaxel	45 / 103 (43.7)	7.6 [2.0; 20.7]	44 / 105 (41.9)	6.9 [3.4; 10.3]	1.0020 [0.6525; 1.5362] 0.9974	
Paclitaxel	21 / 67 (31.3)	6.9 [3.6; NE]	28 / 68 (41.2)	2.1 [0.8; 4.2]	0.4438 [0.2467; 0.7864] 0.0049	
ECOG						0.0490
0	90 / 252 (35.7)	8.4 [4.2; 15.9]	124 / 257 (48.2)	2.1 [2.0; 3.4]	0.5909 [0.4481; 0.7763] 0.0001	
>=1	67 / 179 (37.4)	6.9 [4.2; 11.6]	59 / 164 (36.0)	5.6 [2.8; 10.3]	0.8839 [0.6221; 1.2588] 0.4981	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.11 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Insomnia						
Prior Taxane Use In The Non-Metastatic Setting						0.0414
Yes	53 / 179 (29.6)	14.5 [6.2; 30.4]	70 / 177 (39.5)	4.8 [2.8; 7.5]	0.6305 [0.4364; 0.9050] 0.0117	
No	95 / 257 (37.0)	7.7 [4.9; 11.8]	83 / 253 (32.8)	5.5 [4.1; 10.4]	1.0107 [0.7529; 1.3595] 0.9429	
ER/PR status I						0.0332
ER+, PR+	82 / 253 (32.4)	9.6 [6.2; 15.9]	93 / 237 (39.2)	4.8 [3.2; 6.3]	0.6646 [0.4924; 0.8953] 0.0069	
ER+, PR-	65 / 167 (38.9)	7.8 [3.5; 12.4]	57 / 181 (31.5)	8.3 [3.5; NE]	1.1105 [0.7760; 1.5933] 0.5685	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.11.11 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Appetite Loss						
Age at randomization						0.0307
<65 years of age	143 / 302 (47.4)	2.1 [1.5; 2.9]	113 / 297 (38.0)	5.6 [4.8; 9.6]	1.5002 [1.1729; 1.9234] 0.0012	
>=65 years of age	58 / 134 (43.3)	2.2 [1.5; 4.2]	66 / 133 (49.6)	2.2 [1.5; 3.7]	0.9486 [0.6645; 1.3503] 0.7736	
Liver metastases						0.0108
Yes	125 / 296 (42.2)	2.8 [2.1; 4.4]	118 / 283 (41.7)	4.2 [2.2; 6.9]	1.0804 [0.8399; 1.3907] 0.5477	
No	76 / 140 (54.3)	1.5 [1.4; 2.2]	61 / 147 (41.5)	4.9 [3.5; 7.5]	1.8824 [1.3427; 2.6506] 0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 15:43; Program name: T.2.11.11_EORTC_C30_TTFDet_FAS_SUB_SIG.sas; Output name: T.2.11.11_EORTC_C30_TTFDet_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.11.11 EORTC QLQ-C30 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

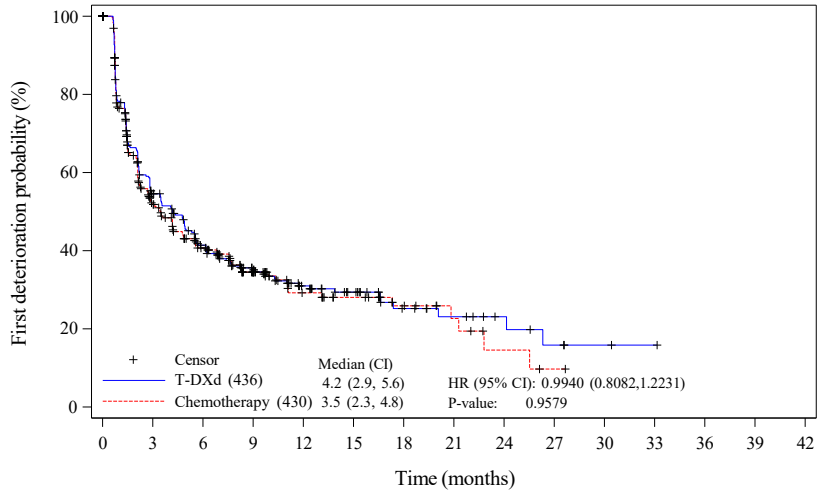
DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Common Symptoms/Diarrhea						
Prior Taxane Use In The Non-Metastatic Setting						0.0259
Yes	73 / 179 (40.8)	4.4 [2.8; 9.7]	66 / 177 (37.3)	7.7 [4.1; 11.1]	1.1626 [0.8309; 1.6287] 0.3827	
No	99 / 257 (38.5)	8.2 [4.9; 11.0]	108 / 253 (42.7)	4.1 [2.8; 6.8]	0.7052 [0.5353; 0.9281] 0.0121	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 15:43; Program name: T.2.11.11_EORTC_C30_TTFDet_FAS_SUB_SIG.sas; Output name: T.2.11.11_EORTC_C30_TTFDet_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.11.5 EORTC-QLQ-C30 – Zeit bis zur erstmaligen Verschlechterung – Kaplan-Meier-Plot – FAS

Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Global Health Status



Patients still at risk:

T-DXd(436)	436	144	97	69	42	30	15	11	7	4	2	1	0
Chemotherapy (430)	430	125	83	47	25	18	12	7	3	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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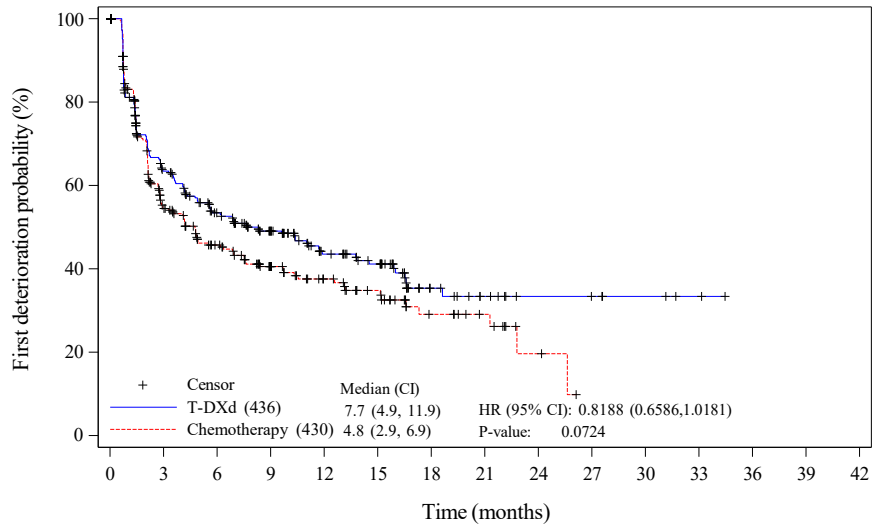
Run date: 10DEC2024 10:29; Program name: F.2.11.5_EORTC_C30_TTFDet_FAS.sas; Output name: F.2.11.5_EORTC_C30_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Physical Functioning



Patients still at risk:

T-DXd(436)	436	172	128	97	63	50	19	12	7	6	4	2	0
Chemotherapy (430)	430	135	95	63	43	31	15	10	3	0			

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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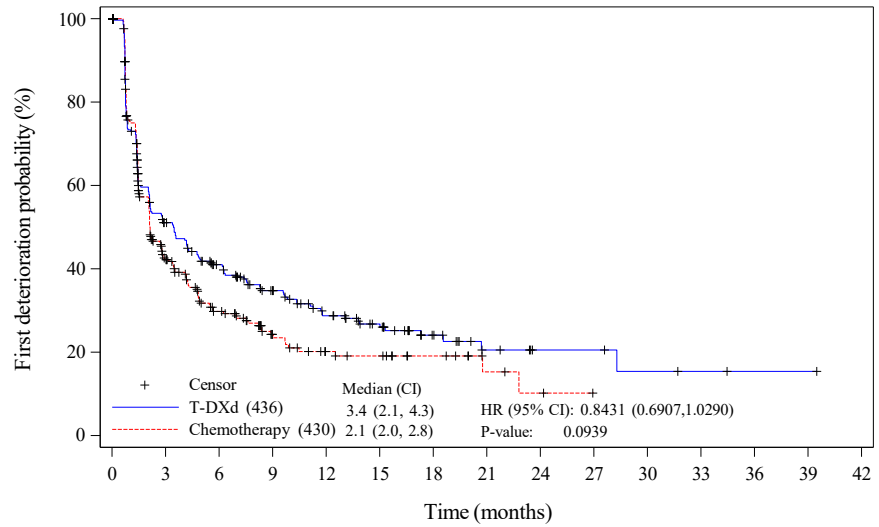
Run date: 10DEC2024 10:29; Program name: F.2.11.5_EORTC_C30_TTFDet_FAS.sas; Output name: F.2.11.5_EORTC_C30_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Role Functioning



Patients still at risk:

T-DXd(436)	436	134	97	70	49	36	18	9	5	5	3	2	1	1	0
Chemotherapy (430)	430	102	58	30	19	16	10	4	2	0					

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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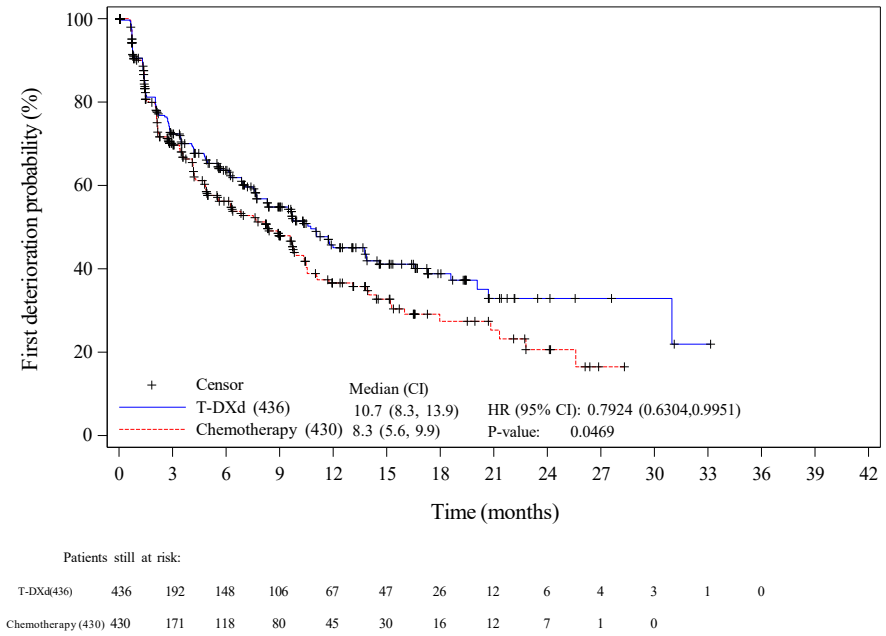
Run date: 10DEC2024 10:29; Program name: F.2.11.5_EORTC_C30_TTFDet_FAS.sas; Output name: F.2.11.5_EORTC_C30_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Emotional Functioning



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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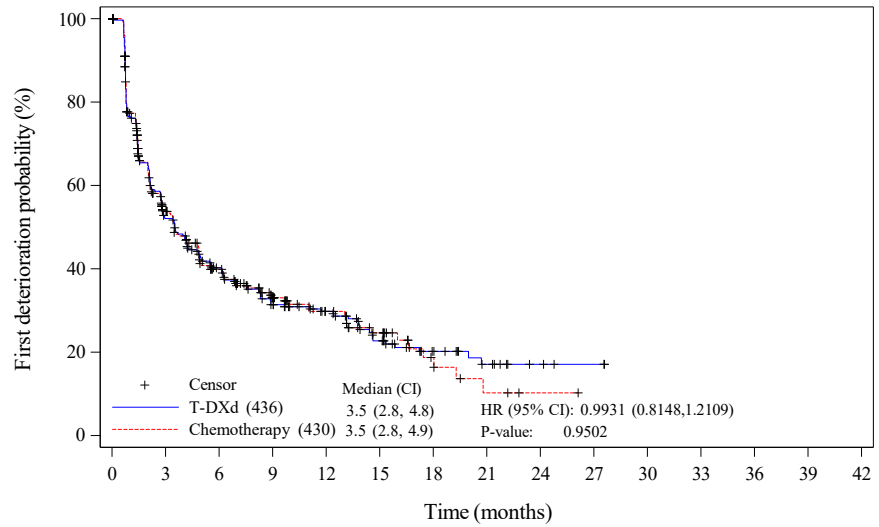
Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Cognitive Functioning



Patients still at risk:

T-DXd(436)	436	141	97	66	52	33	18	10	4	2	0
Chemotherapy (430)	430	131	84	51	32	19	8	3	1	0	

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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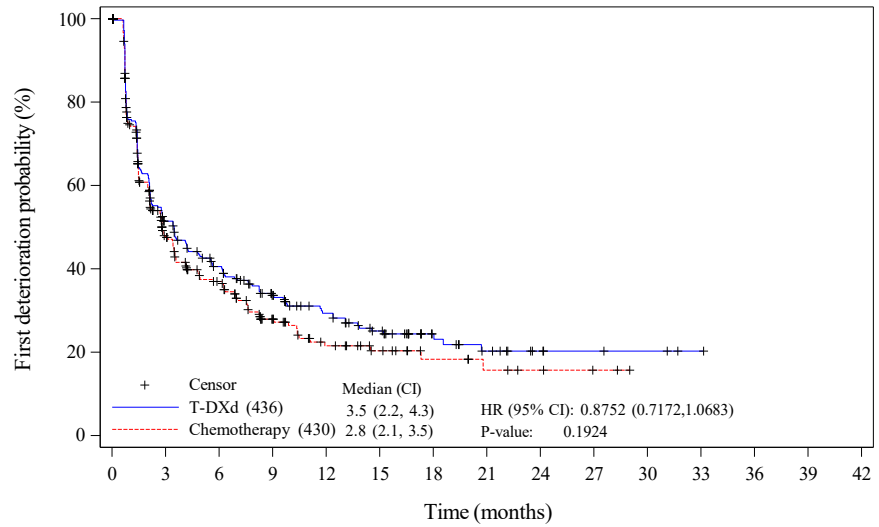
Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Social Functioning



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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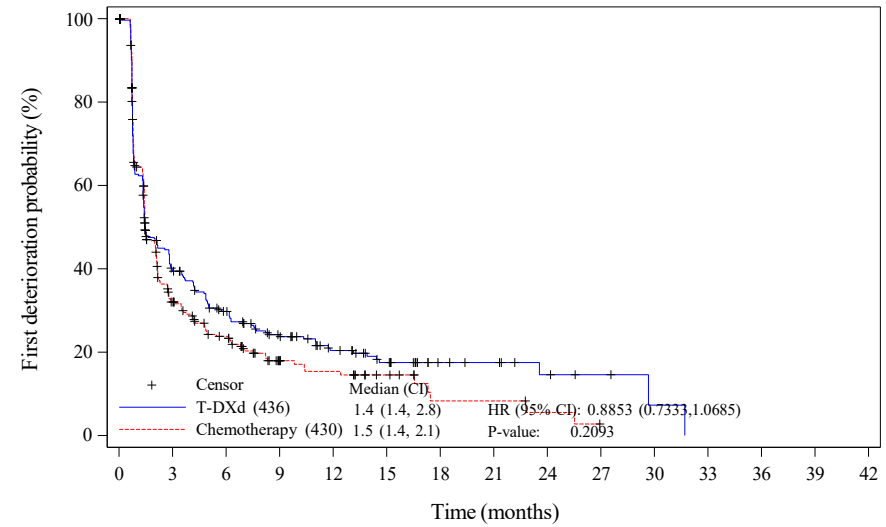
Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Fatigue



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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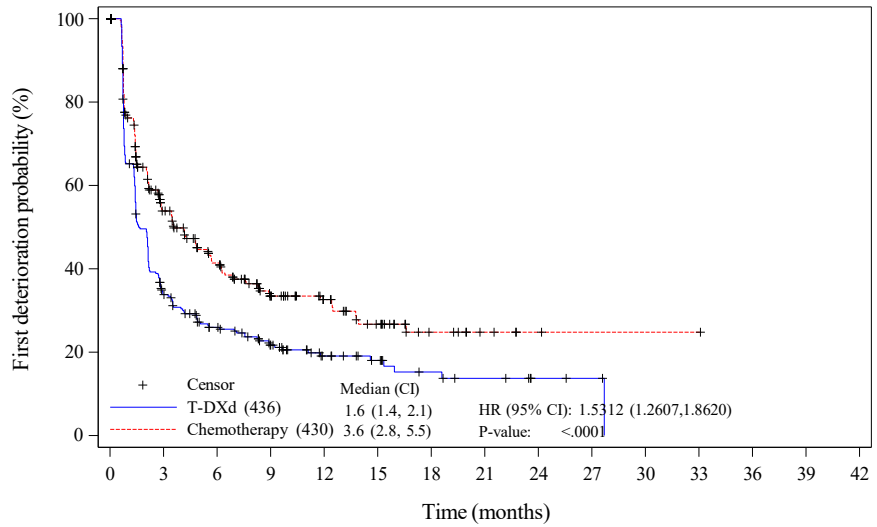
Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Nausea and Vomiting



Patients still at risk:

T-DXd(436)	436	91	60	41	23	16	10	7	3	2	0	
Chemotherapy (430)	430	135	89	52	37	23	10	5	2	1	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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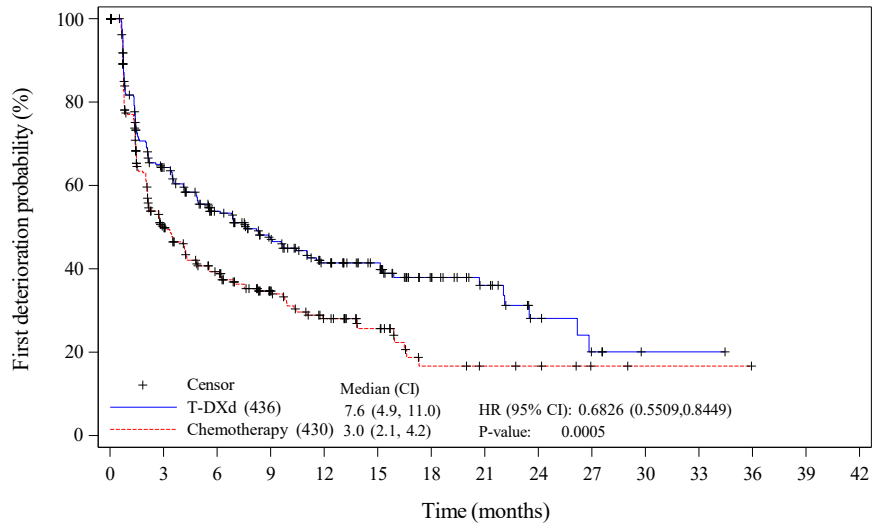
Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Pain



Patients still at risk:

T-DXd(436)	436	166	120	91	66	52	28	18	8	4	1	1	0
Chemotherapy (430)	430	121	83	51	33	21	8	6	5	2	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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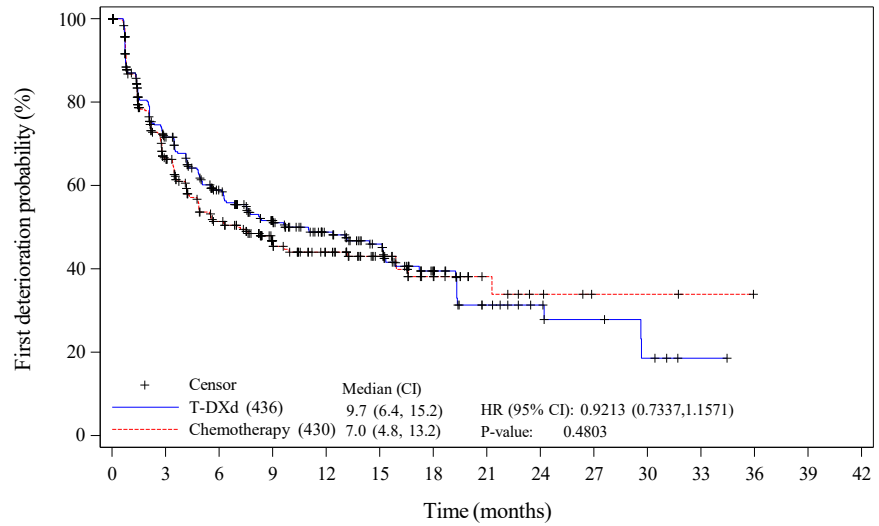
Run date: 10DEC2024 10:29; Program name: F.2.11.5_EORTC_C30_TTFDet_FAS.sas; Output name: F.2.11.5_EORTC_C30_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Dyspnoea



Patients still at risk:

T-DXd(436)	436	189	136	101	74	56	30	15	10	7	4	1	0
Chemotherapy (430)	430	168	112	71	51	33	18	9	5	2	2	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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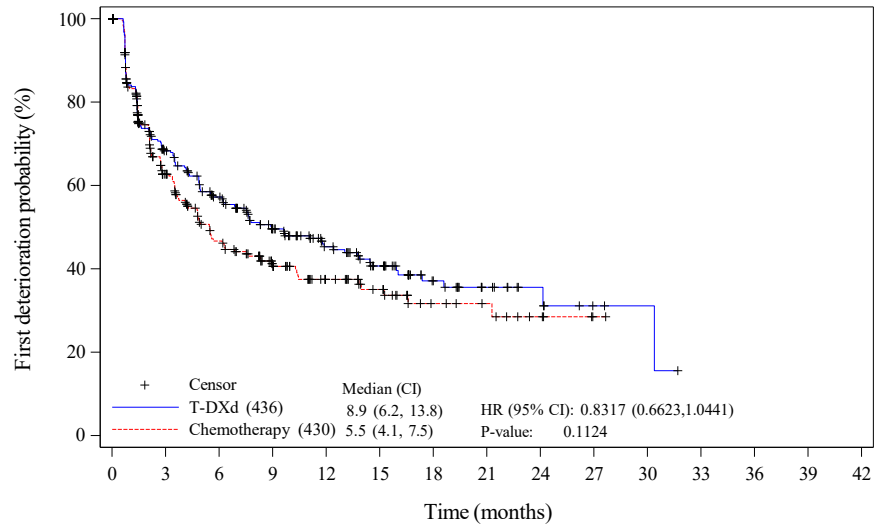
Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Insomnia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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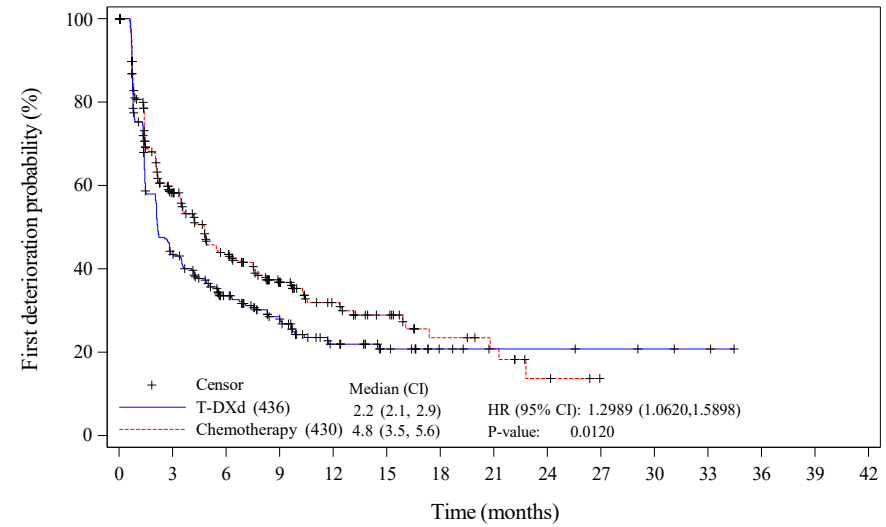
Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Appetite Loss



Patients still at risk:

T-DXd(436)	436	116	74	50	26	16	8	5	5	4	3	2	0
Chemotherapy (430)	430	144	95	58	33	22	11	8	3	0			

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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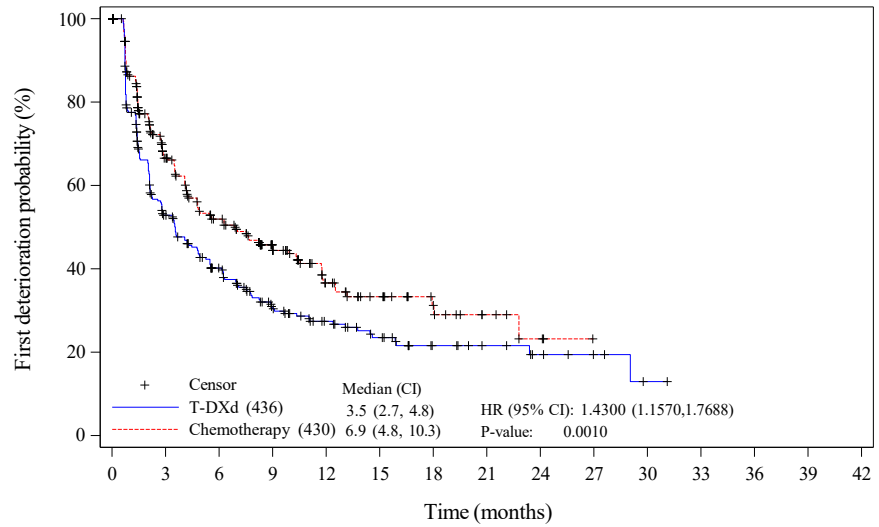
Run date: 10DEC2024 10:29; Program name: F.2.11.5_EORTC_C30_TTFDet_FAS.sas; Output name: F.2.11.5_EORTC_C30_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Constipation



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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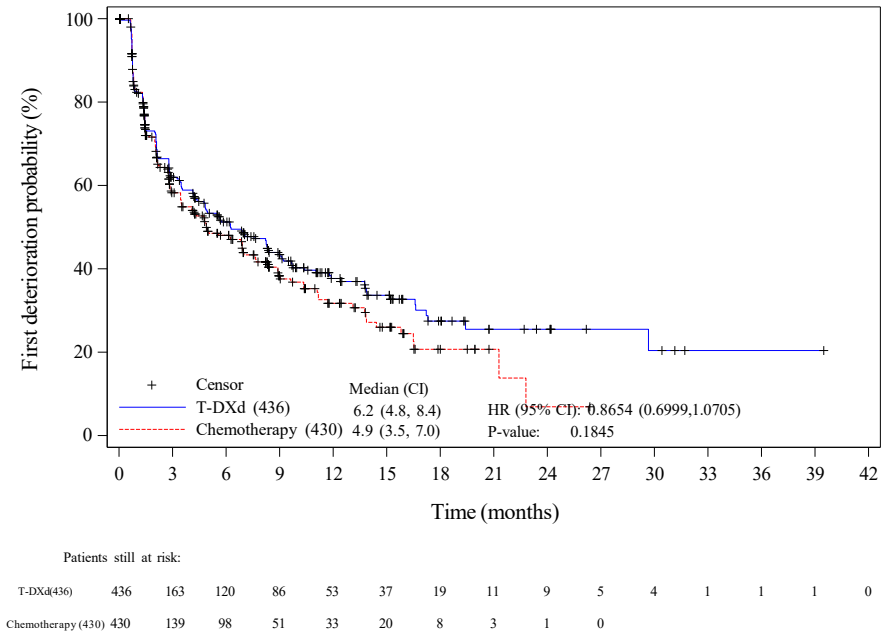
Run date: 10DEC2024 10:29; Program name: F.2.11.5_EORTC_C30_TTFDet_FAS.sas; Output name: F.2.11.5_EORTC_C30_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

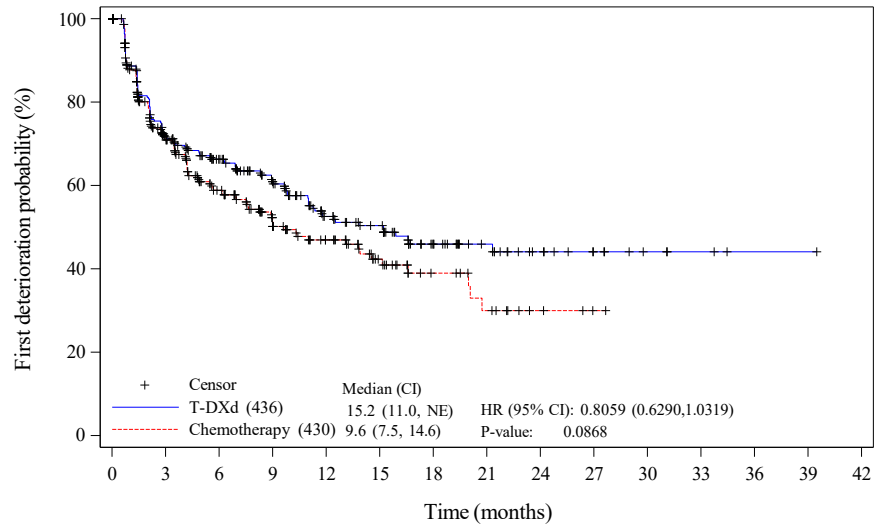
Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Diarrhea



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10DEC2024 10:29; Program name: F.2.11.5_EORTC_C30_TTFDet_FAS.sas; Output name: F.2.11.5_EORTC_C30_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.5 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Common Symptoms/Financial Difficulties



Patients still at risk:

T-DXd(436)	436	183	148	117	77	64	38	25	15	9	5	3	1	1	0
Chemotherapy (430)	430	167	111	74	50	30	16	10	4	1	0				

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 10DEC2024 10:29; Program name: F.2.11.5_EORTC_C30_TTFDet_FAS.sas; Output name: F.2.11.5_EORTC_C30_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.11.2 EORTC-QLQ-C30 – Zeit bis zur erstmaligen Verschlechterung – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

Daiichi Sankyo Europe GmbH
Data Intelligence – Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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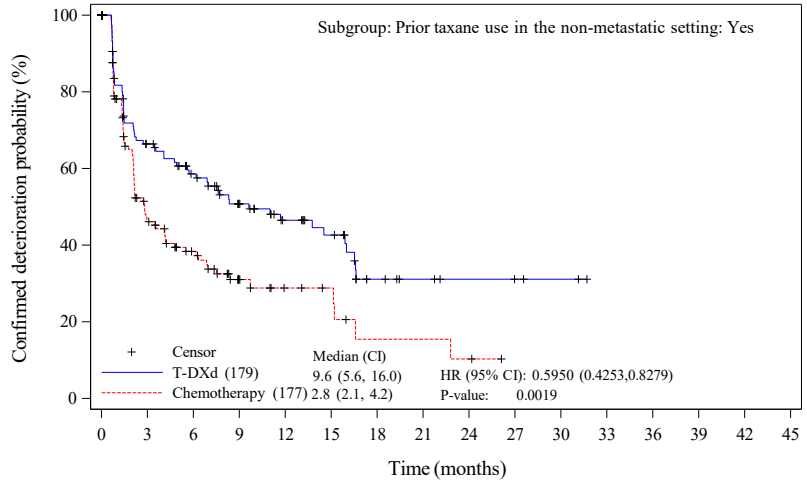
Final
Statistical analyses for AMNOG (HTA Germany)

Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Physical Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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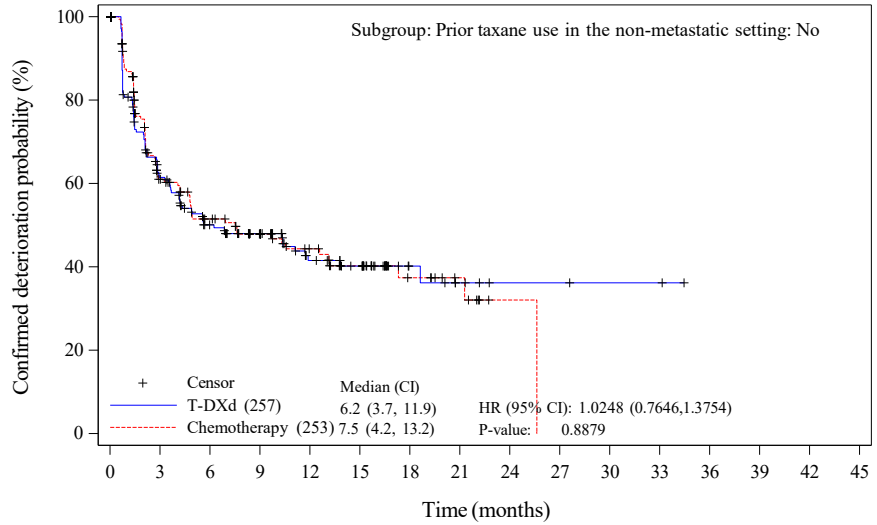
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Physical Functioning



Patients still at risk:

T-DXd(257)	257	101	72	57	35	28	10	6	3	3	2	2	0
Chemotherapy (253)	253	83	61	48	34	24	12	7	1	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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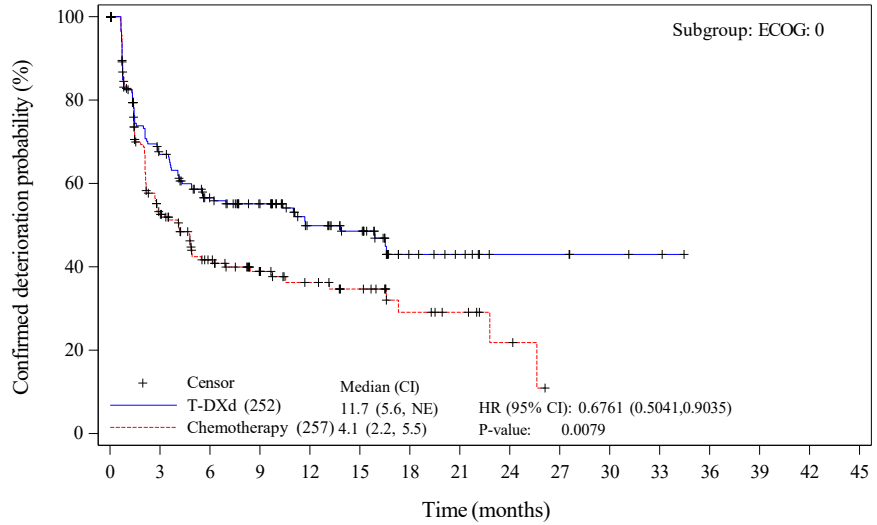
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Physical Functioning



Patients still at risk:

T-DXd(252)	252	106	79	66	44	36	14	10	5	5	3	2	0
Chemotherapy (257)	257	81	51	34	25	19	10	7	3	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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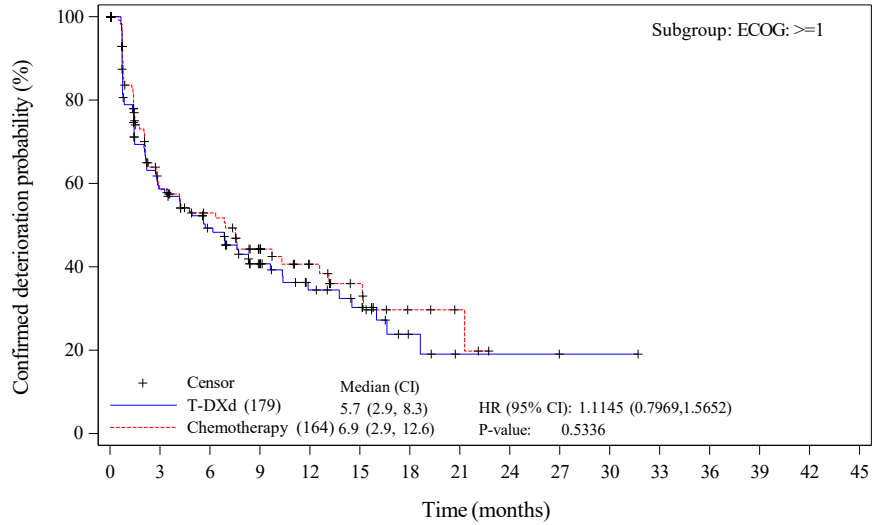
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Physical Functioning



Patients still at risk:

T-DXd(179)	179	66	49	31	19	14	5	2	2	1	1	0
Chemotherapy (164)	164	54	44	29	18	12	5	3	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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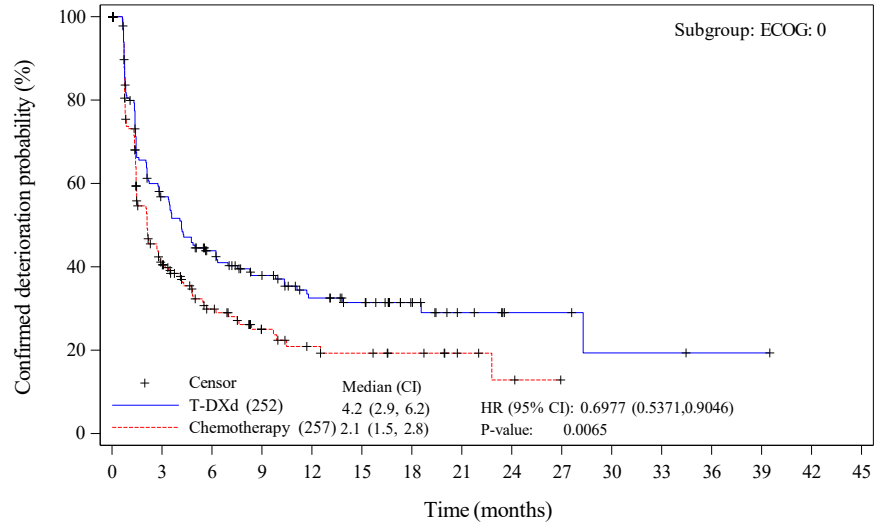
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Role Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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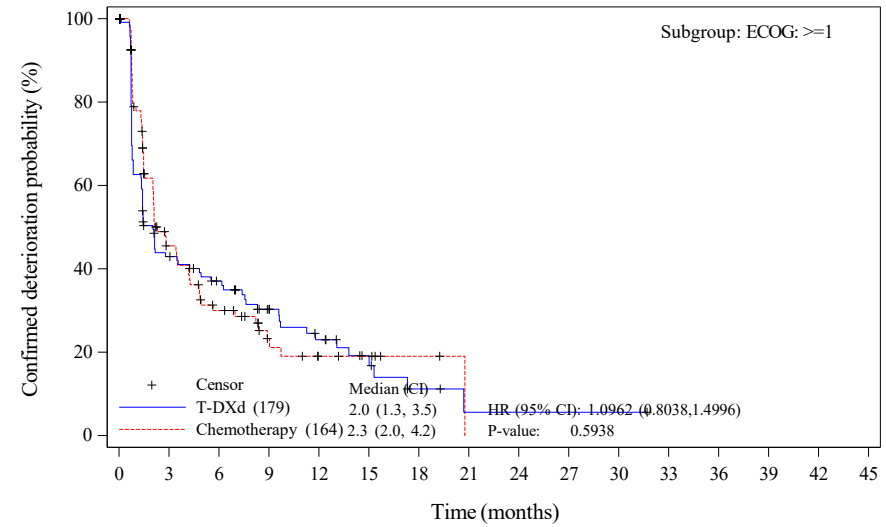
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Role Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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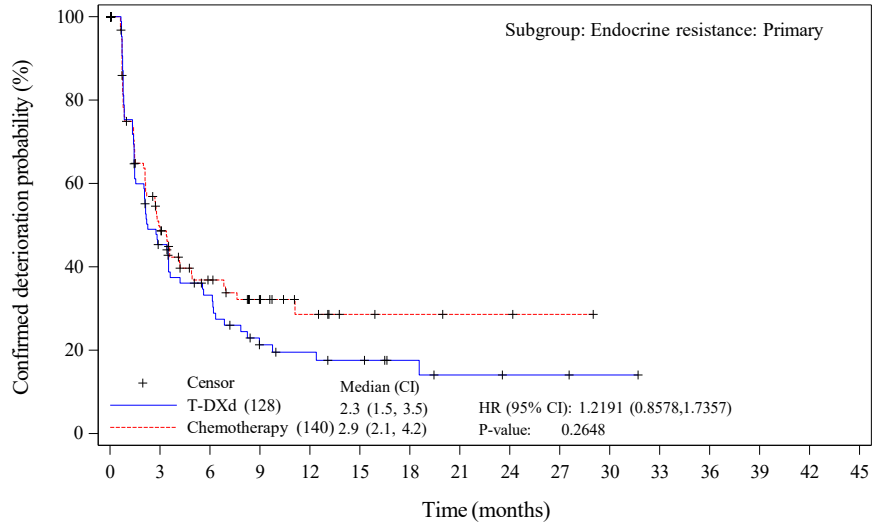
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Social Functioning



Patients still at risk:

T-DXd(128)	128	36	23	12	10	8	5	3	2	2	1	0
Chemotherapy (140)	140	41	25	14	8	4	3	2	2	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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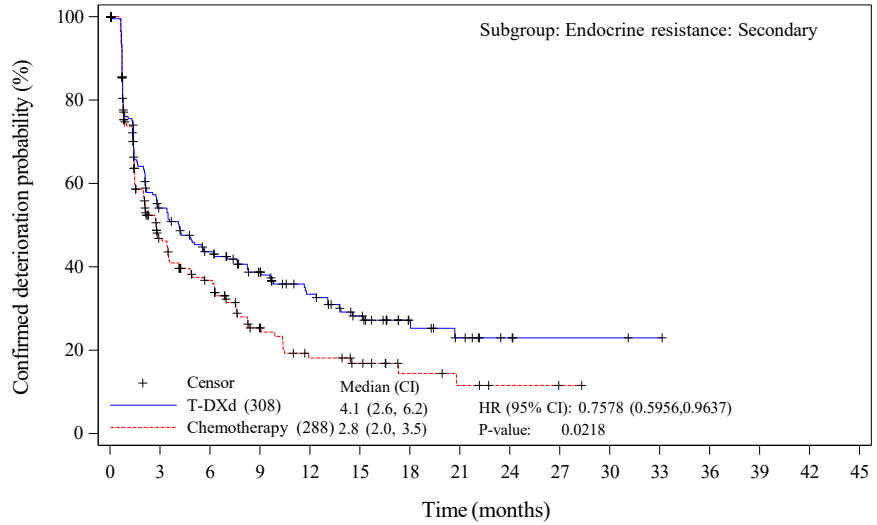
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Social Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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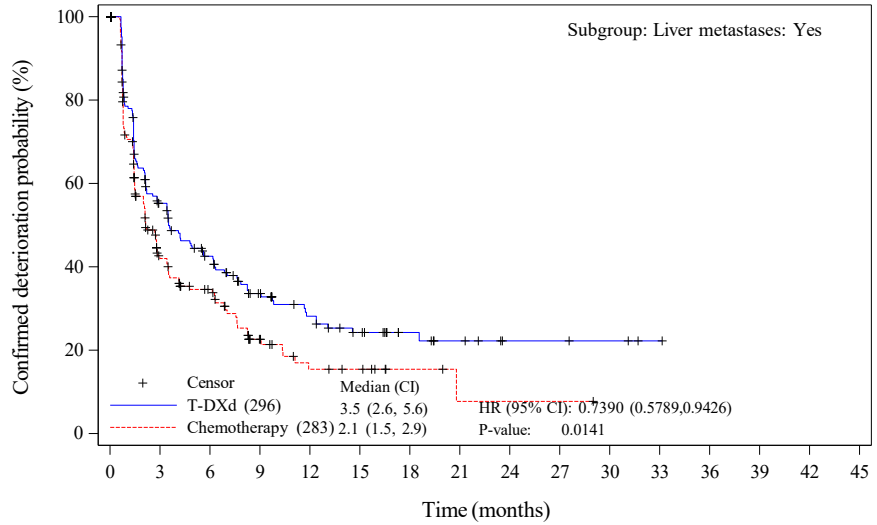
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Social Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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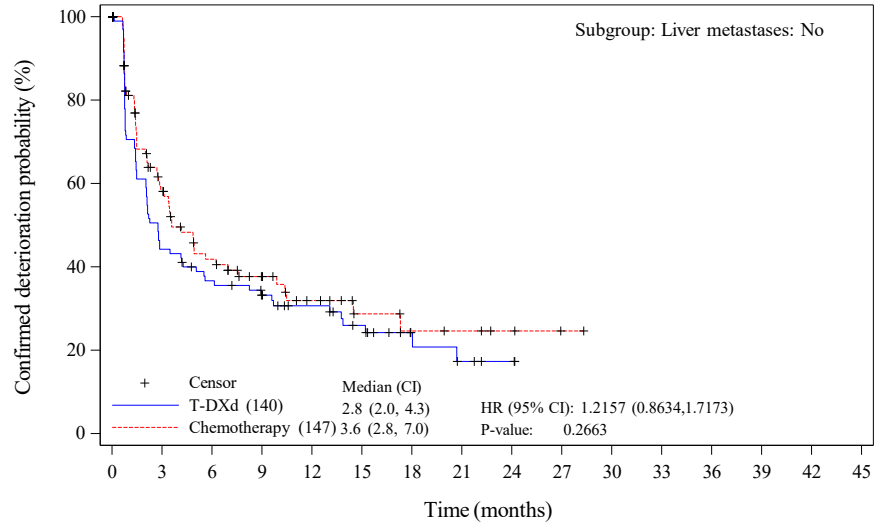
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Social Functioning



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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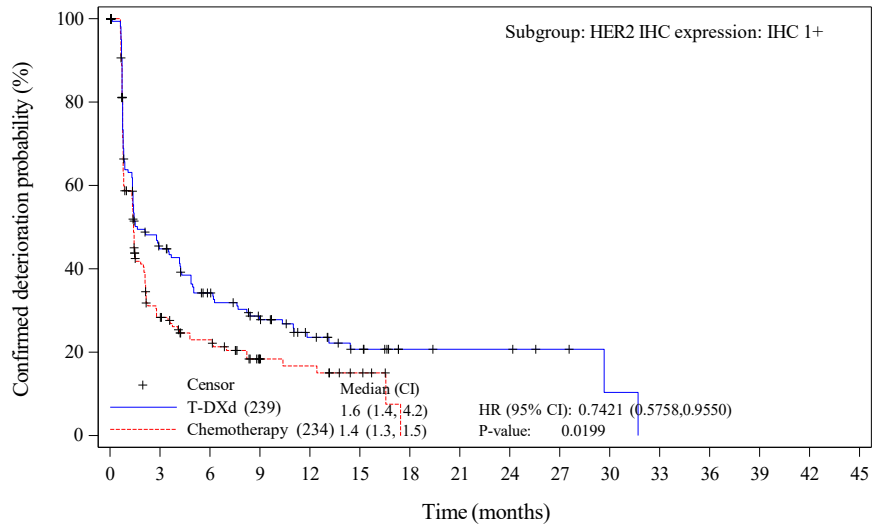
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Fatigue



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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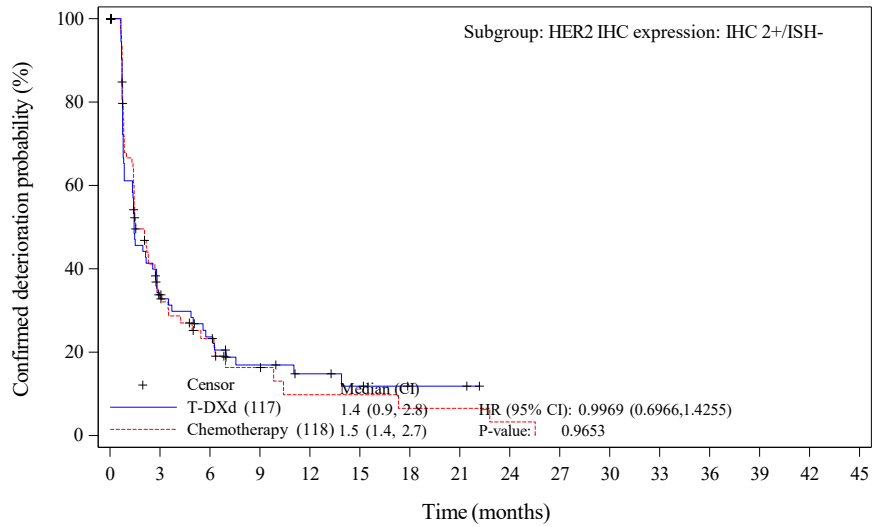
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Fatigue



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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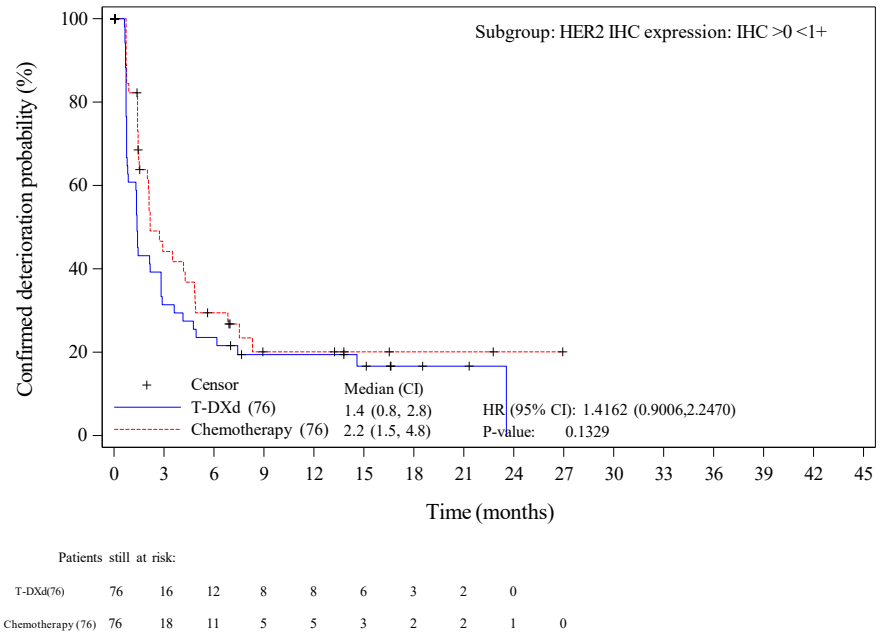
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Fatigue



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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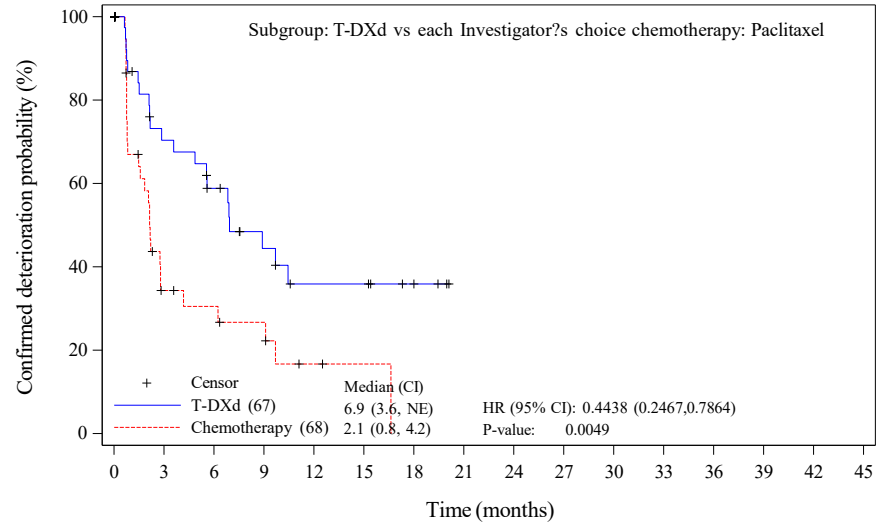
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Pain



Patients still at risk:

T-DXd(67)	67	25	18	11	7	7	4	0
Chemotherapy (68)	68	10	8	6	2	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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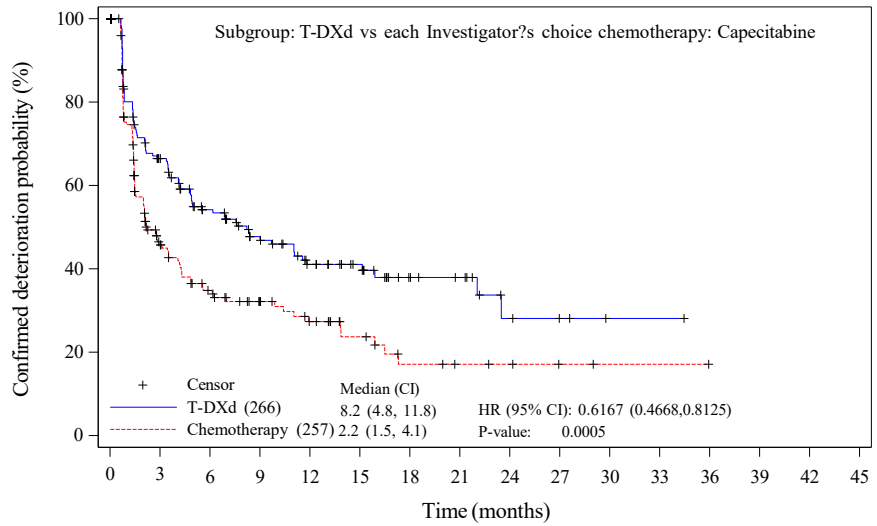
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Pain



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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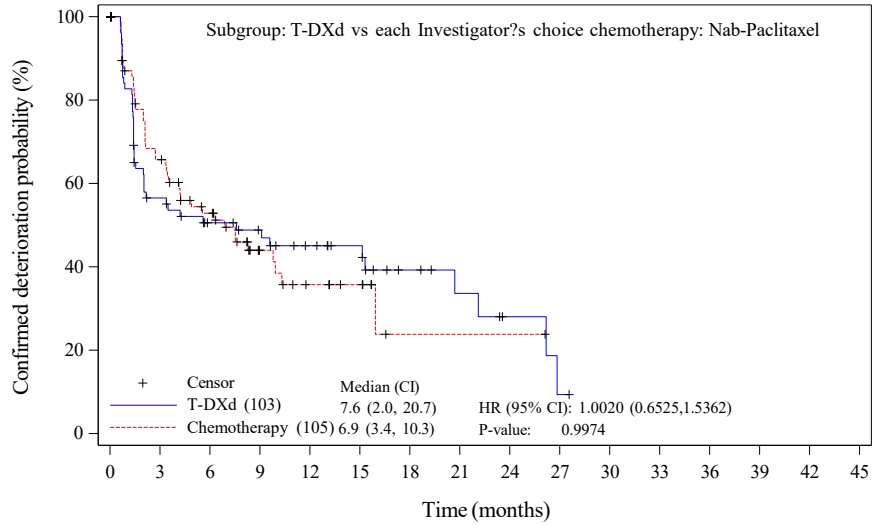
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Pain



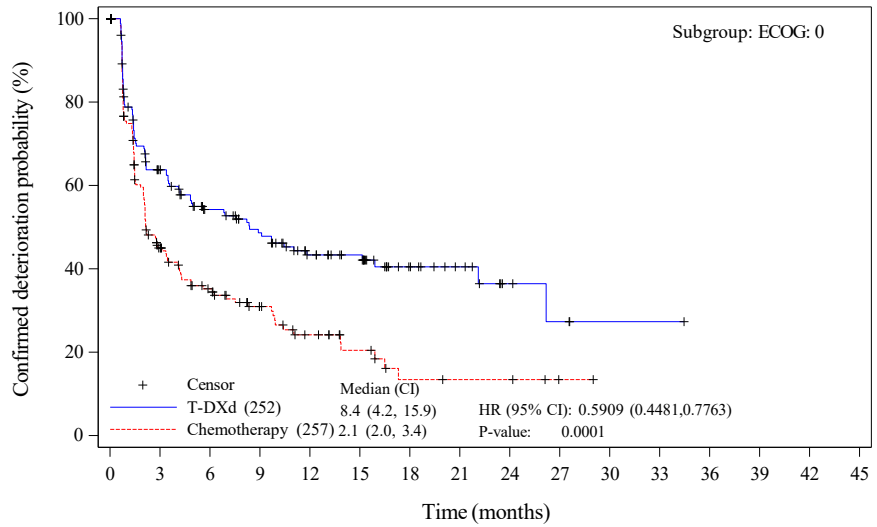
Patients still at risk:

T-DXd(103)	103	39	30	26	20	16	9	6	3	1	0
Chemotherapy (105)	105	49	34	16	10	7	1	1	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 02AUG2024 7:49; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Pain



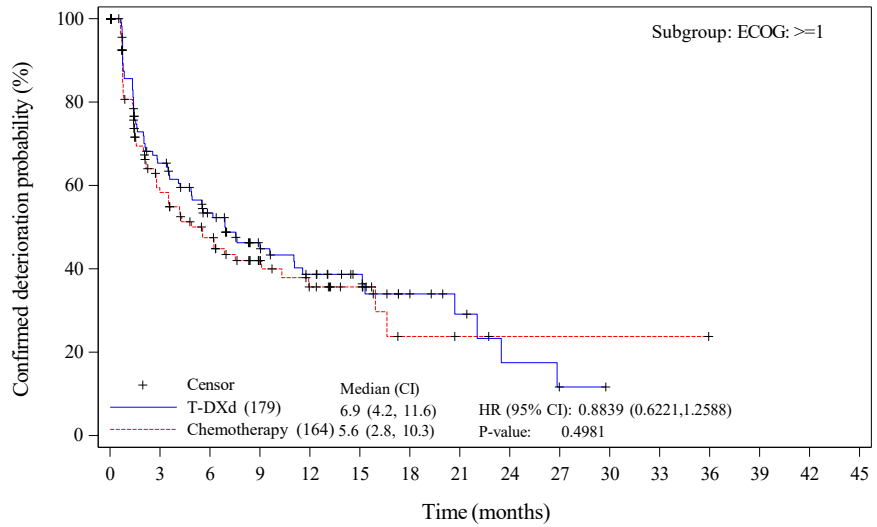
Patients still at risk:

T-DXd(252)	252	97	72	59	42	35	18	12	5	3	1	1	0
Chemotherapy (257)	257	69	46	29	18	11	5	4	4	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 02AUG2024 7:49; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Pain



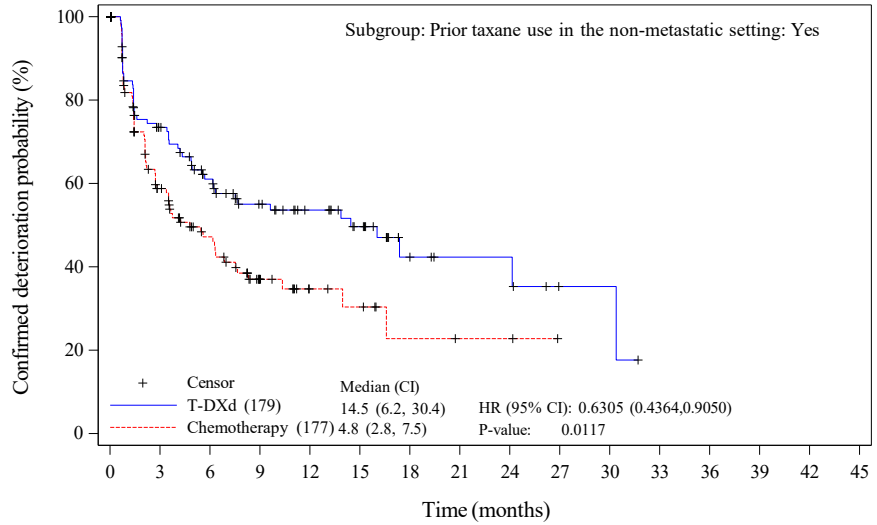
Patients still at risk:

T-DXd(179)	179	69	48	32	24	17	10	6	3	1	0	
Chemotherapy (164)	164	51	37	22	15	10	3	2	1	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 02AUG2024 7:49; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Insomnia



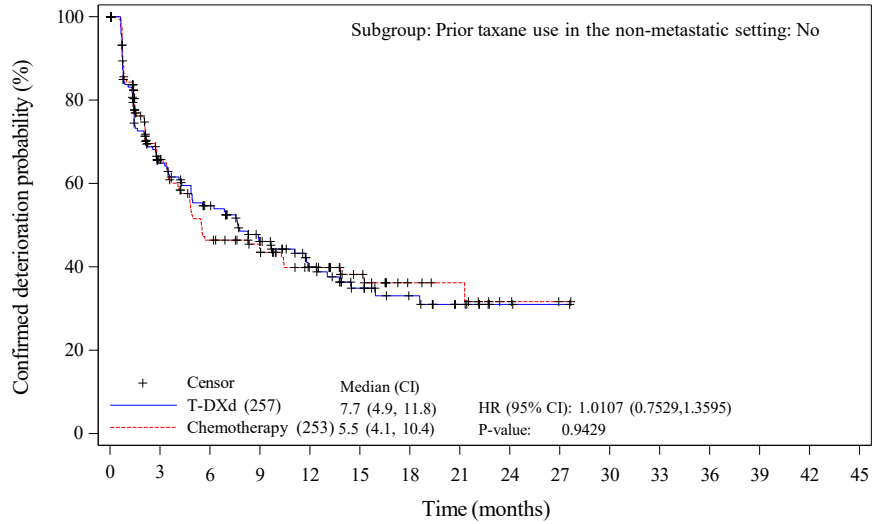
Patients still at risk:

T-DXd(179)	179	74	54	40	31	23	9	6	6	2	2	0
Chemotherapy (177)	177	61	39	18	9	7	3	2	2	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 02AUG2024 7:49; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Insomnia



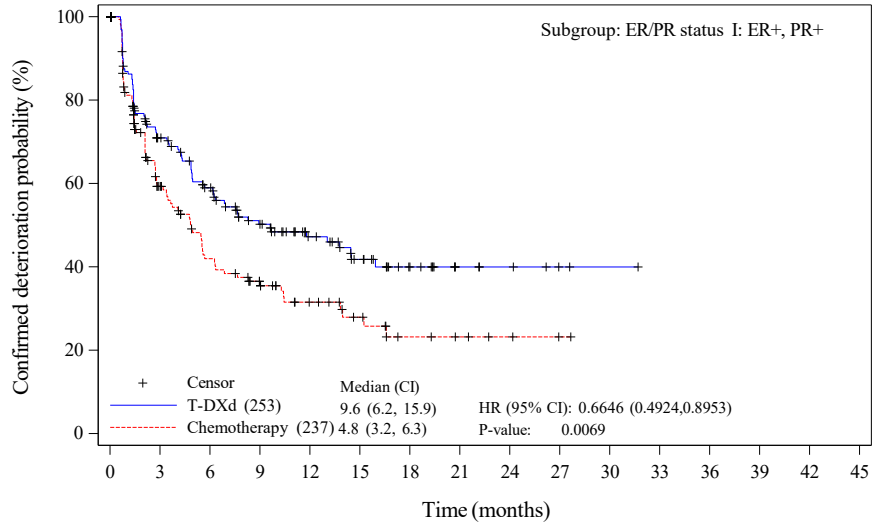
Patients still at risk:

T-DXd(257)	257	98	76	55	35	23	16	8	2	1	0
Chemotherapy (253)	253	83	54	45	30	20	10	8	3	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 02AUG2024 7:49; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Insomnia



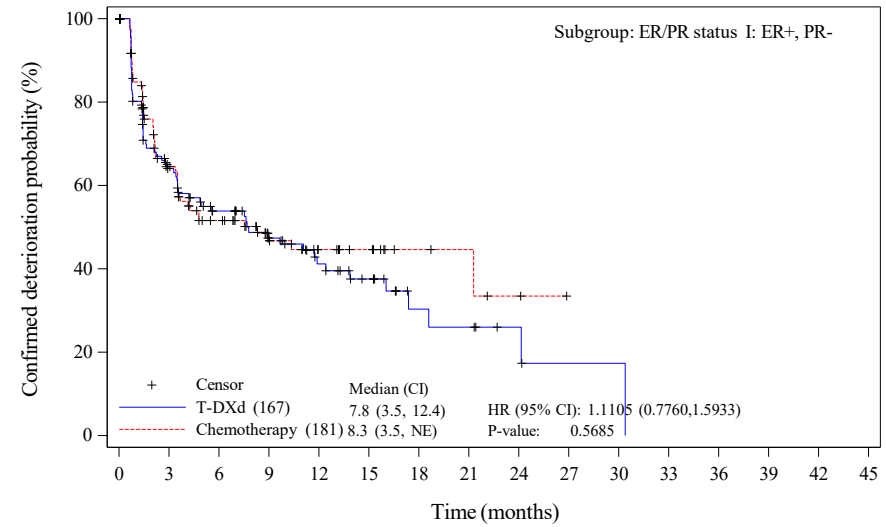
Patients still at risk:

T-DXd(253)	253	105	80	58	39	27	16	7	5	2	1	0
Chemotherapy (237)	237	73	47	34	21	14	7	5	3	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 02AUG2024 7:49; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Insomnia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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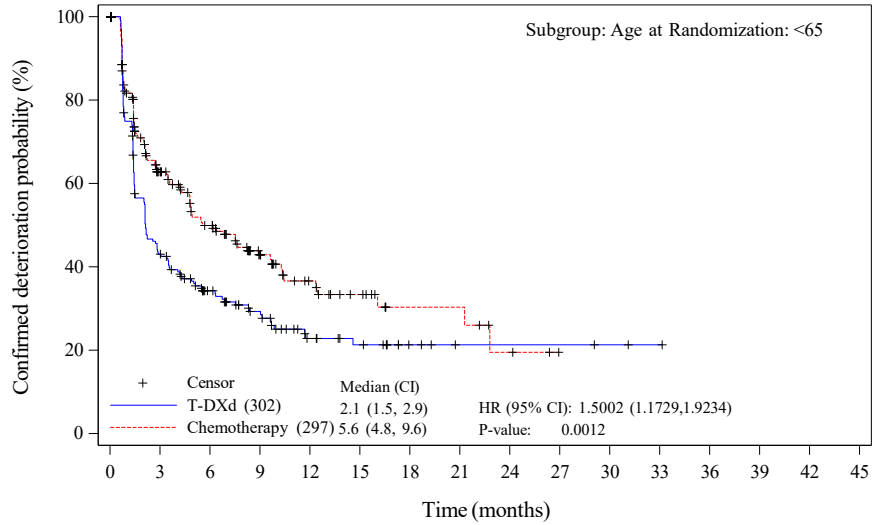
Run date: 02AUG2024 7:49; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Appetite Loss



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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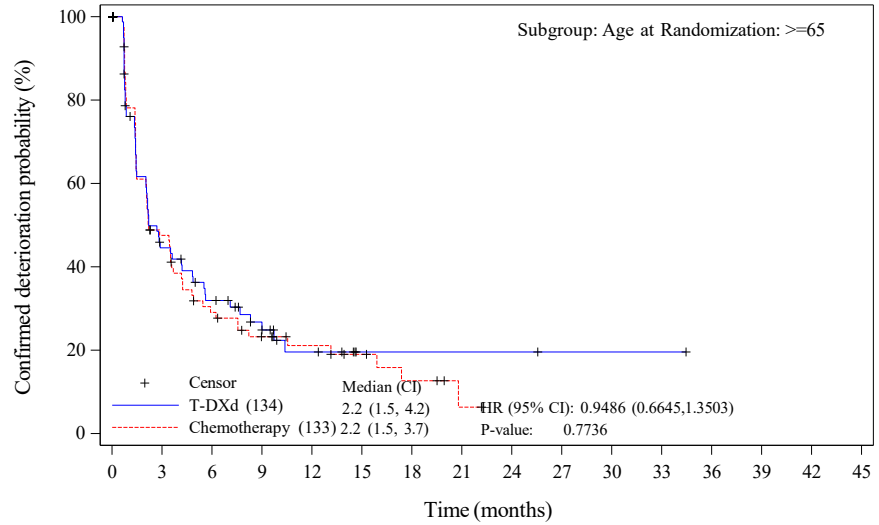
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Appetite Loss



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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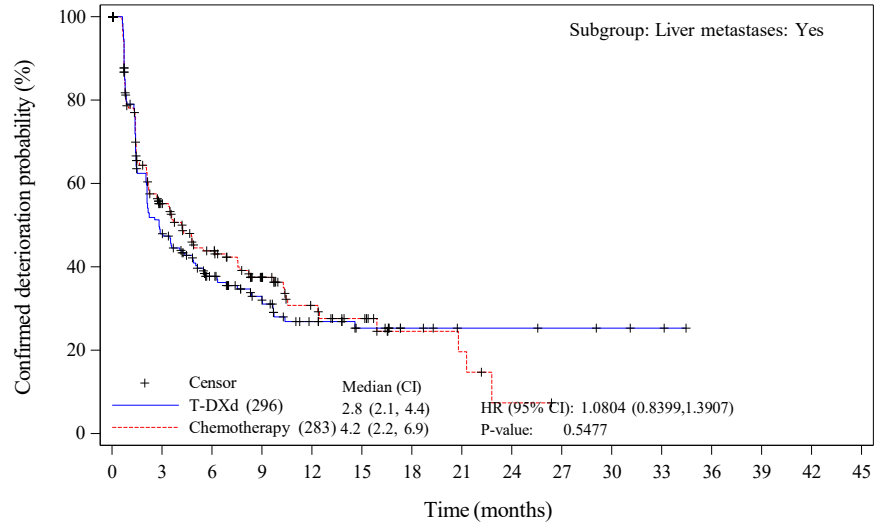
Run date: 02AUG2024 7:50; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Appetite Loss



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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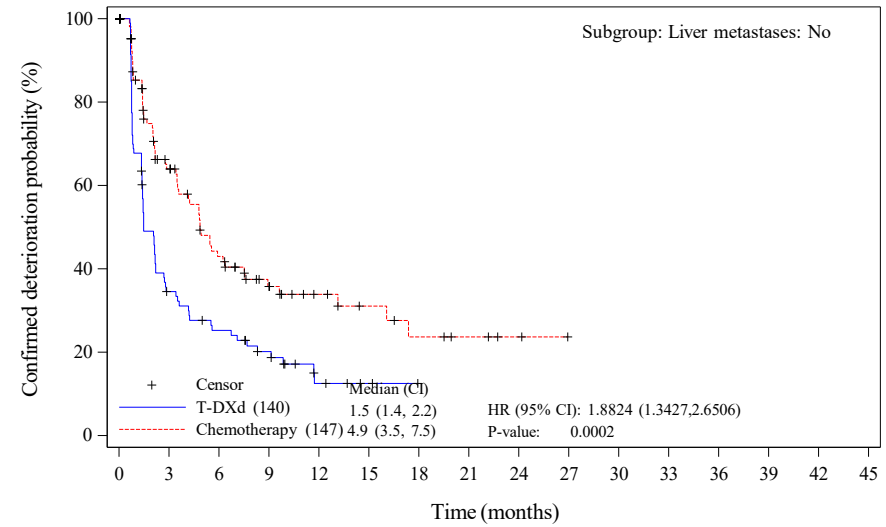
Run date: 02AUG2024 7:50; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

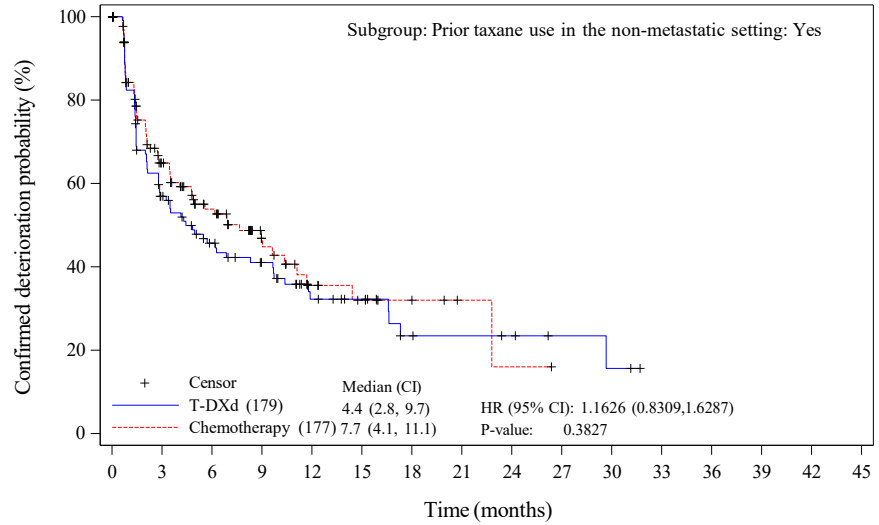
Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Appetite Loss



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 02AUG2024 7:50; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Diarrhea



Patients still at risk:

T-DXd(179)	179	59	41	32	18	14	7	6	5	3	2	0
Chemotherapy (177)	177	70	46	23	12	8	5	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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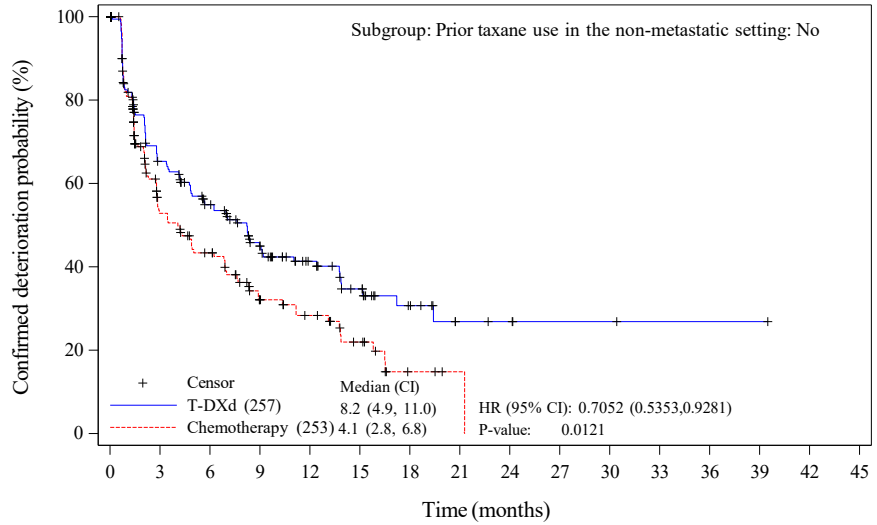
Run date: 02AUG2024 7:50; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.2 EORTC-QLQ-C30 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Common Symptoms/Diarrhea



Patients still at risk:

T-DXd(257)	257	104	79	54	35	23	12	5	4	2	2	1	1	1	0
Chemotherapy (253)	253	69	52	28	21	12	3	1	0						

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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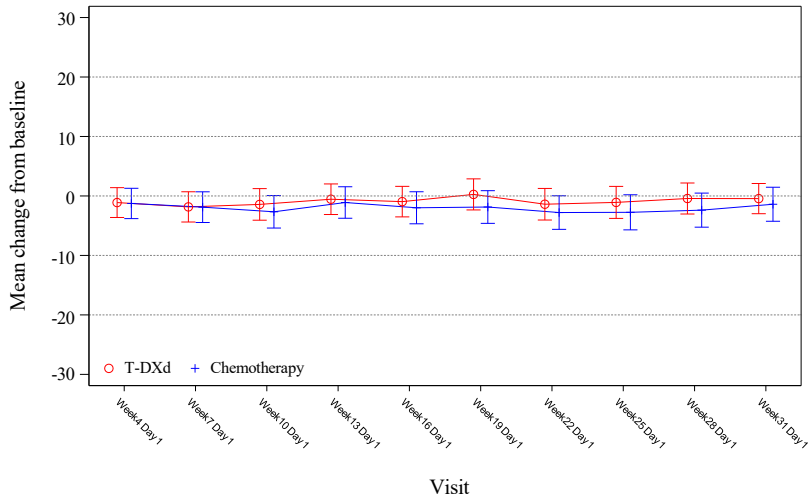
Run date: 02AUG2024 7:50; Program name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.sas; Output name: F.2.11.6_EORTC_C30_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.11.9 EORTC-QLQ-C30 – Mean change from baseline-Plot – FAS

Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Global Health Status
Mean baseline values: T-Dxd:69.5; Chemotherapy:65.9



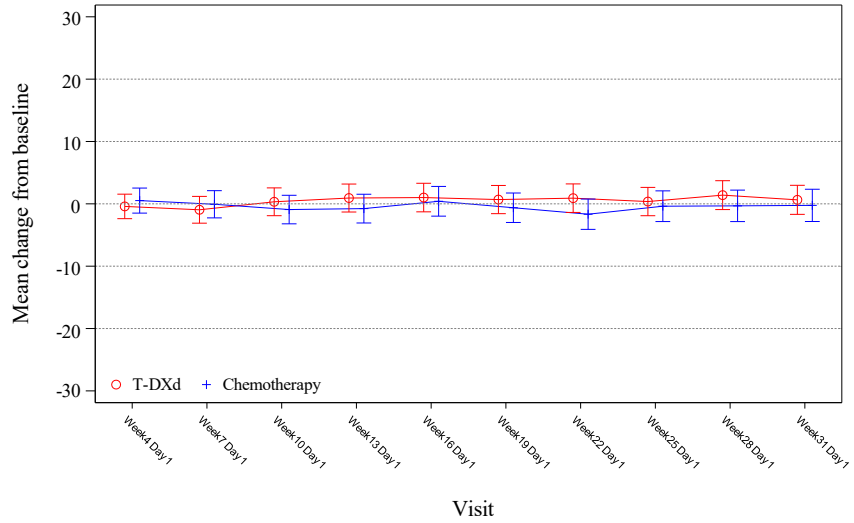
Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	211	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 31JUL2024 7:43; Program name: F.2.11.9_EORTC_CHG_FAS.sas; Output name: F.2.11.9_EORTC_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Functional Scales/Physical Functioning
Mean baseline values: T-Dxd:80.7; Chemotherapy:79.6



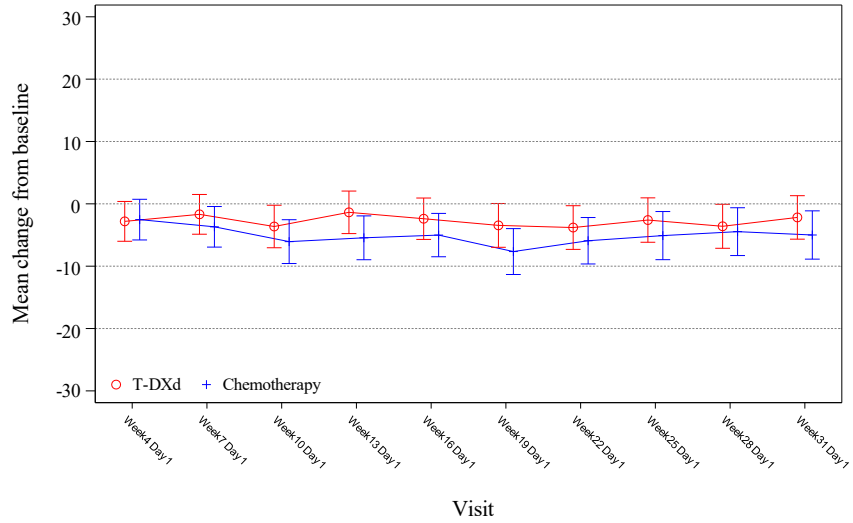
Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	210	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 31JUL2024 7:43; Program name: F.2.11.9_EORTC_CHG_FAS.sas; Output name: F.2.11.9_EORTC_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Functional Scales/Role Functioning
Mean baseline values: T-Dxd:80.0; Chemotherapy:79.7



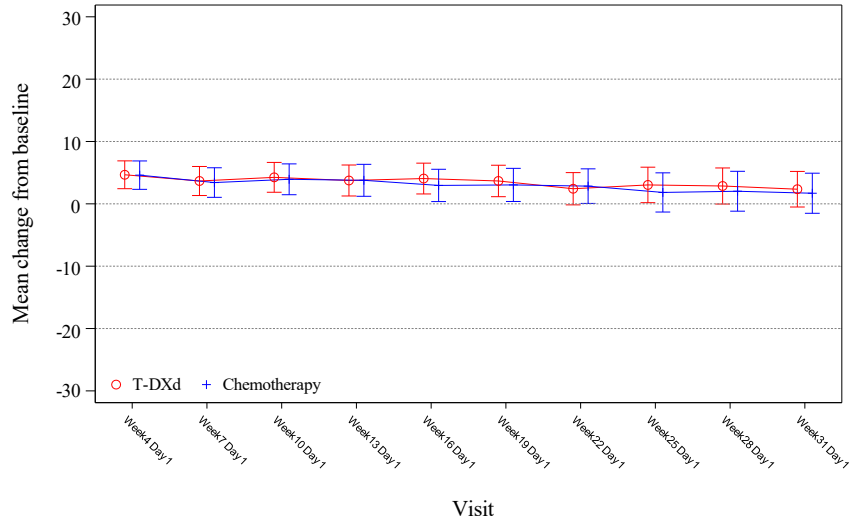
Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	210	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 31JUL2024 7:43; Program name: F.2.11.9_EORTC_CHG_FAS.sas; Output name: F.2.11.9_EORTC_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Functional Scales/Emotional Functioning
Mean baseline values: T-Dxd:73.5; Chemotherapy:71.8



Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	211	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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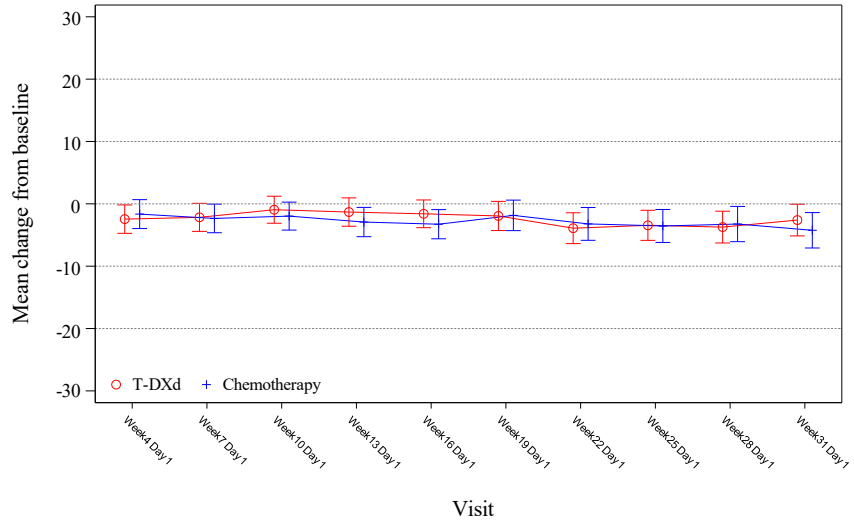
Run date: 31JUL2024 7:43; Program name: F.2.11.9_EORTC_CHG_FAS.sas; Output name: F.2.11.9_EORTC_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Functional Scales/Cognitive Functioning
Mean baseline values: T-Dxd:87.8; Chemotherapy:85.9



Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	211	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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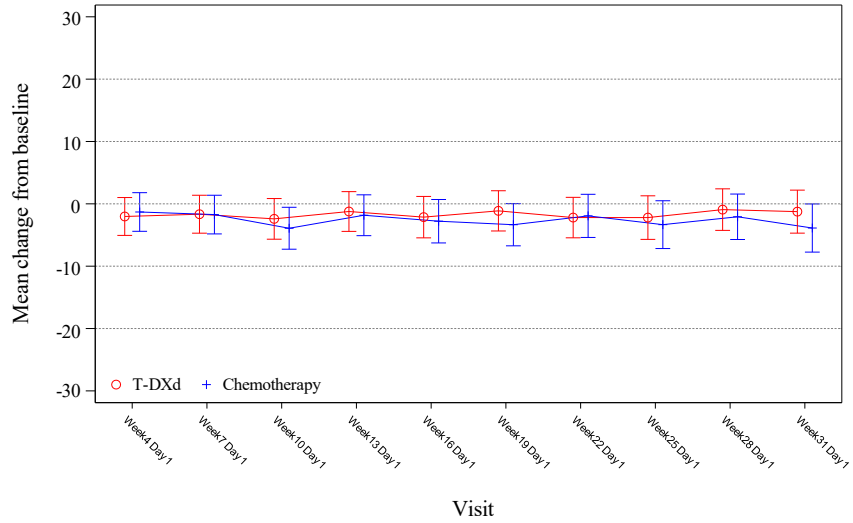
Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Functional Scales/Social Functioning
Mean baseline values: T-Dxd:80.4; Chemotherapy:79.8



Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	211	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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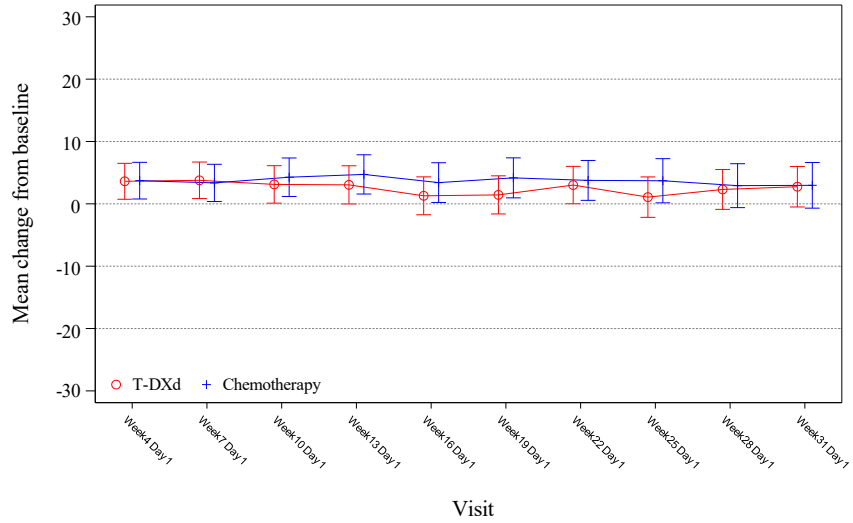
Run date: 31JUL2024 7:43; Program name: F.2.11.9_EORTC_CHG_FAS.sas; Output name: F.2.11.9_EORTC_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Symptom Scales/Fatigue
Mean baseline values: T-Dxd:30.5; Chemotherapy:31.4



Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	210	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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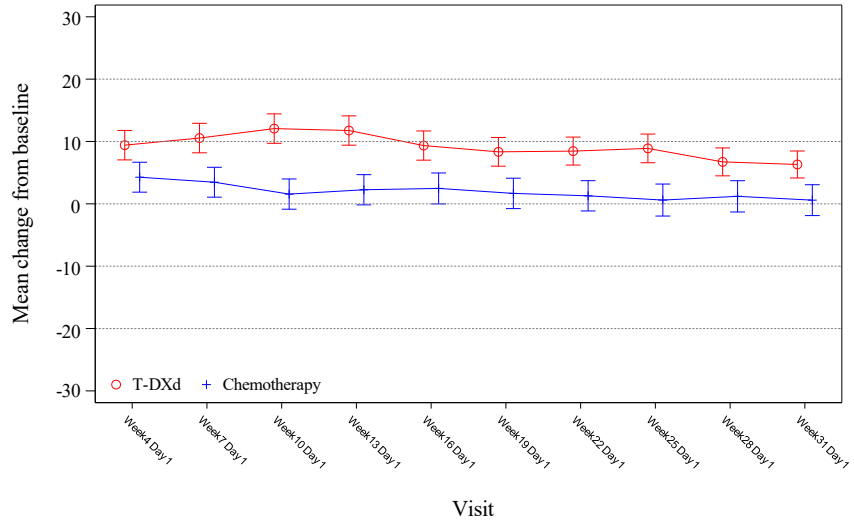
Run date: 31JUL2024 7:43; Program name: F.2.11.9_EORTC_CHG_FAS.sas; Output name: F.2.11.9_EORTC_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Symptom Scales/Nausea and Vomiting
Mean baseline values: T-Dxd:7.0; Chemotherapy:5.7



Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	210	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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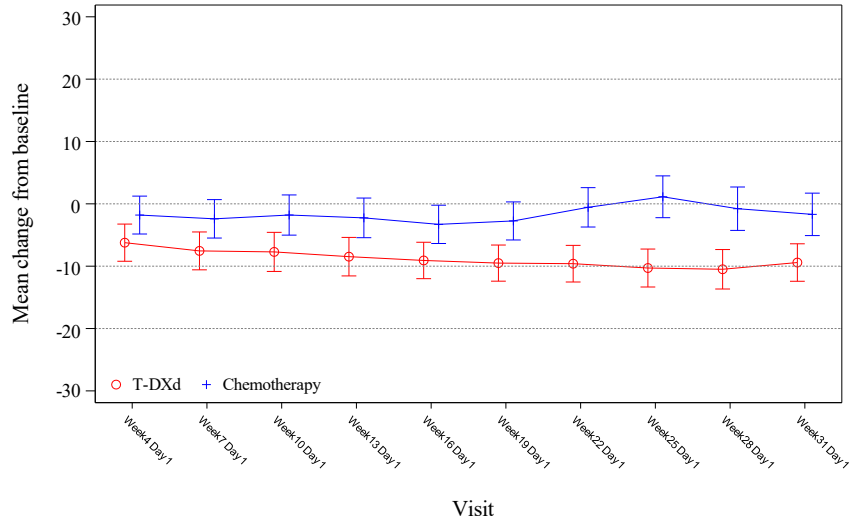
Run date: 31JUL2024 7:43; Program name: F.2.11.9_EORTC_CHG_FAS.sas; Output name: F.2.11.9_EORTC_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Symptom Scales/Pain
Mean baseline values: T-Dxd:25.5; Chemotherapy:28.1



Number of subjects with an observation:

T-DXd	265	248	244	226	224	216	212	204	194	181
Chemotherapy	259	245	226	211	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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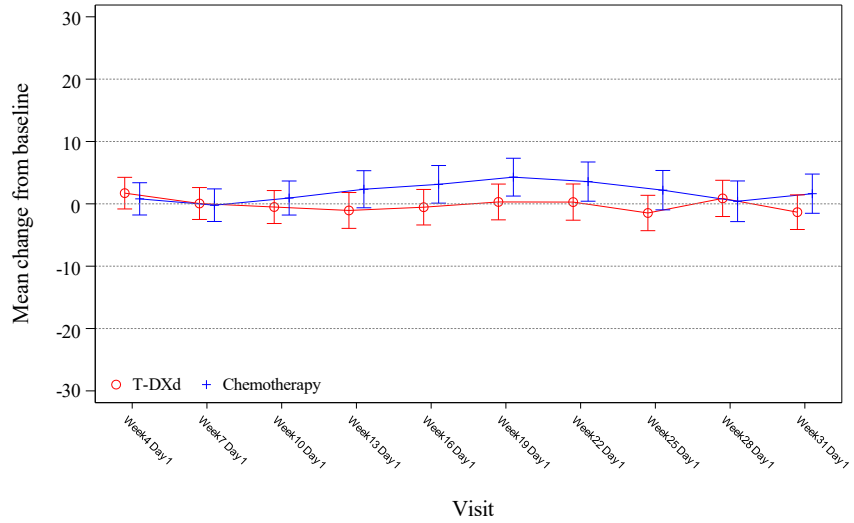
Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Common Symptoms/Dyspnoea
Mean baseline values: T-Dxd:14.4; Chemotherapy:15.1



Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	210	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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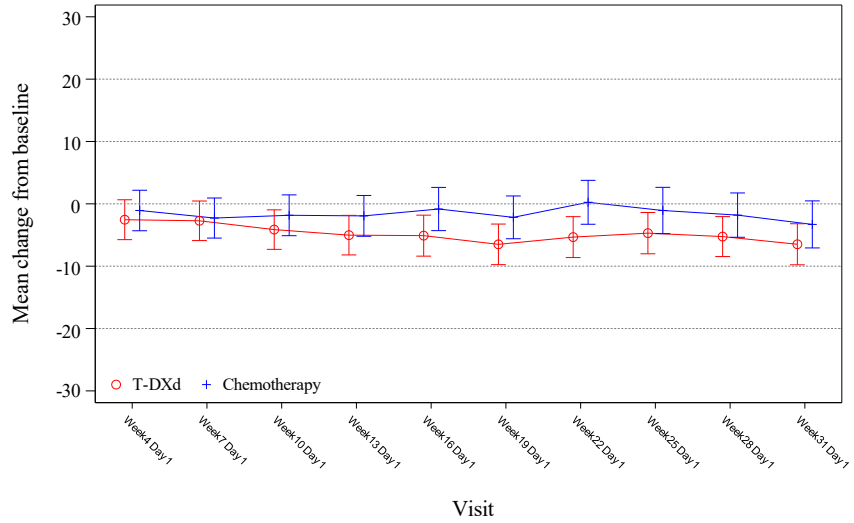
Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Common Symptoms/Insomnia
Mean baseline values: T-Dxd:25.5; Chemotherapy:29.1



Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	210	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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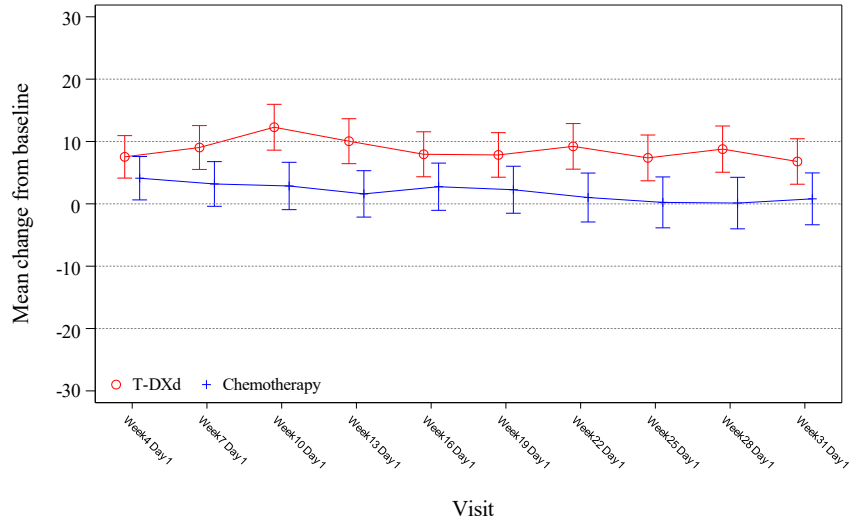
Run date: 31JUL2024 7:43; Program name: F.2.11.9_EORTC_CHG_FAS.sas; Output name: F.2.11.9_EORTC_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Common Symptoms/Appetite Loss
Mean baseline values: T-Dxd:17.5; Chemotherapy:16.4



Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	210	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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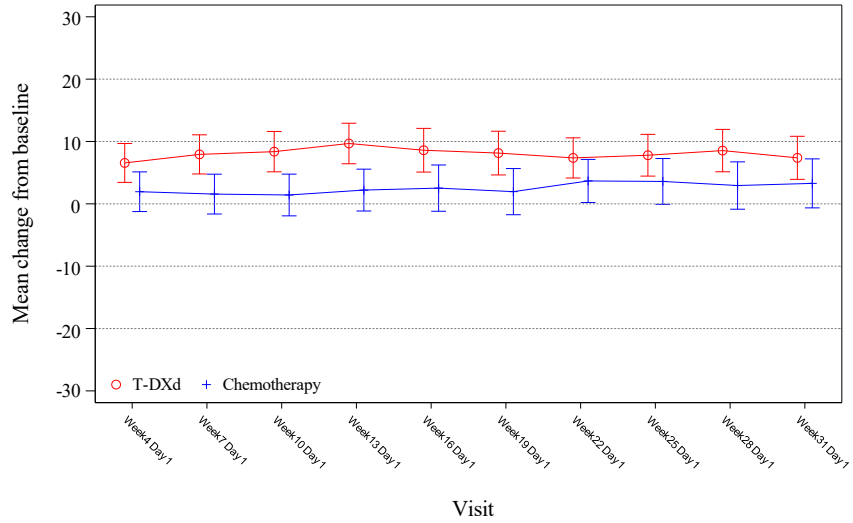
Run date: 31JUL2024 7:43; Program name: F.2.11.9_EORTC_CHG_FAS.sas; Output name: F.2.11.9_EORTC_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Common Symptoms/Constipation
Mean baseline values: T-Dxd:13.0; Chemotherapy:13.0



Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	210	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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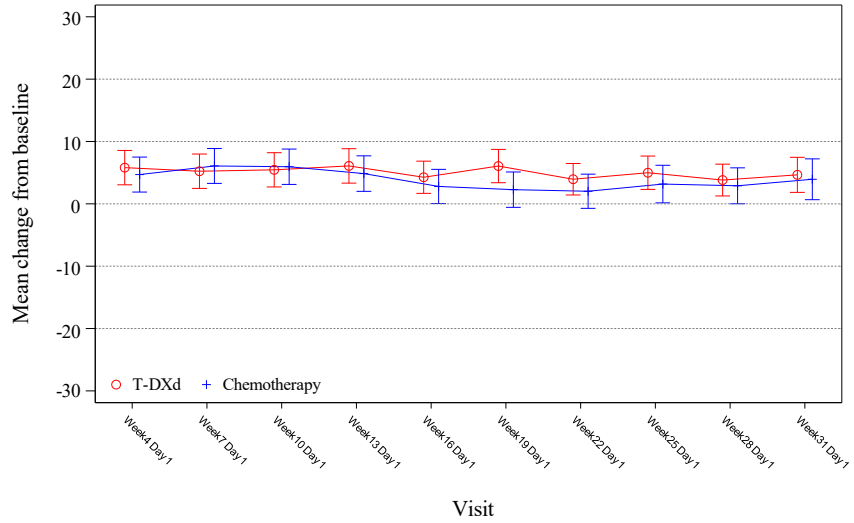
Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Common Symptoms/Diarrhea
Mean baseline values: T-Dxd:4.5; Chemotherapy:6.1



Number of subjects with an observation:

T-DXd	265	247	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	211	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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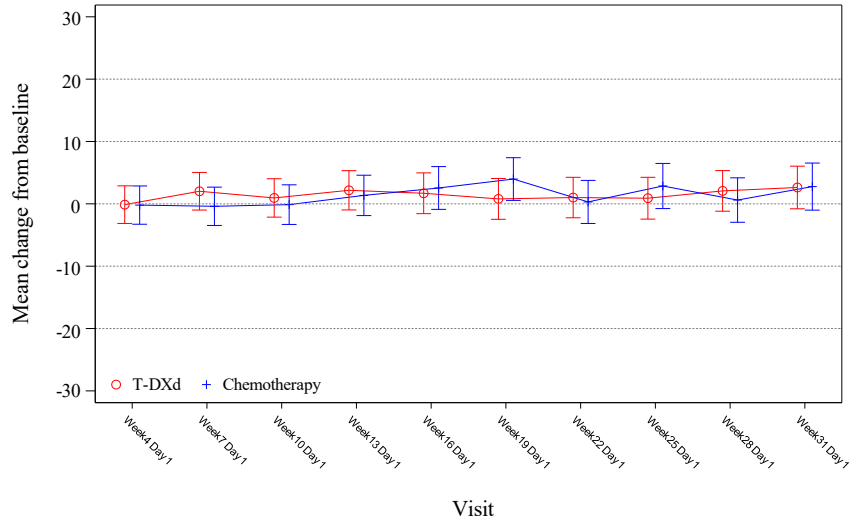
Figure 2.11.9 EORTC-QLQ-C30 - Mean change from baseline- Full Analysis Set
Common Symptoms/Financial Difficulties
Mean baseline values: T-Dxd:19.3; Chemotherapy:18.2



Number of subjects with an observation:

T-DXd	265	248	244	226	224	217	212	204	194	181
Chemotherapy	259	245	226	211	188	188	170	146	137	119

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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Run date: 31JUL2024 7:43; Program name: F.2.11.9_EORTC_CHG_FAS.sas; Output name: F.2.11.9_EORTC_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.11.15 EORTC-QLQ-C30 – Mixed Model for Repeated Measurement – FAS

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Global Health Status			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	-1.11 [-3.62; 1.40]	-1.26 [-3.81; 1.29]	
Standard error	1.28	1.30	
Difference of LS Means [95% CI]			0.15 [-2.80; 3.10]
Standard error for difference			1.50
p-value			0.9203
Hedges' g [95% CI]			0.01 [-0.16; 0.18]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	-1.84 [-4.38; 0.71]	-1.88 [-4.46; 0.70]	
Standard error	1.29	1.31	
Difference of LS Means [95% CI]			0.05 [-2.97; 3.06]
Standard error for difference			1.54
p-value			0.9764
Hedges' g [95% CI]			0.00 [-0.17; 0.18]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	-1.42 [-4.08; 1.23]	-2.66 [-5.39; 0.07]	
Standard error	1.35	1.39	
Difference of LS Means [95% CI]			1.24 [-2.00; 4.48]
Standard error for difference			1.65
p-value			0.4524
Hedges' g [95% CI]			0.06 [-0.12; 0.24]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	211	
LS Means [95% CI]	-0.55 [-3.12; 2.02]	-1.10 [-3.75; 1.55]	
Standard error	1.31	1.35	
Difference of LS Means [95% CI]			0.55 [-2.55; 3.66]
Standard error for difference			1.58
p-value			0.7265
Hedges' g [95% CI]			0.03 [-0.16; 0.22]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	-0.95 [-3.52; 1.61]	-1.99 [-4.68; 0.71]	
Standard error	1.31	1.37	
Difference of LS Means [95% CI]			1.03 [-2.12; 4.18]
Standard error for difference			1.60
p-value			0.5197
Hedges' g [95% CI]			0.05 [-0.14; 0.25]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	0.26 [-2.35; 2.87]	-1.86 [-4.61; 0.89]	
Standard error	1.33	1.40	
Difference of LS Means [95% CI]			2.12 [-1.11; 5.35]
Standard error for difference			1.64
p-value			0.1975
Hedges' g [95% CI]			0.11 [-0.09; 0.30]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	-1.39 [-4.04; 1.26]	-2.79 [-5.62; 0.04]	
Standard error	1.35	1.44	
Difference of LS Means [95% CI]			1.40 [-1.93; 4.73]
Standard error for difference			1.70
p-value			0.4095
Hedges' g [95% CI]			0.07 [-0.13; 0.27]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	-1.08 [-3.77; 1.61]	-2.75 [-5.70; 0.20]	
Standard error	1.37	1.50	
Difference of LS Means [95% CI]			1.67 [-1.81; 5.14]
Standard error for difference			1.77
p-value			0.3458
Hedges' g [95% CI]			0.09 [-0.12; 0.30]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	-0.43 [-3.04; 2.18]	-2.39 [-5.25; 0.48]	
Standard error	1.33	1.46	
Difference of LS Means [95% CI]			1.96 [-1.38; 5.29]
Standard error for difference			1.70
p-value			0.2492
Hedges' g [95% CI]			0.11 [-0.11; 0.33]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	-0.45 [-2.98; 2.09]	-1.39 [-4.25; 1.47]	
Standard error	1.29	1.46	
Difference of LS Means [95% CI]			0.95 [-2.33; 4.23]
Standard error for difference			1.67
p-value			0.5700
Hedges' g [95% CI]			0.06 [-0.18; 0.29]
Average [b]			
n	286	299	
LS Means [95% CI]	-0.90 [-3.03; 1.24]	-2.01 [-4.22; 0.20]	
Standard error	1.09	1.13	
Difference of LS Means [95% CI]			1.11 [-1.23; 3.45]
Standard error for difference			1.19
p-value			0.3506
Hedges' g [95% CI]			0.06 [-0.10; 0.22]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Functional Scales/Physical Functioning			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	-0.41 [-2.38; 1.55]	0.52 [-1.49; 2.53]	
Standard error	1.00	1.02	
Difference of LS Means [95% CI]			-0.94 [-3.12; 1.25]
Standard error for difference			1.11
p-value			0.4008
Hedges' g [95% CI]			-0.06 [-0.23; 0.11]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	-0.95 [-3.10; 1.19]	-0.07 [-2.25; 2.11]	
Standard error	1.09	1.11	
Difference of LS Means [95% CI]			-0.88 [-3.40; 1.63]
Standard error for difference			1.28
p-value			0.4896
Hedges' g [95% CI]			-0.05 [-0.23; 0.13]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	0.33 [-1.90; 2.56]	-0.92 [-3.21; 1.37]	
Standard error	1.14	1.17	
Difference of LS Means [95% CI]			1.25 [-1.43; 3.92]
Standard error for difference			1.36
p-value			0.3604
Hedges' g [95% CI]			0.07 [-0.11; 0.25]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	210	
LS Means [95% CI]	0.93 [-1.31; 3.17]	-0.76 [-3.07; 1.54]	
Standard error	1.14	1.17	
Difference of LS Means [95% CI]			1.70 [-1.00; 4.40]
Standard error for difference			1.37
p-value			0.2174
Hedges' g [95% CI]			0.10 [-0.09; 0.29]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	1.01 [-1.28; 3.30]	0.41 [-1.97; 2.79]	
Standard error	1.17	1.21	
Difference of LS Means [95% CI]			0.60 [-2.21; 3.41]
Standard error for difference			1.43
p-value			0.6752
Hedges' g [95% CI]			0.03 [-0.16; 0.23]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	0.69 [-1.58; 2.95]	-0.63 [-2.99; 1.74]	
Standard error	1.15	1.20	
Difference of LS Means [95% CI]			1.31 [-1.46; 4.08]
Standard error for difference			1.41
p-value			0.3527
Hedges' g [95% CI]			0.08 [-0.12; 0.27]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	0.91 [-1.38; 3.20]	-1.66 [-4.10; 0.77]	
Standard error	1.16	1.24	
Difference of LS Means [95% CI]			2.57 [-0.28; 5.43]
Standard error for difference			1.45
p-value			0.0767
Hedges' g [95% CI]			0.15 [-0.05; 0.36]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	0.37 [-1.90; 2.64]	-0.38 [-2.84; 2.08]	
Standard error	1.16	1.25	
Difference of LS Means [95% CI]			0.75 [-2.12; 3.62]
Standard error for difference			1.46
p-value			0.6090
Hedges' g [95% CI]			0.05 [-0.17; 0.26]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	1.40 [-0.92; 3.71]	-0.32 [-2.85; 2.20]	
Standard error	1.18	1.29	
Difference of LS Means [95% CI]			1.72 [-1.24; 4.68]
Standard error for difference			1.50
p-value			0.2542
Hedges' g [95% CI]			0.11 [-0.11; 0.33]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	0.64 [-1.69; 2.97]	-0.25 [-2.83; 2.34]	
Standard error	1.18	1.32	
Difference of LS Means [95% CI]			0.89 [-2.13; 3.91]
Standard error for difference			1.54
p-value			0.5630
Hedges' g [95% CI]			0.06 [-0.17; 0.29]
Average [b]			
n	286	299	
LS Means [95% CI]	0.49 [-1.43; 2.41]	-0.41 [-2.39; 1.58]	
Standard error	0.98	1.01	
Difference of LS Means [95% CI]			0.90 [-1.24; 3.03]
Standard error for difference			1.09
p-value			0.4102
Hedges' g [95% CI]			0.05 [-0.11; 0.21]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Functional Scales/Role Functioning			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	-2.81 [-6.00; 0.38]	-2.53 [-5.79; 0.73]	
Standard error	1.63	1.66	
Difference of LS Means [95% CI]			-0.28 [-3.96; 3.40]
Standard error for difference			1.87
p-value			0.8812
Hedges' g [95% CI]			-0.01 [-0.18; 0.16]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	-1.68 [-4.87; 1.50]	-3.68 [-6.94; -0.43]	
Standard error	1.62	1.66	
Difference of LS Means [95% CI]			2.00 [-1.69; 5.69]
Standard error for difference			1.88
p-value			0.2871
Hedges' g [95% CI]			0.08 [-0.10; 0.25]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	-3.63 [-7.04; -0.22]	-6.06 [-9.57; -2.54]	
Standard error	1.74	1.79	
Difference of LS Means [95% CI]			2.42 [-1.67; 6.52]
Standard error for difference			2.09
p-value			0.2456
Hedges' g [95% CI]			0.09 [-0.09; 0.27]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	210	
LS Means [95% CI]	-1.36 [-4.77; 2.05]	-5.45 [-8.96; -1.93]	
Standard error	1.74	1.79	
Difference of LS Means [95% CI]			4.09 [-0.02; 8.19]
Standard error for difference			2.09
p-value			0.0510
Hedges' g [95% CI]			0.16 [-0.03; 0.34]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	-2.39 [-5.71; 0.93]	-5.01 [-8.49; -1.54]	
Standard error	1.69	1.77	
Difference of LS Means [95% CI]			2.63 [-1.38; 6.63]
Standard error for difference			2.04
p-value			0.1982
Hedges' g [95% CI]			0.11 [-0.09; 0.30]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	-3.46 [-6.97; 0.06]	-7.65 [-11.33; -3.97]	
Standard error	1.79	1.87	
Difference of LS Means [95% CI]			4.20 [-0.14; 8.53]
Standard error for difference			2.21
p-value			0.0577
Hedges' g [95% CI]			0.16 [-0.03; 0.36]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	-3.80 [-7.31; -0.30]	-5.92 [-9.64; -2.19]	
Standard error	1.78	1.90	
Difference of LS Means [95% CI]			2.12 [-2.25; 6.48]
Standard error for difference			2.22
p-value			0.3414
Hedges' g [95% CI]			0.08 [-0.12; 0.28]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	-2.60 [-6.16; 0.96]	-5.09 [-8.95; -1.23]	
Standard error	1.81	1.97	
Difference of LS Means [95% CI]			2.49 [-2.04; 7.02]
Standard error for difference			2.31
p-value			0.2800
Hedges' g [95% CI]			0.10 [-0.11; 0.31]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	-3.60 [-7.13; -0.07]	-4.46 [-8.29; -0.63]	
Standard error	1.80	1.95	
Difference of LS Means [95% CI]			0.86 [-3.62; 5.34]
Standard error for difference			2.28
p-value			0.7065
Hedges' g [95% CI]			0.04 [-0.18; 0.25]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	-2.18 [-5.67; 1.31]	-5.00 [-8.87; -1.12]	
Standard error	1.78	1.97	
Difference of LS Means [95% CI]			2.82 [-1.67; 7.31]
Standard error for difference			2.28
p-value			0.2178
Hedges' g [95% CI]			0.12 [-0.11; 0.35]
Average [b]			
n	286	299	
LS Means [95% CI]	-2.75 [-5.65; 0.14]	-5.09 [-8.08; -2.09]	
Standard error	1.47	1.52	
Difference of LS Means [95% CI]			2.33 [-0.86; 5.53]
Standard error for difference			1.63
p-value			0.1517
Hedges' g [95% CI]			0.09 [-0.07; 0.25]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Functional Scales/Emotional Functioning			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	4.66 [2.43; 6.89]	4.60 [2.32; 6.88]	
Standard error	1.14	1.16	
Difference of LS Means [95% CI]			0.06 [-2.50; 2.61]
Standard error for difference			1.30
p-value			0.9635
Hedges' g [95% CI]			0.00 [-0.17; 0.17]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	3.66 [1.33; 5.99]	3.42 [1.04; 5.79]	
Standard error	1.19	1.21	
Difference of LS Means [95% CI]			0.25 [-2.49; 2.98]
Standard error for difference			1.39
p-value			0.8588
Hedges' g [95% CI]			0.01 [-0.16; 0.19]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	4.25 [1.86; 6.64]	3.94 [1.46; 6.41]	
Standard error	1.22	1.26	
Difference of LS Means [95% CI]			0.31 [-2.56; 3.19]
Standard error for difference			1.46
p-value			0.8305
Hedges' g [95% CI]			0.02 [-0.16; 0.20]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	211	
LS Means [95% CI]	3.75 [1.26; 6.23]	3.77 [1.21; 6.34]	
Standard error	1.26	1.31	
Difference of LS Means [95% CI]			-0.03 [-3.06; 3.01]
Standard error for difference			1.54
p-value			0.9851
Hedges' g [95% CI]			-0.00 [-0.19; 0.19]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	4.06 [1.59; 6.53]	2.95 [0.36; 5.55]	
Standard error	1.26	1.32	
Difference of LS Means [95% CI]			1.10 [-1.95; 4.15]
Standard error for difference			1.55
p-value			0.4782
Hedges' g [95% CI]			0.06 [-0.13; 0.25]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	3.67 [1.15; 6.19]	3.04 [0.38; 5.69]	
Standard error	1.28	1.35	
Difference of LS Means [95% CI]			0.63 [-2.52; 3.78]
Standard error for difference			1.60
p-value			0.6932
Hedges' g [95% CI]			0.03 [-0.16; 0.23]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	2.42 [-0.16; 5.01]	2.84 [0.07; 5.61]	
Standard error	1.32	1.41	
Difference of LS Means [95% CI]			-0.42 [-3.71; 2.88]
Standard error for difference			1.68
p-value			0.8040
Hedges' g [95% CI]			-0.02 [-0.22; 0.18]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	3.03 [0.19; 5.88]	1.83 [-1.31; 4.97]	
Standard error	1.45	1.60	
Difference of LS Means [95% CI]			1.20 [-2.60; 5.01]
Standard error for difference			1.93
p-value			0.5342
Hedges' g [95% CI]			0.06 [-0.15; 0.27]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	2.86 [-0.03; 5.75]	2.02 [-1.18; 5.22]	
Standard error	1.47	1.63	
Difference of LS Means [95% CI]			0.84 [-3.04; 4.73]
Standard error for difference			1.98
p-value			0.6700
Hedges' g [95% CI]			0.04 [-0.18; 0.26]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	2.35 [-0.51; 5.20]	1.70 [-1.52; 4.91]	
Standard error	1.45	1.64	
Difference of LS Means [95% CI]			0.65 [-3.22; 4.52]
Standard error for difference			1.97
p-value			0.7425
Hedges' g [95% CI]			0.03 [-0.20; 0.27]
Average [b]			
n	286	299	
LS Means [95% CI]	3.47 [1.38; 5.56]	3.01 [0.84; 5.18]	
Standard error	1.06	1.11	
Difference of LS Means [95% CI]			0.46 [-1.89; 2.81]
Standard error for difference			1.20
p-value			0.7005
Hedges' g [95% CI]			0.02 [-0.14; 0.19]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Functional Scales/Cognitive Functioning			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	-2.45 [-4.73; -0.17]	-1.65 [-3.96; 0.67]	
Standard error	1.16	1.18	
Difference of LS Means [95% CI]			-0.80 [-3.48; 1.87]
Standard error for difference			1.36
p-value			0.5556
Hedges' g [95% CI]			-0.04 [-0.21; 0.13]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	-2.17 [-4.42; 0.09]	-2.34 [-4.63; -0.05]	
Standard error	1.15	1.17	
Difference of LS Means [95% CI]			0.17 [-2.47; 2.82]
Standard error for difference			1.35
p-value			0.8971
Hedges' g [95% CI]			0.01 [-0.17; 0.19]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	-0.94 [-3.11; 1.22]	-1.97 [-4.21; 0.28]	
Standard error	1.10	1.14	
Difference of LS Means [95% CI]			1.02 [-1.50; 3.55]
Standard error for difference			1.28
p-value			0.4259
Hedges' g [95% CI]			0.06 [-0.12; 0.24]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	211	
LS Means [95% CI]	-1.32 [-3.59; 0.96]	-2.92 [-5.27; -0.57]	
Standard error	1.16	1.20	
Difference of LS Means [95% CI]			1.60 [-1.11; 4.32]
Standard error for difference			1.38
p-value			0.2466
Hedges' g [95% CI]			0.09 [-0.10; 0.28]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	-1.60 [-3.82; 0.62]	-3.27 [-5.61; -0.93]	
Standard error	1.13	1.19	
Difference of LS Means [95% CI]			1.67 [-1.01; 4.34]
Standard error for difference			1.36
p-value			0.2210
Hedges' g [95% CI]			0.10 [-0.09; 0.29]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	-1.94 [-4.28; 0.39]	-1.85 [-4.30; 0.60]	
Standard error	1.19	1.25	
Difference of LS Means [95% CI]			-0.09 [-2.95; 2.76]
Standard error for difference			1.45
p-value			0.9485
Hedges' g [95% CI]			-0.01 [-0.20; 0.19]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	-3.91 [-6.38; -1.44]	-3.22 [-5.85; -0.59]	
Standard error	1.26	1.34	
Difference of LS Means [95% CI]			-0.69 [-3.80; 2.43]
Standard error for difference			1.59
p-value			0.6651
Hedges' g [95% CI]			-0.04 [-0.24; 0.16]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	-3.45 [-5.86; -1.03]	-3.55 [-6.19; -0.91]	
Standard error	1.23	1.34	
Difference of LS Means [95% CI]			0.11 [-2.98; 3.19]
Standard error for difference			1.57
p-value			0.9463
Hedges' g [95% CI]			0.01 [-0.21; 0.22]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	-3.73 [-6.28; -1.18]	-3.24 [-6.07; -0.41]	
Standard error	1.30	1.44	
Difference of LS Means [95% CI]			-0.49 [-3.84; 2.86]
Standard error for difference			1.70
p-value			0.7742
Hedges' g [95% CI]			-0.03 [-0.25; 0.19]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	-2.60 [-5.14; -0.06]	-4.24 [-7.08; -1.40]	
Standard error	1.29	1.45	
Difference of LS Means [95% CI]			1.64 [-1.71; 4.99]
Standard error for difference			1.71
p-value			0.3367
Hedges' g [95% CI]			0.10 [-0.13; 0.33]
Average [b]			
n	286	299	
LS Means [95% CI]	-2.41 [-4.36; -0.46]	-2.82 [-4.85; -0.80]	
Standard error	0.99	1.03	
Difference of LS Means [95% CI]			0.41 [-1.73; 2.56]
Standard error for difference			1.09
p-value			0.7044
Hedges' g [95% CI]			0.02 [-0.14; 0.19]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Functional Scales/Social Functioning			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	-2.03 [-5.06; 1.01]	-1.31 [-4.41; 1.79]	
Standard error	1.55	1.58	
Difference of LS Means [95% CI]			-0.72 [-4.22; 2.78]
Standard error for difference			1.78
p-value			0.6872
Hedges' g [95% CI]			-0.03 [-0.20; 0.14]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	-1.66 [-4.71; 1.38]	-1.72 [-4.82; 1.38]	
Standard error	1.55	1.58	
Difference of LS Means [95% CI]			0.06 [-3.47; 3.58]
Standard error for difference			1.79
p-value			0.9744
Hedges' g [95% CI]			0.00 [-0.17; 0.18]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	-2.41 [-5.67; 0.85]	-3.92 [-7.28; -0.55]	
Standard error	1.66	1.71	
Difference of LS Means [95% CI]			1.50 [-2.43; 5.44]
Standard error for difference			2.00
p-value			0.4527
Hedges' g [95% CI]			0.06 [-0.12; 0.24]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	211	
LS Means [95% CI]	-1.23 [-4.42; 1.96]	-1.83 [-5.10; 1.45]	
Standard error	1.62	1.67	
Difference of LS Means [95% CI]			0.60 [-3.20; 4.40]
Standard error for difference			1.94
p-value			0.7568
Hedges' g [95% CI]			0.02 [-0.16; 0.21]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	-2.13 [-5.45; 1.19]	-2.79 [-6.27; 0.69]	
Standard error	1.69	1.77	
Difference of LS Means [95% CI]			0.65 [-3.44; 4.75]
Standard error for difference			2.08
p-value			0.7540
Hedges' g [95% CI]			0.03 [-0.17; 0.22]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	-1.13 [-4.35; 2.10]	-3.35 [-6.73; 0.04]	
Standard error	1.64	1.72	
Difference of LS Means [95% CI]			2.22 [-1.71; 6.16]
Standard error for difference			2.00
p-value			0.2678
Hedges' g [95% CI]			0.09 [-0.10; 0.29]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	-2.20 [-5.45; 1.04]	-1.93 [-5.39; 1.53]	
Standard error	1.65	1.76	
Difference of LS Means [95% CI]			-0.27 [-4.29; 3.75]
Standard error for difference			2.05
p-value			0.8949
Hedges' g [95% CI]			-0.01 [-0.21; 0.19]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	-2.21 [-5.70; 1.29]	-3.34 [-7.17; 0.50]	
Standard error	1.78	1.95	
Difference of LS Means [95% CI]			1.13 [-3.41; 5.67]
Standard error for difference			2.31
p-value			0.6244
Hedges' g [95% CI]			0.05 [-0.17; 0.26]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	-0.93 [-4.26; 2.41]	-2.08 [-5.72; 1.57]	
Standard error	1.70	1.86	
Difference of LS Means [95% CI]			1.15 [-3.11; 5.41]
Standard error for difference			2.17
p-value			0.5957
Hedges' g [95% CI]			0.05 [-0.17; 0.27]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	-1.25 [-4.70; 2.20]	-3.88 [-7.74; -0.01]	
Standard error	1.76	1.97	
Difference of LS Means [95% CI]			2.63 [-1.91; 7.16]
Standard error for difference			2.31
p-value			0.2553
Hedges' g [95% CI]			0.12 [-0.12; 0.35]
Average [b]			
n	286	299	
LS Means [95% CI]	-1.72 [-4.44; 1.00]	-2.61 [-5.43; 0.21]	
Standard error	1.39	1.44	
Difference of LS Means [95% CI]			0.90 [-2.10; 3.89]
Standard error for difference			1.52
p-value			0.5566
Hedges' g [95% CI]			0.04 [-0.13; 0.20]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Symptom Scales/Fatigue			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	3.62 [0.73; 6.50]	3.72 [0.78; 6.66]	
Standard error	1.47	1.50	
Difference of LS Means [95% CI]			-0.10 [-3.42; 3.22]
Standard error for difference			1.69
p-value			0.9520
Hedges' g [95% CI]			-0.00 [-0.18; 0.17]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	3.77 [0.84; 6.70]	3.36 [0.38; 6.34]	
Standard error	1.49	1.52	
Difference of LS Means [95% CI]			0.41 [-3.00; 3.83]
Standard error for difference			1.74
p-value			0.8130
Hedges' g [95% CI]			0.02 [-0.16; 0.19]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	3.11 [0.11; 6.12]	4.27 [1.18; 7.36]	
Standard error	1.53	1.57	
Difference of LS Means [95% CI]			-1.16 [-4.73; 2.41]
Standard error for difference			1.82
p-value			0.5250
Hedges' g [95% CI]			-0.05 [-0.23; 0.13]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	210	
LS Means [95% CI]	3.05 [-0.02; 6.11]	4.72 [1.57; 7.87]	
Standard error	1.56	1.60	
Difference of LS Means [95% CI]			-1.67 [-5.35; 2.00]
Standard error for difference			1.87
p-value			0.3710
Hedges' g [95% CI]			-0.07 [-0.26; 0.12]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	1.29 [-1.75; 4.33]	3.40 [0.22; 6.59]	
Standard error	1.55	1.62	
Difference of LS Means [95% CI]			-2.12 [-5.82; 1.58]
Standard error for difference			1.88
p-value			0.2617
Hedges' g [95% CI]			-0.09 [-0.29; 0.10]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	1.44 [-1.62; 4.49]	4.17 [0.96; 7.37]	
Standard error	1.56	1.63	
Difference of LS Means [95% CI]			-2.73 [-6.46; 1.00]
Standard error for difference			1.90
p-value			0.1509
Hedges' g [95% CI]			-0.12 [-0.32; 0.08]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	3.01 [0.02; 6.01]	3.76 [0.56; 6.96]	
Standard error	1.53	1.63	
Difference of LS Means [95% CI]			-0.74 [-4.42; 2.93]
Standard error for difference			1.87
p-value			0.6907
Hedges' g [95% CI]			-0.03 [-0.24; 0.17]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	1.08 [-2.17; 4.32]	3.70 [0.16; 7.25]	
Standard error	1.65	1.80	
Difference of LS Means [95% CI]			-2.63 [-6.79; 1.54]
Standard error for difference			2.12
p-value			0.2159
Hedges' g [95% CI]			-0.11 [-0.33; 0.10]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	2.31 [-0.88; 5.50]	2.92 [-0.61; 6.44]	
Standard error	1.63	1.79	
Difference of LS Means [95% CI]			-0.61 [-4.72; 3.51]
Standard error for difference			2.09
p-value			0.7726
Hedges' g [95% CI]			-0.03 [-0.25; 0.19]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	2.75 [-0.50; 5.99]	2.97 [-0.69; 6.63]	
Standard error	1.65	1.86	
Difference of LS Means [95% CI]			-0.22 [-4.50; 4.06]
Standard error for difference			2.18
p-value			0.9182
Hedges' g [95% CI]			-0.01 [-0.24; 0.22]
Average [b]			
n	286	299	
LS Means [95% CI]	2.54 [-0.03; 5.11]	3.70 [1.04; 6.36]	
Standard error	1.31	1.36	
Difference of LS Means [95% CI]			-1.16 [-3.97; 1.66]
Standard error for difference			1.43
p-value			0.4202
Hedges' g [95% CI]			-0.05 [-0.21; 0.11]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Symptom Scales/Nausea and Vomiting			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	9.41 [7.05; 11.78]	4.27 [1.87; 6.67]	
Standard error	1.20	1.22	
Difference of LS Means [95% CI]			5.14 [2.26; 8.02]
Standard error for difference			1.47
p-value			0.0005
Hedges' g [95% CI]			0.26 [0.09; 0.43]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	10.55 [8.18; 12.91]	3.47 [1.07; 5.86]	
Standard error	1.20	1.22	
Difference of LS Means [95% CI]			7.08 [4.19; 9.97]
Standard error for difference			1.47
p-value			<.0001
Hedges' g [95% CI]			0.37 [0.19; 0.55]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	12.07 [9.71; 14.43]	1.56 [-0.86; 3.99]	
Standard error	1.20	1.24	
Difference of LS Means [95% CI]			10.50 [7.59; 13.42]
Standard error for difference			1.48
p-value			<.0001
Hedges' g [95% CI]			0.56 [0.38; 0.75]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	210	
LS Means [95% CI]	11.76 [9.41; 14.11]	2.26 [-0.16; 4.68]	
Standard error	1.20	1.23	
Difference of LS Means [95% CI]			9.50 [6.59; 12.41]
Standard error for difference			1.48
p-value			<.0001
Hedges' g [95% CI]			0.53 [0.34; 0.72]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	9.35 [7.01; 11.69]	2.47 [-0.01; 4.95]	
Standard error	1.19	1.26	
Difference of LS Means [95% CI]			6.88 [3.92; 9.84]
Standard error for difference			1.51
p-value			<.0001
Hedges' g [95% CI]			0.39 [0.19; 0.59]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	8.34 [6.04; 10.65]	1.68 [-0.76; 4.11]	
Standard error	1.17	1.24	
Difference of LS Means [95% CI]			6.67 [3.78; 9.56]
Standard error for difference			1.47
p-value			<.0001
Hedges' g [95% CI]			0.39 [0.19; 0.58]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	8.46 [6.22; 10.70]	1.29 [-1.14; 3.71]	
Standard error	1.14	1.24	
Difference of LS Means [95% CI]			7.17 [4.34; 10.01]
Standard error for difference			1.44
p-value			<.0001
Hedges' g [95% CI]			0.44 [0.23; 0.64]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	8.89 [6.59; 11.20]	0.61 [-1.96; 3.17]	
Standard error	1.17	1.31	
Difference of LS Means [95% CI]			8.29 [5.28; 11.30]
Standard error for difference			1.53
p-value			<.0001
Hedges' g [95% CI]			0.51 [0.29; 0.72]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	6.73 [4.49; 8.97]	1.20 [-1.30; 3.71]	
Standard error	1.14	1.28	
Difference of LS Means [95% CI]			5.53 [2.62; 8.44]
Standard error for difference			1.48
p-value			0.0002
Hedges' g [95% CI]			0.36 [0.14; 0.58]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	6.32 [4.15; 8.48]	0.59 [-1.88; 3.07]	
Standard error	1.10	1.26	
Difference of LS Means [95% CI]			5.72 [2.90; 8.55]
Standard error for difference			1.44
p-value			<.0001
Hedges' g [95% CI]			0.40 [0.16; 0.63]
Average [b]			
n	286	299	
LS Means [95% CI]	9.19 [7.39; 10.99]	1.94 [0.07; 3.81]	
Standard error	0.91	0.95	
Difference of LS Means [95% CI]			7.25 [5.30; 9.20]
Standard error for difference			0.99
p-value			<.0001
Hedges' g [95% CI]			0.45 [0.29; 0.62]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Symptom Scales/Pain			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	-6.23 [-9.21; -3.24]	-1.80 [-4.84; 1.24]	
Standard error	1.52	1.55	
Difference of LS Means [95% CI]			-4.43 [-7.98; -0.87]
Standard error for difference			1.81
p-value			0.0147
Hedges' g [95% CI]			-0.18 [-0.35; -0.01]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	-7.55 [-10.58; -4.51]	-2.40 [-5.49; 0.68]	
Standard error	1.55	1.57	
Difference of LS Means [95% CI]			-5.15 [-8.80; -1.49]
Standard error for difference			1.86
p-value			0.0058
Hedges' g [95% CI]			-0.21 [-0.39; -0.03]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	-7.71 [-10.84; -4.57]	-1.79 [-5.02; 1.43]	
Standard error	1.60	1.64	
Difference of LS Means [95% CI]			-5.91 [-9.77; -2.06]
Standard error for difference			1.96
p-value			0.0027
Hedges' g [95% CI]			-0.24 [-0.42; -0.06]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	211	
LS Means [95% CI]	-8.47 [-11.56; -5.38]	-2.25 [-5.43; 0.93]	
Standard error	1.57	1.62	
Difference of LS Means [95% CI]			-6.22 [-10.00; -2.44]
Standard error for difference			1.92
p-value			0.0013
Hedges' g [95% CI]			-0.26 [-0.45; -0.07]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	-9.08 [-12.00; -6.16]	-3.29 [-6.36; -0.22]	
Standard error	1.49	1.56	
Difference of LS Means [95% CI]			-5.79 [-9.36; -2.22]
Standard error for difference			1.82
p-value			0.0015
Hedges' g [95% CI]			-0.26 [-0.46; -0.07]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	216	188	
LS Means [95% CI]	-9.50 [-12.40; -6.61]	-2.74 [-5.80; 0.31]	
Standard error	1.48	1.55	
Difference of LS Means [95% CI]			-6.76 [-10.29; -3.23]
Standard error for difference			1.80
p-value			0.0002
Hedges' g [95% CI]			-0.31 [-0.51; -0.12]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	-9.60 [-12.54; -6.66]	-0.56 [-3.72; 2.60]	
Standard error	1.50	1.61	
Difference of LS Means [95% CI]			-9.04 [-12.69; -5.39]
Standard error for difference			1.86
p-value			<.0001
Hedges' g [95% CI]			-0.42 [-0.63; -0.22]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	-10.29 [-13.34; -7.25]	1.13 [-2.22; 4.49]	
Standard error	1.55	1.71	
Difference of LS Means [95% CI]			-11.43 [-15.34; -7.51]
Standard error for difference			1.99
p-value			<.0001
Hedges' g [95% CI]			-0.53 [-0.75; -0.31]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	-10.50 [-13.66; -7.33]	-0.78 [-4.26; 2.70]	
Standard error	1.61	1.77	
Difference of LS Means [95% CI]			-9.72 [-13.83; -5.60]
Standard error for difference			2.09
p-value			<.0001
Hedges' g [95% CI]			-0.45 [-0.67; -0.22]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	-9.41 [-12.42; -6.41]	-1.69 [-5.09; 1.71]	
Standard error	1.53	1.73	
Difference of LS Means [95% CI]			-7.73 [-11.65; -3.80]
Standard error for difference			2.00
p-value			0.0001
Hedges' g [95% CI]			-0.39 [-0.62; -0.15]
Average [b]			
n	286	299	
LS Means [95% CI]	-8.83 [-11.30; -6.37]	-1.62 [-4.17; 0.94]	
Standard error	1.26	1.30	
Difference of LS Means [95% CI]			-7.22 [-9.92; -4.52]
Standard error for difference			1.38
p-value			<.0001
Hedges' g [95% CI]			-0.33 [-0.49; -0.17]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Common Symptoms/Dyspnoea			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	1.72 [-0.82; 4.25]	0.80 [-1.79; 3.39]	
Standard error	1.29	1.32	
Difference of LS Means [95% CI]			0.92 [-2.07; 3.91]
Standard error for difference			1.52
p-value			0.5475
Hedges' g [95% CI]			0.04 [-0.13; 0.21]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	0.05 [-2.51; 2.61]	-0.22 [-2.83; 2.40]	
Standard error	1.30	1.33	
Difference of LS Means [95% CI]			0.27 [-2.78; 3.32]
Standard error for difference			1.55
p-value			0.8626
Hedges' g [95% CI]			0.01 [-0.16; 0.19]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	-0.51 [-3.16; 2.13]	0.93 [-1.80; 3.66]	
Standard error	1.35	1.39	
Difference of LS Means [95% CI]			-1.44 [-4.66; 1.77]
Standard error for difference			1.64
p-value			0.3777
Hedges' g [95% CI]			-0.07 [-0.25; 0.11]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	210	
LS Means [95% CI]	-1.06 [-3.93; 1.82]	2.34 [-0.63; 5.32]	
Standard error	1.46	1.51	
Difference of LS Means [95% CI]			-3.40 [-7.02; 0.21]
Standard error for difference			1.84
p-value			0.0651
Hedges' g [95% CI]			-0.15 [-0.34; 0.03]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	-0.54 [-3.39; 2.31]	3.13 [0.11; 6.15]	
Standard error	1.45	1.54	
Difference of LS Means [95% CI]			-3.67 [-7.30; -0.03]
Standard error for difference			1.85
p-value			0.0479
Hedges' g [95% CI]			-0.17 [-0.37; 0.02]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	0.30 [-2.57; 3.17]	4.28 [1.25; 7.31]	
Standard error	1.46	1.54	
Difference of LS Means [95% CI]			-3.98 [-7.64; -0.31]
Standard error for difference			1.86
p-value			0.0334
Hedges' g [95% CI]			-0.19 [-0.38; 0.01]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	0.28 [-2.63; 3.19]	3.57 [0.42; 6.71]	
Standard error	1.48	1.60	
Difference of LS Means [95% CI]			-3.29 [-7.07; 0.50]
Standard error for difference			1.93
p-value			0.0887
Hedges' g [95% CI]			-0.15 [-0.36; 0.05]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	-1.47 [-4.30; 1.37]	2.19 [-0.96; 5.35]	
Standard error	1.44	1.61	
Difference of LS Means [95% CI]			-3.66 [-7.41; 0.09]
Standard error for difference			1.91
p-value			0.0556
Hedges' g [95% CI]			-0.18 [-0.39; 0.03]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	0.87 [-2.03; 3.78]	0.41 [-2.85; 3.67]	
Standard error	1.48	1.66	
Difference of LS Means [95% CI]			0.46 [-3.43; 4.35]
Standard error for difference			1.98
p-value			0.8152
Hedges' g [95% CI]			0.02 [-0.20; 0.24]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	-1.34 [-4.12; 1.44]	1.63 [-1.52; 4.78]	
Standard error	1.41	1.60	
Difference of LS Means [95% CI]			-2.97 [-6.66; 0.72]
Standard error for difference			1.88
p-value			0.1147
Hedges' g [95% CI]			-0.16 [-0.39; 0.07]
Average [b]			
n	286	299	
LS Means [95% CI]	-0.17 [-2.32; 1.98]	1.91 [-0.33; 4.15]	
Standard error	1.10	1.14	
Difference of LS Means [95% CI]			-2.08 [-4.45; 0.29]
Standard error for difference			1.21
p-value			0.0857
Hedges' g [95% CI]			-0.11 [-0.27; 0.05]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Common Symptoms/Insomnia			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	-2.54 [-5.74; 0.65]	-1.07 [-4.32; 2.18]	
Standard error	1.63	1.65	
Difference of LS Means [95% CI]			-1.48 [-5.33; 2.38]
Standard error for difference			1.96
p-value			0.4521
Hedges' g [95% CI]			-0.06 [-0.23; 0.12]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	-2.72 [-5.89; 0.45]	-2.28 [-5.49; 0.94]	
Standard error	1.62	1.64	
Difference of LS Means [95% CI]			-0.44 [-4.25; 3.37]
Standard error for difference			1.94
p-value			0.8203
Hedges' g [95% CI]			-0.02 [-0.19; 0.16]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	-4.13 [-7.30; -0.96]	-1.84 [-5.11; 1.44]	
Standard error	1.61	1.67	
Difference of LS Means [95% CI]			-2.29 [-6.15; 1.56]
Standard error for difference			1.96
p-value			0.2426
Hedges' g [95% CI]			-0.09 [-0.27; 0.09]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	210	
LS Means [95% CI]	-5.02 [-8.19; -1.85]	-1.93 [-5.20; 1.34]	
Standard error	1.62	1.67	
Difference of LS Means [95% CI]			-3.09 [-6.96; 0.78]
Standard error for difference			1.97
p-value			0.1178
Hedges' g [95% CI]			-0.13 [-0.32; 0.06]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	-5.10 [-8.39; -1.82]	-0.83 [-4.30; 2.63]	
Standard error	1.67	1.76	
Difference of LS Means [95% CI]			-4.27 [-8.40; -0.14]
Standard error for difference			2.10
p-value			0.0428
Hedges' g [95% CI]			-0.17 [-0.37; 0.02]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	-6.50 [-9.75; -3.24]	-2.17 [-5.60; 1.26]	
Standard error	1.66	1.75	
Difference of LS Means [95% CI]			-4.33 [-8.41; -0.25]
Standard error for difference			2.07
p-value			0.0373
Hedges' g [95% CI]			-0.18 [-0.37; 0.02]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	-5.33 [-8.61; -2.06]	0.25 [-3.27; 3.77]	
Standard error	1.67	1.79	
Difference of LS Means [95% CI]			-5.58 [-9.76; -1.41]
Standard error for difference			2.12
p-value			0.0089
Hedges' g [95% CI]			-0.23 [-0.44; -0.03]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	-4.70 [-8.01; -1.39]	-1.07 [-4.78; 2.65]	
Standard error	1.69	1.89	
Difference of LS Means [95% CI]			-3.63 [-8.01; 0.74]
Standard error for difference			2.23
p-value			0.1035
Hedges' g [95% CI]			-0.15 [-0.37; 0.06]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	-5.25 [-8.45; -2.05]	-1.81 [-5.36; 1.75]	
Standard error	1.63	1.81	
Difference of LS Means [95% CI]			-3.44 [-7.60; 0.71]
Standard error for difference			2.11
p-value			0.1040
Hedges' g [95% CI]			-0.16 [-0.37; 0.06]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	-6.48 [-9.78; -3.19]	-3.30 [-7.07; 0.47]	
Standard error	1.68	1.92	
Difference of LS Means [95% CI]			-3.19 [-7.60; 1.23]
Standard error for difference			2.24
p-value			0.1566
Hedges' g [95% CI]			-0.14 [-0.38; 0.09]
Average [b]			
n	286	299	
LS Means [95% CI]	-4.78 [-7.31; -2.24]	-1.60 [-4.23; 1.03]	
Standard error	1.29	1.34	
Difference of LS Means [95% CI]			-3.17 [-5.92; -0.43]
Standard error for difference			1.40
p-value			0.0236
Hedges' g [95% CI]			-0.14 [-0.30; 0.02]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Common Symptoms/Appetite Loss			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	7.54 [4.13; 10.94]	4.11 [0.63; 7.59]	
Standard error	1.73	1.77	
Difference of LS Means [95% CI]			3.42 [-0.61; 7.45]
Standard error for difference			2.05
p-value			0.0959
Hedges' g [95% CI]			0.12 [-0.05; 0.29]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	9.03 [5.52; 12.55]	3.19 [-0.40; 6.77]	
Standard error	1.79	1.83	
Difference of LS Means [95% CI]			5.85 [1.61; 10.08]
Standard error for difference			2.16
p-value			0.0069
Hedges' g [95% CI]			0.21 [0.03; 0.38]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	12.29 [8.61; 15.96]	2.87 [-0.93; 6.66]	
Standard error	1.87	1.93	
Difference of LS Means [95% CI]			9.42 [4.88; 13.96]
Standard error for difference			2.31
p-value			<.0001
Hedges' g [95% CI]			0.32 [0.14; 0.50]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	210	
LS Means [95% CI]	10.05 [6.45; 13.65]	1.60 [-2.13; 5.32]	
Standard error	1.84	1.90	
Difference of LS Means [95% CI]			8.45 [4.03; 12.88]
Standard error for difference			2.25
p-value			0.0002
Hedges' g [95% CI]			0.31 [0.12; 0.50]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	7.95 [4.34; 11.56]	2.75 [-1.04; 6.54]	
Standard error	1.84	1.93	
Difference of LS Means [95% CI]			5.20 [0.71; 9.70]
Standard error for difference			2.29
p-value			0.0233
Hedges' g [95% CI]			0.19 [-0.00; 0.39]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	7.84 [4.27; 11.42]	2.26 [-1.51; 6.03]	
Standard error	1.82	1.92	
Difference of LS Means [95% CI]			5.58 [1.13; 10.03]
Standard error for difference			2.27
p-value			0.0141
Hedges' g [95% CI]			0.21 [0.01; 0.41]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	9.22 [5.56; 12.88]	1.01 [-2.91; 4.94]	
Standard error	1.86	2.00	
Difference of LS Means [95% CI]			8.21 [3.55; 12.86]
Standard error for difference			2.37
p-value			0.0006
Hedges' g [95% CI]			0.31 [0.10; 0.51]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	7.37 [3.70; 11.04]	0.23 [-3.85; 4.31]	
Standard error	1.87	2.08	
Difference of LS Means [95% CI]			7.14 [2.32; 11.95]
Standard error for difference			2.45
p-value			0.0038
Hedges' g [95% CI]			0.27 [0.06; 0.49]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	8.78 [5.07; 12.49]	0.12 [-4.01; 4.25]	
Standard error	1.89	2.10	
Difference of LS Means [95% CI]			8.65 [3.78; 13.53]
Standard error for difference			2.48
p-value			0.0005
Hedges' g [95% CI]			0.34 [0.12; 0.56]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	6.79 [3.15; 10.44]	0.80 [-3.36; 4.96]	
Standard error	1.86	2.12	
Difference of LS Means [95% CI]			5.99 [1.13; 10.85]
Standard error for difference			2.47
p-value			0.0158
Hedges' g [95% CI]			0.25 [0.01; 0.48]
Average [b]			
n	286	299	
LS Means [95% CI]	8.69 [5.80; 11.57]	1.89 [-1.11; 4.90]	
Standard error	1.47	1.53	
Difference of LS Means [95% CI]			6.79 [3.60; 9.98]
Standard error for difference			1.62
p-value			<.0001
Hedges' g [95% CI]			0.26 [0.10; 0.43]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Common Symptoms/Constipation			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	6.56 [3.44; 9.68]	1.95 [-1.24; 5.13]	
Standard error	1.59	1.62	
Difference of LS Means [95% CI]			4.62 [0.92; 8.31]
Standard error for difference			1.88
p-value			0.0144
Hedges' g [95% CI]			0.18 [0.01; 0.35]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	7.93 [4.79; 11.07]	1.56 [-1.63; 4.76]	
Standard error	1.60	1.63	
Difference of LS Means [95% CI]			6.37 [2.63; 10.11]
Standard error for difference			1.90
p-value			0.0009
Hedges' g [95% CI]			0.25 [0.07; 0.43]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	8.37 [5.14; 11.61]	1.42 [-1.93; 4.77]	
Standard error	1.65	1.70	
Difference of LS Means [95% CI]			6.95 [3.01; 10.90]
Standard error for difference			2.01
p-value			0.0006
Hedges' g [95% CI]			0.27 [0.09; 0.45]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	210	
LS Means [95% CI]	9.68 [6.43; 12.93]	2.21 [-1.15; 5.56]	
Standard error	1.66	1.71	
Difference of LS Means [95% CI]			7.47 [3.50; 11.45]
Standard error for difference			2.02
p-value			0.0002
Hedges' g [95% CI]			0.30 [0.11; 0.49]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	8.60 [5.10; 12.10]	2.52 [-1.19; 6.23]	
Standard error	1.78	1.89	
Difference of LS Means [95% CI]			6.08 [1.60; 10.56]
Standard error for difference			2.28
p-value			0.0080
Hedges' g [95% CI]			0.23 [0.04; 0.42]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	8.14 [4.64; 11.65]	1.96 [-1.75; 5.66]	
Standard error	1.78	1.89	
Difference of LS Means [95% CI]			6.19 [1.71; 10.66]
Standard error for difference			2.28
p-value			0.0069
Hedges' g [95% CI]			0.24 [0.04; 0.43]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	7.37 [4.14; 10.59]	3.67 [0.21; 7.13]	
Standard error	1.64	1.76	
Difference of LS Means [95% CI]			3.70 [-0.35; 7.75]
Standard error for difference			2.06
p-value			0.0735
Hedges' g [95% CI]			0.16 [-0.04; 0.36]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	7.80 [4.45; 11.14]	3.59 [-0.08; 7.27]	
Standard error	1.70	1.87	
Difference of LS Means [95% CI]			4.20 [-0.14; 8.54]
Standard error for difference			2.21
p-value			0.0576
Hedges' g [95% CI]			0.18 [-0.04; 0.39]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	8.54 [5.14; 11.94]	2.94 [-0.86; 6.74]	
Standard error	1.73	1.93	
Difference of LS Means [95% CI]			5.60 [1.12; 10.09]
Standard error for difference			2.28
p-value			0.0145
Hedges' g [95% CI]			0.24 [0.02; 0.46]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	7.38 [3.93; 10.83]	3.28 [-0.65; 7.21]	
Standard error	1.76	2.00	
Difference of LS Means [95% CI]			4.10 [-0.54; 8.74]
Standard error for difference			2.36
p-value			0.0833
Hedges' g [95% CI]			0.18 [-0.05; 0.41]
Average [b]			
n	286	299	
LS Means [95% CI]	8.04 [5.40; 10.68]	2.51 [-0.24; 5.26]	
Standard error	1.34	1.40	
Difference of LS Means [95% CI]			5.53 [2.61; 8.45]
Standard error for difference			1.49
p-value			0.0002
Hedges' g [95% CI]			0.23 [0.07; 0.40]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Common Symptoms/Diarrhea			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	5.81 [3.05; 8.56]	4.69 [1.89; 7.50]	
Standard error	1.40	1.43	
Difference of LS Means [95% CI]			1.11 [-2.33; 4.55]
Standard error for difference			1.75
p-value			0.5267
Hedges' g [95% CI]			0.05 [-0.12; 0.22]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	247	245	
LS Means [95% CI]	5.23 [2.47; 7.99]	6.08 [3.28; 8.87]	
Standard error	1.40	1.42	
Difference of LS Means [95% CI]			-0.84 [-4.30; 2.61]
Standard error for difference			1.76
p-value			0.6311
Hedges' g [95% CI]			-0.04 [-0.21; 0.14]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	5.45 [2.71; 8.20]	5.95 [3.12; 8.78]	
Standard error	1.40	1.44	
Difference of LS Means [95% CI]			-0.49 [-3.97; 2.98]
Standard error for difference			1.77
p-value			0.7797
Hedges' g [95% CI]			-0.02 [-0.20; 0.16]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	211	
LS Means [95% CI]	6.08 [3.32; 8.85]	4.85 [2.00; 7.70]	
Standard error	1.41	1.45	
Difference of LS Means [95% CI]			1.23 [-2.27; 4.74]
Standard error for difference			1.79
p-value			0.4900
Hedges' g [95% CI]			0.06 [-0.13; 0.25]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	4.26 [1.68; 6.85]	2.79 [0.05; 5.53]	
Standard error	1.31	1.40	
Difference of LS Means [95% CI]			1.47 [-1.82; 4.76]
Standard error for difference			1.67
p-value			0.3790
Hedges' g [95% CI]			0.08 [-0.12; 0.27]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	6.06 [3.39; 8.74]	2.27 [-0.56; 5.11]	
Standard error	1.36	1.44	
Difference of LS Means [95% CI]			3.79 [0.35; 7.22]
Standard error for difference			1.75
p-value			0.0308
Hedges' g [95% CI]			0.19 [-0.01; 0.39]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	3.95 [1.42; 6.47]	2.02 [-0.72; 4.76]	
Standard error	1.28	1.40	
Difference of LS Means [95% CI]			1.93 [-1.31; 5.16]
Standard error for difference			1.65
p-value			0.2425
Hedges' g [95% CI]			0.10 [-0.10; 0.31]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	4.99 [2.32; 7.67]	3.17 [0.16; 6.19]	
Standard error	1.36	1.53	
Difference of LS Means [95% CI]			1.82 [-1.77; 5.41]
Standard error for difference			1.83
p-value			0.3199
Hedges' g [95% CI]			0.10 [-0.12; 0.31]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	3.82 [1.27; 6.36]	2.90 [0.02; 5.78]	
Standard error	1.30	1.47	
Difference of LS Means [95% CI]			0.92 [-2.46; 4.30]
Standard error for difference			1.72
p-value			0.5933
Hedges' g [95% CI]			0.05 [-0.17; 0.27]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	4.65 [1.84; 7.46]	3.94 [0.67; 7.21]	
Standard error	1.43	1.67	
Difference of LS Means [95% CI]			0.71 [-3.20; 4.62]
Standard error for difference			1.99
p-value			0.7216
Hedges' g [95% CI]			0.04 [-0.19; 0.27]
Average [b]			
n	286	299	
LS Means [95% CI]	5.03 [3.07; 6.99]	3.87 [1.82; 5.91]	
Standard error	1.00	1.04	
Difference of LS Means [95% CI]			1.16 [-0.97; 3.30]
Standard error for difference			1.09
p-value			0.2840
Hedges' g [95% CI]			0.07 [-0.10; 0.23]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Common Symptoms/Financial Difficulties			
Week 4 Day 1			
Estimated change from baseline [a]			
n	265	259	
LS Means [95% CI]	-0.13 [-3.14; 2.89]	-0.20 [-3.27; 2.87]	
Standard error	1.54	1.56	
Difference of LS Means [95% CI]			0.07 [-3.43; 3.58]
Standard error for difference			1.78
p-value			0.9668
Hedges' g [95% CI]			0.00 [-0.17; 0.17]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	248	245	
LS Means [95% CI]	2.02 [-1.00; 5.04]	-0.39 [-3.47; 2.68]	
Standard error	1.54	1.56	
Difference of LS Means [95% CI]			2.41 [-1.11; 5.93]
Standard error for difference			1.79
p-value			0.1788
Hedges' g [95% CI]			0.10 [-0.08; 0.28]
Week 10 Day 1			
Estimated change from baseline [a]			
n	244	226	
LS Means [95% CI]	0.95 [-2.13; 4.03]	-0.13 [-3.30; 3.05]	
Standard error	1.57	1.62	
Difference of LS Means [95% CI]			1.07 [-2.59; 4.73]
Standard error for difference			1.86
p-value			0.5651
Hedges' g [95% CI]			0.04 [-0.14; 0.22]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	226	211	
LS Means [95% CI]	2.17 [-0.98; 5.32]	1.35 [-1.88; 4.59]	
Standard error	1.60	1.65	
Difference of LS Means [95% CI]			0.82 [-2.96; 4.60]
Standard error for difference			1.92
p-value			0.6707
Hedges' g [95% CI]			0.03 [-0.15; 0.22]
Week 16 Day 1			
Estimated change from baseline [a]			
n	224	188	
LS Means [95% CI]	1.70 [-1.57; 4.97]	2.54 [-0.89; 5.98]	
Standard error	1.66	1.75	
Difference of LS Means [95% CI]			-0.85 [-4.90; 3.20]
Standard error for difference			2.06
p-value			0.6810
Hedges' g [95% CI]			-0.03 [-0.23; 0.16]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	217	188	
LS Means [95% CI]	0.79 [-2.48; 4.07]	3.98 [0.55; 7.40]	
Standard error	1.67	1.74	
Difference of LS Means [95% CI]			-3.19 [-7.23; 0.86]
Standard error for difference			2.06
p-value			0.1226
Hedges' g [95% CI]			-0.13 [-0.33; 0.06]
Week 22 Day 1			
Estimated change from baseline [a]			
n	212	170	
LS Means [95% CI]	1.01 [-2.24; 4.25]	0.31 [-3.15; 3.76]	
Standard error	1.65	1.76	
Difference of LS Means [95% CI]			0.70 [-3.35; 4.75]
Standard error for difference			2.06
p-value			0.7332
Hedges' g [95% CI]			0.03 [-0.17; 0.23]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	204	146	
LS Means [95% CI]	0.91 [-2.45; 4.26]	2.86 [-0.76; 6.48]	
Standard error	1.71	1.84	
Difference of LS Means [95% CI]			-1.96 [-6.23; 2.32]
Standard error for difference			2.17
p-value			0.3685
Hedges' g [95% CI]			-0.08 [-0.30; 0.13]
Week 28 Day 1			
Estimated change from baseline [a]			
n	194	137	
LS Means [95% CI]	2.08 [-1.18; 5.33]	0.61 [-2.96; 4.17]	
Standard error	1.66	1.82	
Difference of LS Means [95% CI]			1.47 [-2.70; 5.63]
Standard error for difference			2.12
p-value			0.4895
Hedges' g [95% CI]			0.07 [-0.15; 0.28]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 10SEP2024 7:10; Program name: T.2.11.15_EORTC_C30_MMRM_FAS.sas; Output name: T.2.11.15_EORTC_C30_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.11.15 EORTC-QLQ-C30 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	181	119	
LS Means [95% CI]	2.62 [-0.79; 6.04]	2.77 [-1.01; 6.54]	
Standard error	1.74	1.92	
Difference of LS Means [95% CI]			-0.14 [-4.60; 4.32]
Standard error for difference			2.27
p-value			0.9506
Hedges' g [95% CI]			-0.01 [-0.24; 0.23]
Average [b]			
n	286	299	
LS Means [95% CI]	1.41 [-1.27; 4.10]	1.37 [-1.40; 4.14]	
Standard error	1.37	1.41	
Difference of LS Means [95% CI]			0.04 [-2.92; 3.00]
Standard error for difference			1.51
p-value			0.9779
Hedges' g [95% CI]			0.00 [-0.16; 0.16]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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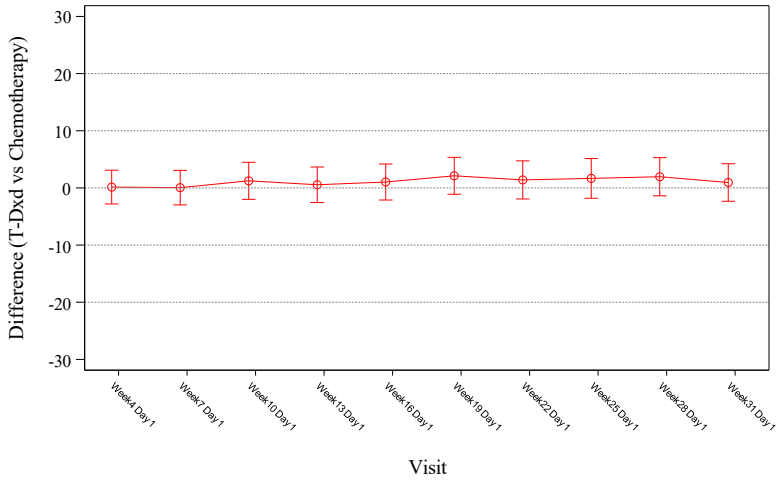
Abbildung 2.11.10 EORTC-QLQ-C30 – Plot of least-square means of repeated measures analysis of change from baseline – FAS

Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Global Health Status



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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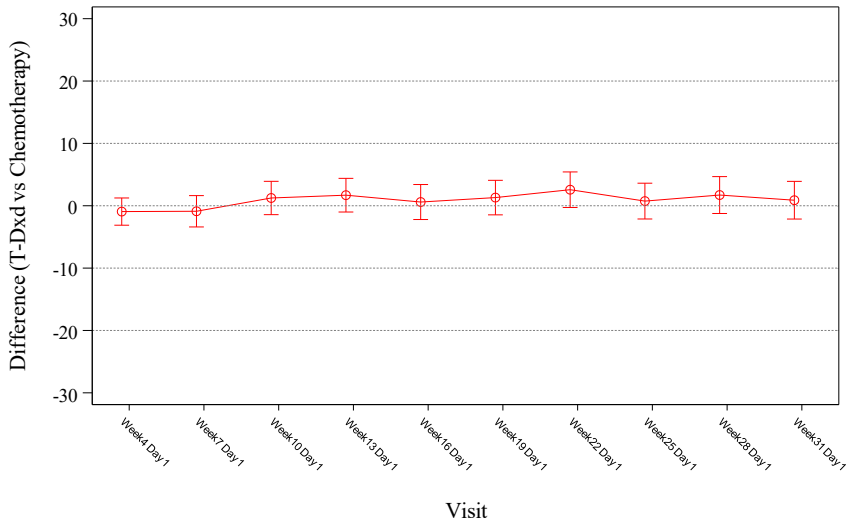
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Functional Scales/Physical Functioning



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CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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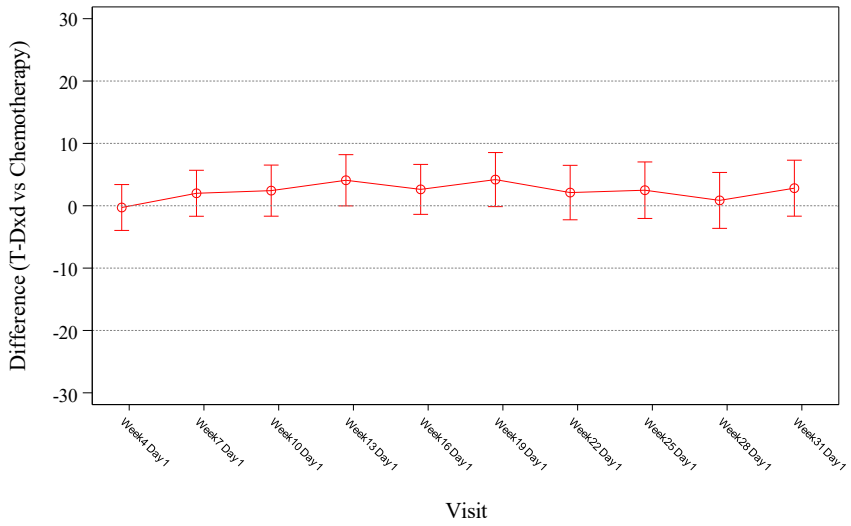
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Functional Scales/Role Functioning



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The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
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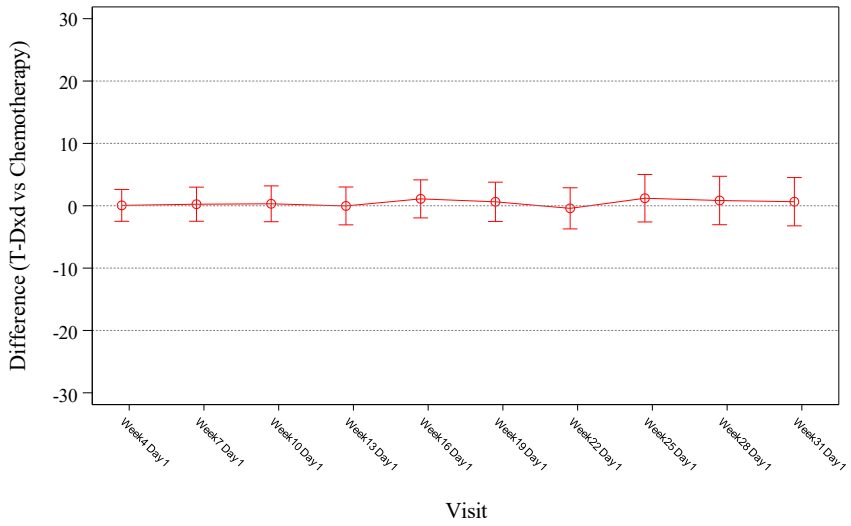
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Functional Scales/Emotional Functioning



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
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CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Functional Scales/Cognitive Functioning

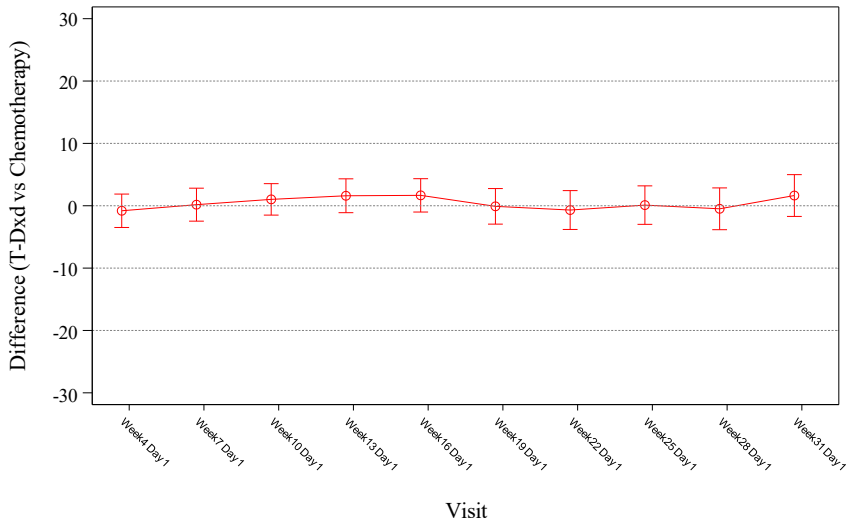

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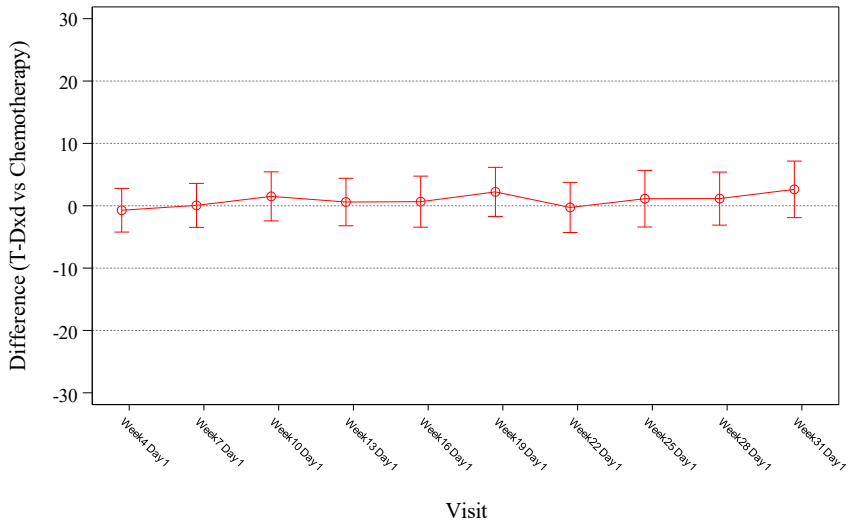
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Functional Scales/Social Functioning



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
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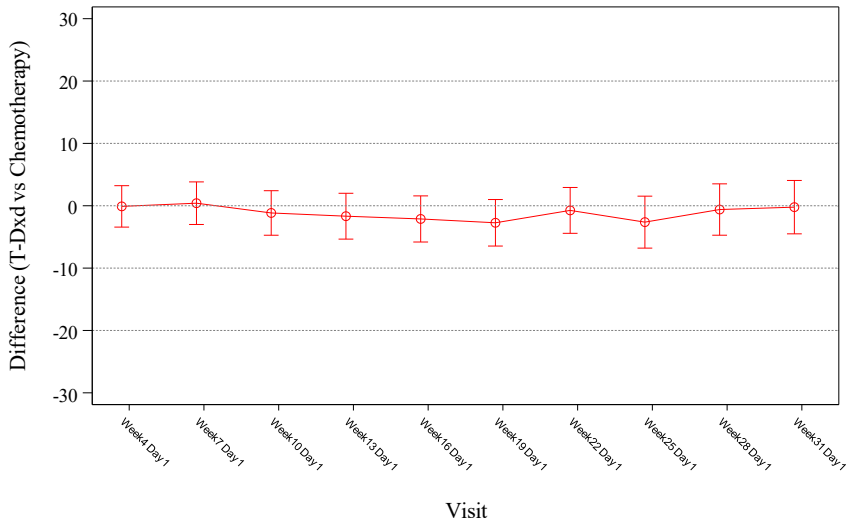
Run date: 31JUL2024 9:45; Program name: F.2.11.10_EORTC_C30_MMRM_CHG_FAS.sas; Output name: F.2.11.10_EORTC_C30_MMRM_CHG_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Symptom Scales/Fatigue



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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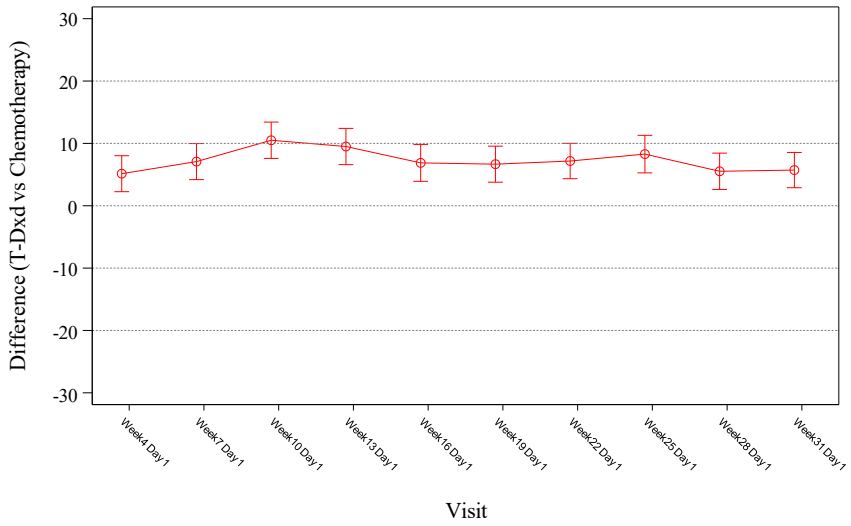
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Symptom Scales/Nausea and Vomiting



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
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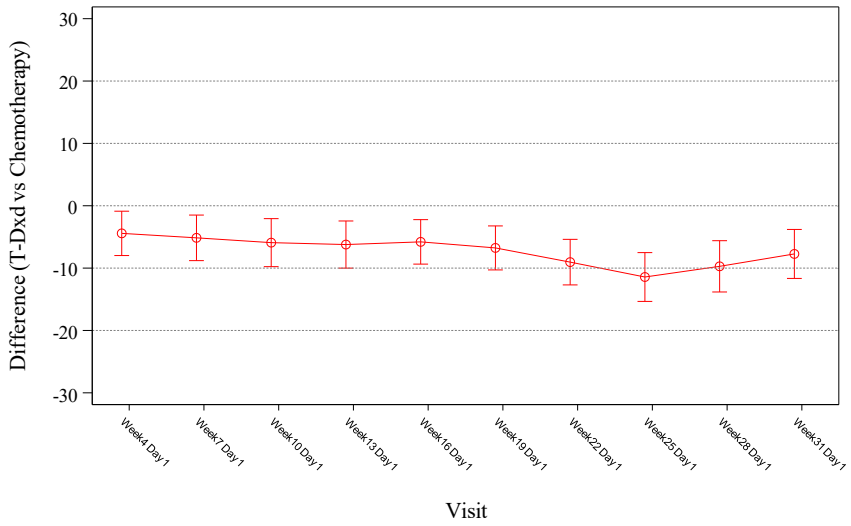
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Symptom Scales/Pain



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
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CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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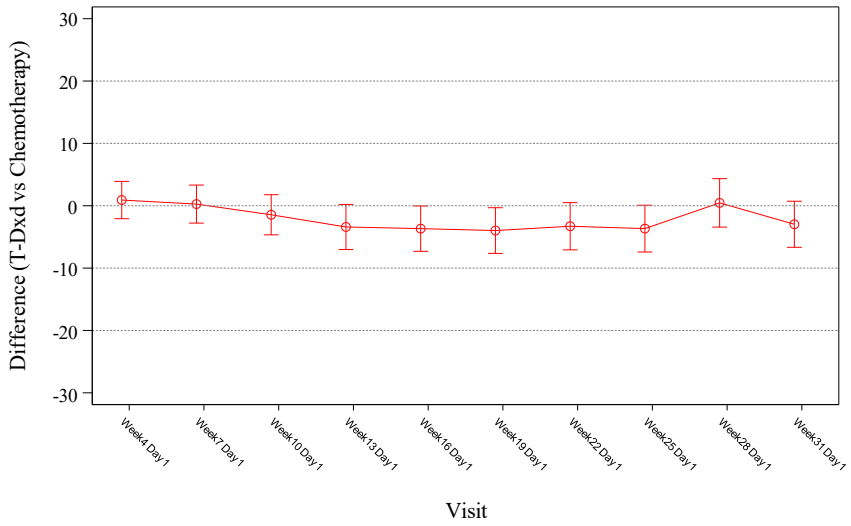
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Common Symptoms/Dyspnoea



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
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CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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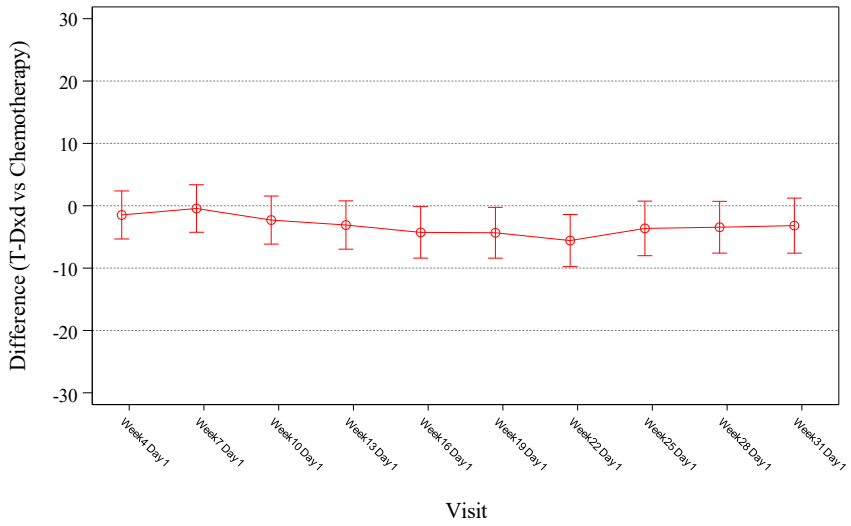
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Common Symptoms/Insomnia



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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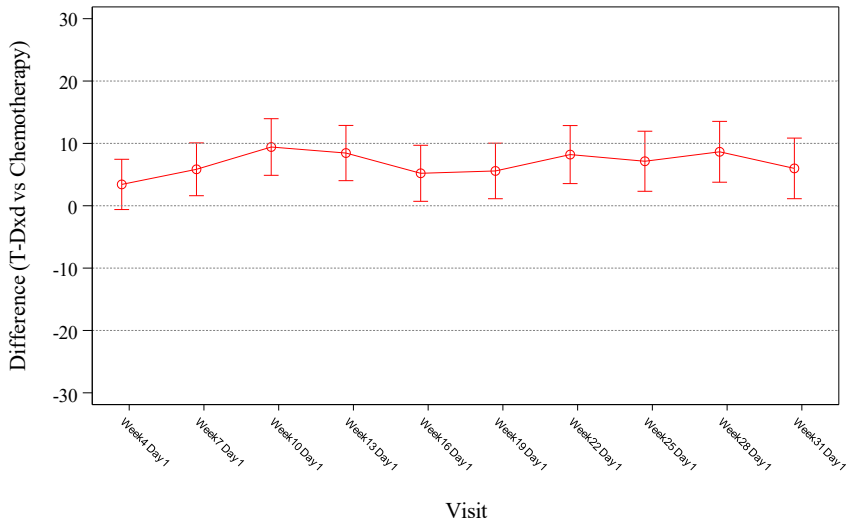
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Common Symptoms/Appetite Loss



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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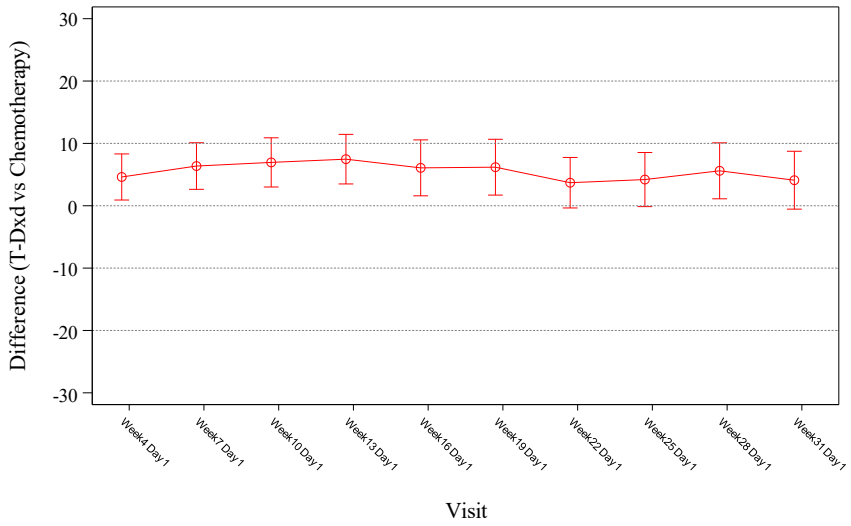
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Common Symptoms/Constipation



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
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CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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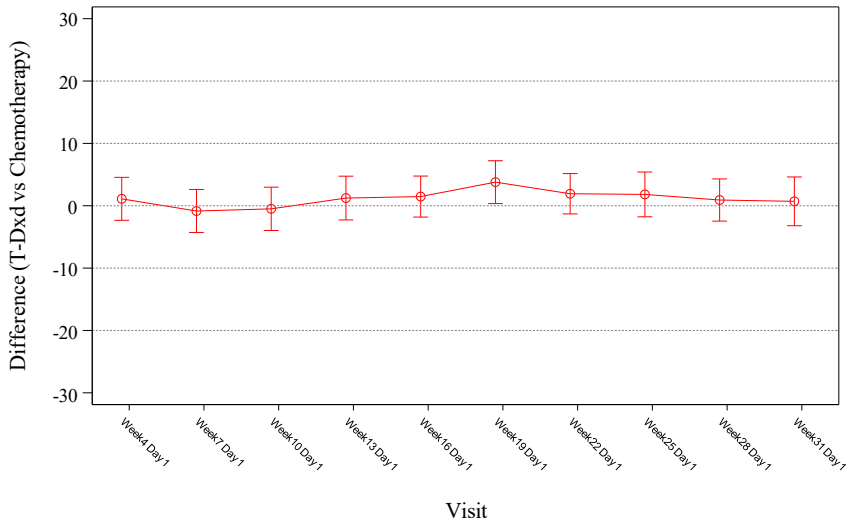
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Common Symptoms/Diarrhea



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The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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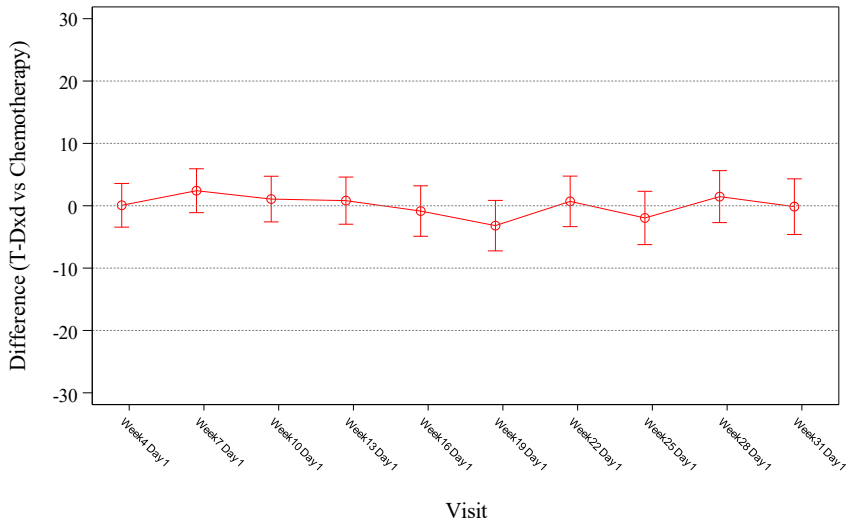
Figure 2.11.10 EORTC-QLQ-C30 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Common Symptoms/Financial Difficulties



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
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CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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Anhang 4-G 3.3 EORTC QLQ-BR45

Tabelle 2.12.1 EORTC-QLQ-BR45 – Zeit bis zur bestätigten Verschlechterung – FAS

Table 2.12.1 EORTC QLQ-BR45 - Time to confirmed deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Body Image	114 (26.1)	18.6 [11.3; NE]	127 (29.5)	9.7 [6.9; 15.1]	0.8609 [0.6674; 1.1092] 0.2472	0.2459
Functional Scales/Sexual Functioning	50 (11.5)	2.0 [1.4; 4.9]	62 (14.4)	4.1 [1.5; 5.5]	1.2178 [0.8355; 1.7663] 0.3007	0.3020
Functional Scales/Breast Satisfaction	104 (23.9)	5.0 [3.4; 9.6]	115 (26.7)	4.2 [2.8; 7.0]	0.9381 [0.7184; 1.2235] 0.6377	0.6419
Functional Scales/Sexual Enjoyment	16 (3.7)	20.6 [4.9; NE]	14 (3.3)	NE [8.4; NE]	1.5975 [0.7762; 3.3268] 0.2022	0.1988
Functional Scales/Future Perspective	72 (16.5)	20.7 [15.9; NE]	89 (20.7)	20.1 [11.3; NE]	0.7816 [0.5710; 1.0662] 0.1211	0.1225
Symptom Scales/Arm Symptoms	107 (24.5)	16.7 [13.9; 31.0]	129 (30.0)	12.4 [7.4; 19.3]	0.7231 [0.5583; 0.9345] 0.0135	0.0135

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

Table 2.12.1 EORTC QLQ-BR45 - Time to confirmed deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Breast Symptoms	43 (9.9)	NE [NE; NE]	61 (14.2)	NE [NE; NE]	0.5840 [0.3924; 0.8620] 0.0072	0.0066
Symptom Scales/Systemic Therapy Side Effects	163 (37.4)	7.6 [4.3; 10.3]	147 (34.2)	7.1 [4.3; 10.5]	1.1108 [0.8888; 1.3896] 0.3564	0.3585
Symptom Scales/Endocrine Therapy Symptoms	81 (18.6)	26.3 [20.0; NE]	108 (25.1)	15.1 [11.1; 24.9]	0.5947 [0.4430; 0.7950] 0.0005	0.0004
Symptom Scales/Skin Mucosis Symptoms	118 (27.1)	15.3 [13.1; 21.4]	198 (46.0)	2.8 [2.1; 3.5]	0.3677 [0.2907; 0.4632] <.0001	<.0001
Symptom Scales/Endocrine Sexual Symptoms	115 (26.4)	17.2 [11.8; NE]	87 (20.2)	22.2 [17.4; NE]	1.3644 [1.0337; 1.8073] 0.0290	0.0292
Symptom Scales/Upset by Hair Loss	41 (9.4)	2.5 [1.4; 6.3]	32 (7.4)	10.3 [2.9; NE]	1.4695 [0.9267; 2.3498] 0.1033	0.1063

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

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Tabelle 2.12.2 EORTC-QLQ-BR45 – Zeit bis zur bestätigten Verschlechterung – Subgruppenanalyse – FAS

Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Body Image						
Age at randomization						0.4624
<65 years of age	82 / 302 (27.2)	17.9 [8.9; NE]	90 / 297 (30.3)	9.0 [6.2; 15.2]	0.8127 [0.6011; 1.0981] 0.1762	
>=65 years of age	32 / 134 (23.9)	18.6 [6.2; NE]	37 / 133 (27.8)	13.1 [6.9; NE]	0.9877 [0.6121; 1.5853] 0.9459	
Race						0.1396
Asian	49 / 154 (31.8)	NE [14.6; NE]	61 / 151 (40.4)	9.0 [5.6; NE]	0.6855 [0.4682; 0.9985] 0.0478	
White	56 / 231 (24.2)	12.4 [5.6; 22.1]	60 / 230 (26.1)	10.4 [6.9; 15.2]	1.0514 [0.7286; 1.5147] 0.7914	
Other	9 / 51 (17.6)	11.0 [1.5; NE]	6 / 49 (12.2)	13.2 [4.1; NE]	1.4523 [0.5199; 4.3591] 0.4796	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0368
Asia	48 / 149 (32.2)	NE [14.6; NE]	60 / 147 (40.8)	9.0 [5.6; NE]	0.6940 [0.4723; 1.0143] 0.0581	
Europe	52 / 227 (22.9)	12.4 [5.7; NE]	57 / 213 (26.8)	9.1 [4.9; 13.2]	0.8868 [0.6069; 1.2928] 0.5294	
Rest of the World	14 / 60 (23.3)	8.9 [1.5; NE]	10 / 70 (14.3)	NE [8.4; NE]	2.1140 [0.9423; 4.9195] 0.0660	
HER2 IHC expression						0.2374
IHC 1+	56 / 239 (23.4)	NE [11.3; NE]	70 / 234 (29.9)	11.0 [6.9; NE]	0.7800 [0.5463; 1.1086] 0.1646	
IHC 2+/ISH-	31 / 117 (26.5)	18.6 [4.9; NE]	39 / 118 (33.1)	7.0 [4.2; 13.1]	0.7457 [0.4607; 1.1967] 0.2223	
IHC >0 <1+	26 / 76 (34.2)	8.9 [2.8; NE]	18 / 76 (23.7)	13.1 [4.3; NE]	1.3338 [0.7355; 2.4726] 0.3450	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5854
Yes	102 / 394 (25.9)	17.9 [10.4; NE]	116 / 389 (29.8)	9.7 [6.2; 13.2]	0.8401 [0.6423; 1.0967] 0.1979	
No	12 / 42 (28.6)	NE [4.9; NE]	11 / 41 (26.8)	NE [6.9; NE]	1.0577 [0.4632; 2.4391] 0.8932	
Prior Taxane Use In The Non-Metastatic Setting						0.8772
Yes	45 / 179 (25.1)	15.1 [7.7; NE]	52 / 177 (29.4)	9.0 [6.2; NE]	0.8525 [0.5683; 1.2730] 0.4310	
No	69 / 257 (26.8)	18.6 [8.9; NE]	75 / 253 (29.6)	10.4 [6.2; 15.1]	0.8651 [0.6225; 1.2005] 0.3838	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4401
1	19 / 65 (29.2)	10.4 [1.5; NE]	20 / 82 (24.4)	10.4 [5.6; NE]	1.2022 [0.6364; 2.2632] 0.5682	
2	71 / 295 (24.1)	22.1 [11.3; NE]	81 / 288 (28.1)	13.1 [6.9; NE]	0.8490 [0.6155; 1.1683] 0.3108	
>=3	23 / 75 (30.7)	13.1 [5.6; NE]	25 / 58 (43.1)	6.3 [3.5; 11.1]	0.6794 [0.3819; 1.2027] 0.1796	
ER/PR status I						0.7798
ER+, PR+	68 / 253 (26.9)	17.9 [8.9; NE]	67 / 237 (28.3)	9.9 [6.2; NE]	0.9009 [0.6422; 1.2648] 0.5432	
ER+, PR-	45 / 167 (26.9)	18.6 [7.7; NE]	55 / 181 (30.4)	9.7 [6.2; 13.1]	0.8360 [0.5600; 1.2413] 0.3701	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.0312
ER <=10%	7 / 21 (33.3)	8.9 [1.4; NE]	8 / 14 (57.1)	1.4 [0.7; 3.5]	0.1956 [0.0503; 0.6484] 0.0042	
ER >10%	94 / 364 (25.8)	18.6 [8.9; NE]	98 / 355 (27.6)	9.9 [8.3; NE]	0.9296 [0.6995; 1.2346] 0.6091	
Positive	13 / 51 (25.5)	NE [11.7; NE]	21 / 61 (34.4)	10.4 [4.2; NE]	0.6806 [0.3301; 1.3511] 0.2727	
Endocrine Resistance						0.1232
Primary	37 / 128 (28.9)	7.7 [4.1; NE]	37 / 140 (26.4)	11.0 [5.7; NE]	1.1744 [0.7428; 1.8567] 0.4873	
Secondary	77 / 308 (25.0)	22.1 [12.4; NE]	89 / 288 (30.9)	9.1 [6.2; 13.2]	0.7568 [0.5561; 1.0277] 0.0719	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3623
Capecitabine	64 / 266 (24.1)	22.1 [11.3; NE]	70 / 257 (27.2)	11.9 [9.0; NE]	0.9661 [0.6865; 1.3571] 0.8337	
Nab-Paclitaxel	28 / 103 (27.2)	NE [7.0; NE]	35 / 105 (33.3)	8.4 [4.2; NE]	0.6973 [0.4209; 1.1447] 0.1528	
Paclitaxel	22 / 67 (32.8)	6.9 [2.1; 17.9]	22 / 68 (32.4)	3.5 [2.0; 9.1]	0.6596 [0.3571; 1.2146] 0.1757	
Prior anthracycline use						0.5916
Yes	54 / 199 (27.1)	13.1 [6.2; NE]	61 / 208 (29.3)	9.1 [6.2; NE]	0.9394 [0.6488; 1.3563] 0.7364	
No	60 / 237 (25.3)	22.1 [12.4; NE]	66 / 222 (29.7)	10.4 [6.2; 15.1]	0.8029 [0.5644; 1.1399] 0.2185	
Liver metastases						0.5156
Yes	71 / 296 (24.0)	18.6 [11.3; NE]	74 / 283 (26.1)	13.1 [8.4; NE]	0.9216 [0.6637; 1.2787] 0.6246	
No	43 / 140 (30.7)	12.4 [6.9; NE]	53 / 147 (36.1)	6.9 [5.6; 11.9]	0.7649 [0.5087; 1.1438] 0.1878	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.7467
0	67 / 252 (26.6)	22.1 [8.2; NE]	78 / 257 (30.4)	9.1 [5.6; 15.2]	0.8364 [0.6009; 1.1602] 0.2805	
>=1	46 / 179 (25.7)	14.6 [8.9; NE]	47 / 164 (28.7)	11.1 [6.3; NE]	0.9080 [0.6036; 1.3653] 0.6381	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Sexual Functioning						
Age at randomization						0.3403
<65 years of age	40 / 302 (13.2)	2.2 [1.4; 4.9]	54 / 297 (18.2)	3.5 [1.5; 5.5]	1.1316 [0.7470; 1.6999] 0.5461	
>=65 years of age	10 / 134 (7.5)	1.4 [0.7; 8.9]	8 / 133 (6.0)	4.9 [0.7; 10.5]	1.6345 [0.6319; 4.3712] 0.2951	
Race						0.4071
Asian	17 / 154 (11.0)	1.4 [0.8; 9.0]	16 / 151 (10.6)	3.5 [0.8; 8.4]	1.1138 [0.5587; 2.2306] 0.7640	
White	27 / 231 (11.7)	2.2 [1.4; 4.9]	43 / 230 (18.7)	2.9 [1.5; 7.7]	1.2984 [0.7842; 2.1181] 0.2951	
Other	6 / 51 (11.8)	2.4 [0.7; NE]	3 / 49 (6.1)	4.9 [4.1; NE]	2.3619 [0.6108; 11.3463] 0.2242	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.8775
Asia	16 / 149 (10.7)	1.4 [0.8; 6.9]	14 / 147 (9.5)	3.5 [0.8; NE]	1.1800 [0.5731; 2.4584] 0.6593	
Europe	27 / 227 (11.9)	2.2 [1.4; 4.9]	34 / 213 (16.0)	4.1 [1.5; 7.7]	1.4298 [0.8470; 2.3953] 0.1694	
Rest of the World	7 / 60 (11.7)	7.1 [0.7; NE]	14 / 70 (20.0)	4.8 [1.4; 10.5]	1.1116 [0.4169; 2.7208] 0.8124	
HER2 IHC expression						0.3692
IHC 1+	26 / 239 (10.9)	1.4 [1.3; 4.9]	37 / 234 (15.8)	1.8 [0.8; 4.8]	0.9772 [0.5850; 1.6086] 0.9307	
IHC 2+/ISH-	14 / 117 (12.0)	4.1 [1.4; 8.9]	16 / 118 (13.6)	7.7 [2.9; 17.3]	1.3942 [0.6693; 2.8715] 0.3616	
IHC >0 <1+	10 / 76 (13.2)	1.7 [0.7; 6.9]	8 / 76 (10.5)	8.4 [1.4; NE]	2.0089 [0.7873; 5.2970] 0.1378	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5361
Yes	45 / 394 (11.4)	2.2 [1.4; 4.9]	56 / 389 (14.4)	4.1 [1.5; 7.0]	1.1872 [0.7981; 1.7561] 0.3833	
No	5 / 42 (11.9)	1.1 [0.7; NE]	6 / 41 (14.6)	3.1 [0.8; NE]	1.6852 [0.4574; 6.2228] 0.4046	
Prior Taxane Use In The Non-Metastatic Setting						0.7729
Yes	22 / 179 (12.3)	3.5 [1.4; 5.6]	24 / 177 (13.6)	4.9 [2.1; 8.4]	1.3186 [0.7335; 2.3588] 0.3517	
No	28 / 257 (10.9)	1.5 [0.8; 4.7]	38 / 253 (15.0)	1.8 [1.0; 4.8]	1.1656 [0.7082; 1.8956] 0.5226	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.8276
1	9 / 65 (13.8)	2.2 [0.8; 11.0]	13 / 82 (15.9)	3.1 [1.4; 4.9]	1.0093 [0.4102; 2.3741] 0.9975	
2	27 / 295 (9.2)	2.0 [1.3; 5.7]	40 / 288 (13.9)	4.3 [1.5; 7.7]	1.1628 [0.7059; 1.8864] 0.5448	
>=3	13 / 75 (17.3)	1.4 [0.8; 5.6]	9 / 58 (15.5)	5.5 [0.7; 8.9]	1.7583 [0.7198; 4.5764] 0.2111	
ER/PR status I						0.2170
ER+, PR+	27 / 253 (10.7)	1.5 [1.3; 4.9]	35 / 237 (14.8)	4.1 [1.5; 8.4]	1.4929 [0.8935; 2.4679] 0.1172	
ER+, PR-	23 / 167 (13.8)	4.3 [1.3; 6.3]	26 / 181 (14.4)	3.1 [0.8; 4.9]	0.9533 [0.5392; 1.6743] 0.8711	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5284
ER <=10%	5 / 21 (23.8)	4.9 [0.7; NE]	1 / 14 (7.1)	4.1 [NE; NE]	0.6138 [0.0767; 12.5724] 0.6728	
ER >10%	42 / 364 (11.5)	2.2 [1.4; 4.9]	53 / 355 (14.9)	4.8 [1.5; 7.0]	1.2295 [0.8156; 1.8420] 0.3141	
Positive	3 / 51 (5.9)	1.4 [0.7; NE]	8 / 61 (13.1)	1.5 [0.7; NE]	2.2447 [0.4585; 9.2028] 0.2538	
Endocrine Resistance						0.4313
Primary	22 / 128 (17.2)	2.0 [0.8; 4.9]	19 / 140 (13.6)	4.2 [2.0; 8.4]	1.4883 [0.8043; 2.7794] 0.2093	
Secondary	28 / 308 (9.1)	1.6 [1.4; 5.7]	43 / 288 (14.9)	2.8 [1.4; 7.0]	1.1314 [0.6933; 1.8183] 0.6024	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.8035
Capecitabine	29 / 266 (10.9)	2.8 [1.4; 5.6]	43 / 257 (16.7)	3.1 [1.5; 4.9]	1.0464 [0.6468; 1.6679] 0.8526	
Nab-Paclitaxel	19 / 103 (18.4)	1.4 [0.8; 4.3]	11 / 105 (10.5)	2.1 [0.7; 10.4]	1.3567 [0.6526; 2.9629] 0.4041	
Paclitaxel	2 / 67 (3.0)	2.0 [1.4; NE]	8 / 68 (11.8)	7.7 [1.4; 10.5]	2.0738 [0.2864; 10.6938] 0.3911	
Prior anthracycline use						0.5575
Yes	24 / 199 (12.1)	2.2 [1.3; 4.9]	27 / 208 (13.0)	4.8 [2.1; 8.4]	1.3932 [0.7967; 2.4220] 0.2406	
No	26 / 237 (11.0)	2.0 [1.3; 5.7]	35 / 222 (15.8)	1.5 [0.8; 7.0]	1.1077 [0.6599; 1.8359] 0.6734	
Liver metastases						0.8017
Yes	40 / 296 (13.5)	2.8 [1.4; 4.9]	32 / 283 (11.3)	3.5 [1.5; 10.4]	1.3560 [0.8511; 2.1780] 0.1948	
No	10 / 140 (7.1)	0.8 [0.7; 10.3]	30 / 147 (20.4)	4.2 [0.8; 5.5]	1.1938 [0.5463; 2.3998] 0.6509	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.7873
0	32 / 252 (12.7)	2.8 [1.4; 6.3]	42 / 257 (16.3)	4.3 [1.8; 5.5]	1.2496 [0.7792; 1.9881] 0.3399	
>=1	18 / 179 (10.1)	1.5 [0.8; 4.9]	18 / 164 (11.0)	2.8 [0.8; 10.5]	1.3299 [0.6864; 2.5773] 0.3876	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 16:55; Program name: T.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.sas; Output name: T.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Breast Satisfaction						
Age at randomization						0.8060
<65 years of age	77 / 302 (25.5)	5.0 [2.9; 9.6]	76 / 297 (25.6)	4.2 [2.8; 11.8]	0.9627 [0.7002; 1.3238] 0.8180	
>=65 years of age	27 / 134 (20.1)	4.9 [2.1; 16.0]	39 / 133 (29.3)	4.1 [2.2; 6.9]	0.9011 [0.5459; 1.4657] 0.6732	
Race						0.3475
Asian	56 / 154 (36.4)	3.5 [2.1; 5.0]	50 / 151 (33.1)	2.8 [2.1; 7.5]	1.1387 [0.7775; 1.6726] 0.4995	
White	43 / 231 (18.6)	9.7 [3.5; NE]	59 / 230 (25.7)	4.9 [2.9; 11.9]	0.8058 [0.5403; 1.1920] 0.2851	
Other	5 / 51 (9.8)	NE [1.6; NE]	6 / 49 (12.2)	4.9 [0.7; NE]	0.6054 [0.1734; 2.0209] 0.4027	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5599
Asia	54 / 149 (36.2)	3.5 [2.0; 5.0]	50 / 147 (34.0)	2.8 [2.1; 7.5]	1.0792 [0.7340; 1.5899] 0.6918	
Europe	41 / 227 (18.1)	9.7 [3.4; NE]	46 / 213 (21.6)	6.9 [2.9; NE]	0.8743 [0.5714; 1.3329] 0.5339	
Rest of the World	9 / 60 (15.0)	11.0 [2.1; NE]	19 / 70 (27.1)	4.9 [1.5; 11.9]	0.5823 [0.2364; 1.3046] 0.2015	
HER2 IHC expression						0.6829
IHC 1+	61 / 239 (25.5)	3.5 [2.1; 9.6]	67 / 234 (28.6)	3.5 [2.1; 4.9]	0.9309 [0.6567; 1.3171] 0.6958	
IHC 2+/ISH-	26 / 117 (22.2)	7.0 [2.1; NE]	30 / 118 (25.4)	3.6 [2.0; 17.5]	0.8285 [0.4843; 1.4072] 0.4777	
IHC >0 <1+	17 / 76 (22.4)	8.2 [1.3; NE]	17 / 76 (22.4)	11.9 [2.9; NE]	1.2234 [0.6181; 2.4209] 0.5600	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9991
Yes	93 / 394 (23.6)	4.9 [3.4; 10.3]	101 / 389 (26.0)	4.1 [2.8; 7.5]	0.9487 [0.7145; 1.2581] 0.7162	
No	11 / 42 (26.2)	7.6 [0.8; 10.3]	14 / 41 (34.1)	4.9 [1.3; 17.5]	0.9567 [0.4227; 2.1124] 0.9167	
Prior Taxane Use In The Non-Metastatic Setting						0.9695
Yes	40 / 179 (22.3)	5.7 [2.1; 11.0]	53 / 177 (29.9)	4.2 [2.8; 8.4]	0.9208 [0.6058; 1.3875] 0.6916	
No	64 / 257 (24.9)	4.9 [3.5; 10.3]	62 / 253 (24.5)	4.1 [2.7; 10.0]	0.9514 [0.6702; 1.3513] 0.7825	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.2415
1	13 / 65 (20.0)	16.0 [2.1; NE]	17 / 82 (20.7)	4.9 [2.0; NE]	0.7144 [0.3337; 1.4907] 0.3658	
2	72 / 295 (24.4)	4.2 [2.8; 8.2]	75 / 288 (26.0)	4.9 [2.8; 10.0]	1.0864 [0.7850; 1.5018] 0.6181	
>=3	19 / 75 (25.3)	3.5 [1.5; NE]	23 / 58 (39.7)	2.2 [0.8; 4.9]	0.6466 [0.3481; 1.1868] 0.1564	
ER/PR status I						0.3511
ER+, PR+	59 / 253 (23.3)	4.2 [2.8; 10.3]	71 / 237 (30.0)	4.1 [2.7; 7.0]	0.8428 [0.5946; 1.1902] 0.3342	
ER+, PR-	44 / 167 (26.3)	5.6 [2.8; 11.8]	41 / 181 (22.7)	4.9 [2.8; NE]	1.0879 [0.7092; 1.6723] 0.7002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9846
ER <=10%	8 / 21 (38.1)	2.1 [0.7; NE]	4 / 14 (28.6)	3.6 [0.6; NE]	0.9026 [0.2702; 3.4695] 0.8813	
ER >10%	86 / 364 (23.6)	4.9 [3.4; 8.4]	94 / 355 (26.5)	4.2 [2.8; 7.0]	0.9071 [0.6756; 1.2161] 0.5091	
Positive	10 / 51 (19.6)	16.0 [0.9; NE]	17 / 61 (27.9)	9.7 [2.1; NE]	0.8474 [0.3730; 1.8253] 0.6970	
Endocrine Resistance						0.9179
Primary	31 / 128 (24.2)	7.1 [2.1; 11.8]	34 / 140 (24.3)	4.2 [2.0; 20.1]	0.9556 [0.5828; 1.5608] 0.8644	
Secondary	73 / 308 (23.7)	4.2 [2.9; 9.7]	81 / 288 (28.1)	4.1 [2.8; 7.5]	0.9322 [0.6780; 1.2792] 0.6539	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.2427
Capecitabine	66 / 266 (24.8)	4.9 [3.4; 11.0]	70 / 257 (27.2)	4.9 [2.8; 10.0]	1.0174 [0.7256; 1.4250] 0.9179	
Nab-Paclitaxel	32 / 103 (31.1)	2.8 [1.3; 9.6]	31 / 105 (29.5)	2.8 [1.4; 4.9]	1.0038 [0.6086; 1.6599] 0.9908	
Paclitaxel	6 / 67 (9.0)	NE [8.4; NE]	14 / 68 (20.6)	9.7 [1.6; NE]	0.4584 [0.1613; 1.1513] 0.1082	
Prior anthracycline use						0.1342
Yes	48 / 199 (24.1)	3.5 [2.1; 9.6]	53 / 208 (25.5)	6.9 [3.5; 15.1]	1.1612 [0.7834; 1.7167] 0.4528	
No	56 / 237 (23.6)	6.0 [3.5; 11.8]	62 / 222 (27.9)	2.9 [2.0; 4.9]	0.7854 [0.5450; 1.1292] 0.1893	
Liver metastases						0.3240
Yes	67 / 296 (22.6)	7.0 [3.5; 11.9]	80 / 283 (28.3)	4.9 [2.8; 9.7]	0.8483 [0.6111; 1.1738] 0.3216	
No	37 / 140 (26.4)	3.5 [2.0; 7.1]	35 / 147 (23.8)	3.6 [1.6; 16.5]	1.1436 [0.7190; 1.8219] 0.5754	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.1294
0	59 / 252 (23.4)	7.0 [3.6; 16.0]	74 / 257 (28.8)	4.2 [2.8; 7.5]	0.7958 [0.5624; 1.1210] 0.1921	
>=1	45 / 179 (25.1)	3.5 [2.1; 7.6]	39 / 164 (23.8)	3.5 [2.1; NE]	1.2272 [0.7992; 1.8929] 0.3487	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Sexual Enjoyment						
Age at randomization						0.4562
<65 years of age	14 / 302 (4.6)	20.6 [4.9; NE]	13 / 297 (4.4)	NE [8.4; NE]	1.4643 [0.6824; 3.1656] 0.3183	
>=65 years of age	2 / 134 (1.5)	NE [0.7; NE]	1 / 133 (0.8)	NE [7.7; NE]	2.8118 [0.2480; 64.1837] 0.4012	
Race						0.2403
Asian	3 / 154 (1.9)	NE [0.8; NE]	5 / 151 (3.3)	NE [0.8; NE]	0.6190 [0.1267; 2.5291] 0.5051	
White	12 / 231 (5.2)	20.6 [1.5; NE]	7 / 230 (3.0)	NE [8.4; NE]	2.6289 [1.0539; 7.0864] 0.0359	
Other	1 / 51 (2.0)	NE [0.7; NE]	2 / 49 (4.1)	7.7 [2.1; NE]	0.8794 [0.0395; 9.6623] 0.9183	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5584
Asia	3 / 149 (2.0)	NE [0.8; NE]	4 / 147 (2.7)	NE [0.8; NE]	0.7246 [0.1425; 3.2921] 0.6778	
Europe	12 / 227 (5.3)	7.7 [1.4; NE]	9 / 213 (4.2)	NE [4.3; NE]	1.7992 [0.7588; 4.4221] 0.1809	
Rest of the World	1 / 60 (1.7)	NE [0.7; NE]	1 / 70 (1.4)	NE [0.8; NE]	2.7386 [0.1082; 69.3216] 0.4581	
HER2 IHC expression						0.3465
IHC 1+	6 / 239 (2.5)	NE [1.5; NE]	7 / 234 (3.0)	NE [2.1; NE]	1.1403 [0.3666; 3.4375] 0.8149	
IHC 2+/ISH-	8 / 117 (6.8)	4.9 [0.8; NE]	7 / 118 (5.9)	8.4 [2.1; NE]	1.7295 [0.6159; 4.9702] 0.2907	
IHC >0 <1+	2 / 76 (2.6)	20.6 [6.7; NE]	0 / 76 (0.0)	NE [NE; NE]	1.9811E8 [0.5560; NE] 0.1803	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1426
Yes	15 / 394 (3.8)	20.6 [4.9; NE]	14 / 389 (3.6)	NE [7.7; NE]	1.4194 [0.6807; 2.9780] 0.3427	
No	1 / 42 (2.4)	NE [0.8; NE]	0 / 41 (0.0)	NE [NE; NE]	5.6442E8 [0.3433; NE] 0.1573	
Prior Taxane Use In The Non-Metastatic Setting						0.5111
Yes	8 / 179 (4.5)	NE [1.4; NE]	8 / 177 (4.5)	NE [2.1; NE]	1.1492 [0.4218; 3.1307] 0.7764	
No	8 / 257 (3.1)	20.6 [1.4; NE]	6 / 253 (2.4)	NE [NE; NE]	2.0056 [0.6947; 6.1154] 0.1920	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1746
1	4 / 65 (6.2)	1.4 [0.7; NE]	3 / 82 (3.7)	NE [4.3; NE]	5.8139 [1.2339; 30.7542] 0.0122	
2	7 / 295 (2.4)	20.6 [7.7; NE]	9 / 288 (3.1)	NE [7.7; NE]	0.9799 [0.3483; 2.6479] 0.9783	
>=3	5 / 75 (6.7)	6.7 [1.4; NE]	2 / 58 (3.4)	NE [0.8; NE]	1.7681 [0.3737; 12.5188] 0.4999	
ER/PR status I						0.8905
ER+, PR+	6 / 253 (2.4)	NE [4.9; NE]	7 / 237 (3.0)	NE [8.4; NE]	1.3578 [0.4352; 4.1085] 0.5785	
ER+, PR-	10 / 167 (6.0)	7.7 [1.3; NE]	7 / 181 (3.9)	NE [2.1; NE]	1.5249 [0.5664; 4.2782] 0.4027	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4583
ER <=10%	1 / 21 (4.8)	NE [4.9; NE]	1 / 14 (7.1)	2.1 [NE; NE]	0.0000 [NE; 2.9130] 0.1573	
ER >10%	14 / 364 (3.8)	20.6 [2.9; NE]	10 / 355 (2.8)	NE [8.4; NE]	1.8967 [0.8471; 4.4071] 0.1163	
Positive	1 / 51 (2.0)	NE [1.4; NE]	3 / 61 (4.9)	NE [0.8; NE]	1.0923 [0.0538; 8.6102] 0.9393	
Endocrine Resistance						0.2301
Primary	9 / 128 (7.0)	2.9 [0.8; NE]	6 / 140 (4.3)	NE [4.3; NE]	2.4992 [0.8994; 7.4716] 0.0705	
Secondary	7 / 308 (2.3)	NE [6.7; NE]	8 / 288 (2.8)	NE [7.7; NE]	1.0745 [0.3761; 2.9974] 0.8937	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.7189
Capecitabine	11 / 266 (4.1)	NE [1.5; NE]	12 / 257 (4.7)	NE [4.3; NE]	1.4126 [0.6117; 3.2314] 0.4030	
Nab-Paclitaxel	3 / 103 (2.9)	NE [0.8; NE]	1 / 105 (1.0)	NE [2.0; NE]	1.7881 [0.2281; 36.2075] 0.6104	
Paclitaxel	2 / 67 (3.0)	14.2 [7.7; NE]	1 / 68 (1.5)	NE [2.1; NE]	2.0000 [0.0777; 51.5008] 0.6211	
Prior anthracycline use						0.6222
Yes	9 / 199 (4.5)	7.7 [1.4; NE]	9 / 208 (4.3)	NE [2.1; NE]	1.2893 [0.5013; 3.3154] 0.5911	
No	7 / 237 (3.0)	20.6 [2.9; NE]	5 / 222 (2.3)	NE [7.7; NE]	1.9669 [0.6258; 6.6645] 0.2424	
Liver metastases						0.0748
Yes	12 / 296 (4.1)	20.6 [4.9; NE]	11 / 283 (3.9)	NE [2.0; NE]	0.9521 [0.4168; 2.1964] 0.9040	
No	4 / 140 (2.9)	6.7 [0.8; NE]	3 / 147 (2.0)	NE [8.4; NE]	4.3408 [0.9483; 22.2221] 0.0376	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.7724
0	12 / 252 (4.8)	20.6 [1.4; NE]	11 / 257 (4.3)	NE [7.7; NE]	1.7445 [0.7633; 4.0263] 0.1800	
>=1	4 / 179 (2.2)	NE [1.4; NE]	3 / 164 (1.8)	NE [0.8; NE]	1.2318 [0.2715; 6.2541] 0.7656	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Future Perspective						
Age at randomization						0.7833
<65 years of age	46 / 302 (15.2)	20.7 [15.9; NE]	55 / 297 (18.5)	23.6 [11.8; NE]	0.8182 [0.5503; 1.2112] 0.3157	
>=65 years of age	26 / 134 (19.4)	15.8 [9.6; NE]	34 / 133 (25.6)	12.4 [5.5; NE]	0.7375 [0.4377; 1.2282] 0.2456	
Race						0.2289
Asian	36 / 154 (23.4)	NE [17.3; NE]	50 / 151 (33.1)	13.1 [5.6; NE]	0.6206 [0.4008; 0.9515] 0.0289	
White	32 / 231 (13.9)	15.9 [11.9; NE]	34 / 230 (14.8)	NE [10.6; NE]	0.9836 [0.6044; 1.5970] 0.9476	
Other	4 / 51 (7.8)	12.4 [1.4; NE]	5 / 49 (10.2)	22.2 [2.0; NE]	1.3880 [0.3276; 5.8809] 0.6414	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5154
Asia	36 / 149 (24.2)	20.7 [17.3; NE]	48 / 147 (32.7)	13.1 [8.2; NE]	0.6671 [0.4293; 1.0273] 0.0670	
Europe	28 / 227 (12.3)	15.9 [11.3; NE]	31 / 213 (14.6)	22.2 [10.5; NE]	0.9215 [0.5491; 1.5394] 0.7550	
Rest of the World	8 / 60 (13.3)	15.8 [4.1; NE]	10 / 70 (14.3)	NE [2.7; NE]	0.9402 [0.3528; 2.4201] 0.9016	
HER2 IHC expression						0.3343
IHC 1+	38 / 239 (15.9)	NE [17.3; NE]	56 / 234 (23.9)	12.4 [8.3; NE]	0.6668 [0.4377; 1.0048] 0.0540	
IHC 2+/ISH-	17 / 117 (14.5)	NE [12.4; NE]	21 / 118 (17.8)	21.3 [7.6; NE]	0.8397 [0.4356; 1.5965] 0.5985	
IHC >0 <1+	16 / 76 (21.1)	15.8 [7.6; NE]	11 / 76 (14.5)	23.6 [5.6; NE]	1.2608 [0.5874; 2.8080] 0.5455	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8577
Yes	62 / 394 (15.7)	20.7 [15.8; NE]	77 / 389 (19.8)	20.1 [11.3; NE]	0.7894 [0.5629; 1.1025] 0.1658	
No	10 / 42 (23.8)	NE [6.2; NE]	12 / 41 (29.3)	NE [2.1; NE]	0.7480 [0.3147; 1.7405] 0.4966	
Prior Taxane Use In The Non-Metastatic Setting						0.4883
Yes	29 / 179 (16.2)	17.3 [11.3; NE]	34 / 177 (19.2)	NE [7.5; NE]	0.9203 [0.5551; 1.5151] 0.7522	
No	43 / 257 (16.7)	20.7 [15.9; NE]	55 / 253 (21.7)	20.1 [10.6; NE]	0.7205 [0.4810; 1.0723] 0.1065	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4258
1	8 / 65 (12.3)	NE [11.9; NE]	13 / 82 (15.9)	NE [5.6; NE]	0.9114 [0.3598; 2.1689] 0.8392	
2	46 / 295 (15.6)	20.7 [17.3; NE]	63 / 288 (21.9)	20.1 [10.6; NE]	0.7122 [0.4837; 1.0409] 0.0809	
>=3	18 / 75 (24.0)	15.8 [7.6; NE]	12 / 58 (20.7)	21.3 [8.3; NE]	1.3703 [0.6515; 3.0197] 0.4131	
ER/PR status I						0.9744
ER+, PR+	43 / 253 (17.0)	20.7 [15.8; NE]	51 / 237 (21.5)	22.2 [10.5; NE]	0.7801 [0.5169; 1.1714] 0.2334	
ER+, PR-	29 / 167 (17.4)	20.7 [12.4; NE]	36 / 181 (19.9)	20.1 [11.8; NE]	0.7937 [0.4830; 1.2933] 0.3561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3107
ER <=10%	2 / 21 (9.5)	20.7 [7.6; NE]	3 / 14 (21.4)	6.9 [0.7; NE]	0.1269 [0.0061; 1.0355] 0.0410	
ER >10%	58 / 364 (15.9)	NE [13.8; NE]	73 / 355 (20.6)	20.1 [11.3; NE]	0.7787 [0.5494; 1.0986] 0.1566	
Positive	12 / 51 (23.5)	20.7 [9.0; NE]	13 / 61 (21.3)	21.3 [5.0; NE]	0.9980 [0.4446; 2.2257] 0.9952	
Endocrine Resistance						0.3903
Primary	22 / 128 (17.2)	20.7 [11.1; NE]	27 / 140 (19.3)	13.1 [7.6; NE]	0.9481 [0.5338; 1.6654] 0.8558	
Secondary	50 / 308 (16.2)	20.7 [15.9; NE]	62 / 288 (21.5)	21.3 [10.6; NE]	0.7199 [0.4937; 1.0447] 0.0840	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 16:55; Program name: T.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.sas; Output name: T.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.8254
Capecitabine	41 / 266 (15.4)	20.7 [15.9; NE]	51 / 257 (19.8)	21.3 [11.8; NE]	0.7461 [0.4917; 1.1250] 0.1627	
Nab-Paclitaxel	21 / 103 (20.4)	17.3 [7.6; NE]	25 / 105 (23.8)	NE [5.5; NE]	0.9389 [0.5202; 1.6773] 0.8354	
Paclitaxel	10 / 67 (14.9)	15.9 [7.6; NE]	13 / 68 (19.1)	7.6 [4.1; NE]	0.6024 [0.2467; 1.4072] 0.2436	
Prior anthracycline use						0.0341
Yes	36 / 199 (18.1)	17.3 [7.7; NE]	37 / 208 (17.8)	NE [11.8; NE]	1.1729 [0.7383; 1.8612] 0.4943	
No	36 / 237 (15.2)	20.7 [15.9; NE]	52 / 222 (23.4)	12.5 [7.6; 22.2]	0.5708 [0.3702; 0.8709] 0.0089	
Liver metastases						0.1380
Yes	49 / 296 (16.6)	15.9 [11.9; NE]	54 / 283 (19.1)	21.3 [11.3; NE]	0.9324 [0.6309; 1.3745] 0.7230	
No	23 / 140 (16.4)	NE [17.3; NE]	35 / 147 (23.8)	20.1 [7.5; NE]	0.5717 [0.3332; 0.9624] 0.0357	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.3046
0	42 / 252 (16.7)	20.7 [15.9; NE]	47 / 257 (18.3)	22.2 [12.4; NE]	0.8767 [0.5753; 1.3313] 0.5344	
>=1	29 / 179 (16.2)	17.3 [11.1; NE]	42 / 164 (25.6)	11.1 [4.9; NE]	0.6236 [0.3842; 0.9982] 0.0499	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Arm Symptoms						
Age at randomization						0.5718
<65 years of age	75 / 302 (24.8)	23.4 [15.2; 31.7]	88 / 297 (29.6)	13.1 [7.0; 22.0]	0.6788 [0.4955; 0.9270] 0.0147	
>=65 years of age	32 / 134 (23.9)	13.9 [9.7; NE]	41 / 133 (30.8)	12.4 [6.2; NE]	0.8121 [0.5076; 1.2877] 0.3766	
Race						0.9763
Asian	56 / 154 (36.4)	20.0 [13.7; 31.7]	65 / 151 (43.0)	11.1 [5.6; 20.8]	0.7186 [0.5007; 1.0281] 0.0703	
White	43 / 231 (18.6)	31.0 [11.3; NE]	57 / 230 (24.8)	12.4 [6.9; NE]	0.7117 [0.4748; 1.0582] 0.0935	
Other	8 / 51 (15.7)	13.1 [9.0; NE]	7 / 49 (14.3)	17.4 [2.1; NE]	0.9443 [0.3230; 2.9197] 0.9173	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5443
Asia	55 / 149 (36.9)	20.0 [13.7; 31.7]	64 / 147 (43.5)	11.1 [5.6; 20.8]	0.7183 [0.4989; 1.0307] 0.0723	
Europe	43 / 227 (18.9)	15.3 [9.7; NE]	49 / 213 (23.0)	15.9 [6.9; NE]	0.8030 [0.5292; 1.2129] 0.2986	
Rest of the World	9 / 60 (15.0)	16.7 [12.4; NE]	16 / 70 (22.9)	11.2 [4.1; NE]	0.4569 [0.1906; 1.0295] 0.0587	
HER2 IHC expression						0.7499
IHC 1+	59 / 239 (24.7)	20.0 [12.5; 31.7]	75 / 234 (32.1)	12.4 [8.3; 19.3]	0.7249 [0.5132; 1.0191] 0.0644	
IHC 2+/ISH-	26 / 117 (22.2)	31.0 [11.2; NE]	34 / 118 (28.8)	6.9 [4.3; NE]	0.6125 [0.3607; 1.0258] 0.0614	
IHC >0 <1+	21 / 76 (27.6)	15.8 [10.3; NE]	20 / 76 (26.3)	15.9 [4.9; NE]	0.8287 [0.4465; 1.5433] 0.5508	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8372
Yes	93 / 394 (23.6)	15.9 [13.7; 31.0]	115 / 389 (29.6)	11.2 [7.0; 19.3]	0.7146 [0.5425; 0.9394] 0.0160	
No	14 / 42 (33.3)	20.0 [9.7; NE]	14 / 41 (34.1)	13.1 [4.8; NE]	0.7371 [0.3340; 1.6012] 0.4399	
Prior Taxane Use In The Non-Metastatic Setting						0.5356
Yes	47 / 179 (26.3)	15.3 [12.4; 23.4]	63 / 177 (35.6)	6.2 [4.8; 11.2]	0.6575 [0.4467; 0.9611] 0.0307	
No	60 / 257 (23.3)	25.5 [13.7; NE]	66 / 253 (26.1)	17.4 [11.1; 23.6]	0.7808 [0.5482; 1.1097] 0.1674	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3143
1	19 / 65 (29.2)	13.7 [7.7; 16.7]	18 / 82 (22.0)	13.1 [5.6; NE]	0.9932 [0.5121; 1.9256] 0.9851	
2	68 / 295 (23.1)	23.4 [13.2; NE]	92 / 288 (31.9)	11.1 [6.2; 17.4]	0.6475 [0.4712; 0.8855] 0.0064	
>=3	20 / 75 (26.7)	15.8 [10.3; NE]	18 / 58 (31.0)	20.8 [6.9; NE]	0.8902 [0.4653; 1.7096] 0.7274	
ER/PR status I						0.5932
ER+, PR+	56 / 253 (22.1)	25.5 [15.3; NE]	68 / 237 (28.7)	15.8 [8.2; 23.6]	0.6725 [0.4703; 0.9577] 0.0274	
ER+, PR-	50 / 167 (29.9)	13.9 [9.1; 23.4]	57 / 181 (31.5)	11.1 [5.6; 20.8]	0.7887 [0.5359; 1.1567] 0.2248	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6008
ER <=10%	5 / 21 (23.8)	15.9 [5.6; NE]	4 / 14 (28.6)	6.9 [4.2; NE]	0.5131 [0.1301; 2.1466] 0.3277	
ER >10%	87 / 364 (23.9)	20.0 [13.7; 31.0]	106 / 355 (29.9)	11.2 [7.4; 15.9]	0.6768 [0.5067; 0.9010] 0.0074	
Positive	15 / 51 (29.4)	13.9 [9.1; NE]	19 / 61 (31.1)	19.3 [5.5; NE]	0.9862 [0.4897; 1.9537] 0.9706	
Endocrine Resistance						0.4721
Primary	31 / 128 (24.2)	15.2 [12.4; NE]	43 / 140 (30.7)	8.2 [4.8; NE]	0.6129 [0.3806; 0.9743] 0.0388	
Secondary	76 / 308 (24.7)	20.0 [13.1; 32.4]	86 / 288 (29.9)	15.8 [8.4; 20.8]	0.7691 [0.5635; 1.0478] 0.0953	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.2665
Capecitabine	69 / 266 (25.9)	15.2 [10.3; NE]	78 / 257 (30.4)	15.9 [8.2; 22.0]	0.8291 [0.5982; 1.1468] 0.2595	
Nab-Paclitaxel	21 / 103 (20.4)	23.4 [15.3; NE]	35 / 105 (33.3)	13.1 [5.6; NE]	0.4685 [0.2622; 0.8117] 0.0069	
Paclitaxel	17 / 67 (25.4)	25.5 [7.6; NE]	16 / 68 (23.5)	7.4 [4.2; NE]	0.6867 [0.3345; 1.4022] 0.2941	
Prior anthracycline use						0.7810
Yes	54 / 199 (27.1)	15.2 [11.0; 31.0]	68 / 208 (32.7)	8.4 [5.0; 15.8]	0.7440 [0.5177; 1.0639] 0.1065	
No	53 / 237 (22.4)	23.4 [15.2; NE]	61 / 222 (27.5)	15.9 [8.3; 22.8]	0.7011 [0.4824; 1.0150] 0.0594	
Liver metastases						0.4103
Yes	71 / 296 (24.0)	15.9 [13.1; 31.0]	85 / 283 (30.0)	11.1 [6.2; 20.8]	0.6488 [0.4696; 0.8928] 0.0077	
No	36 / 140 (25.7)	20.0 [12.5; NE]	44 / 147 (29.9)	15.9 [8.2; 23.6]	0.8274 [0.5293; 1.2852] 0.4009	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0718
0	52 / 252 (20.6)	31.0 [15.9; 32.4]	78 / 257 (30.4)	12.4 [7.4; 22.8]	0.5832 [0.4060; 0.8300] 0.0027	
>=1	54 / 179 (30.2)	11.2 [9.1; 15.3]	48 / 164 (29.3)	15.8 [5.7; 20.8]	0.9325 [0.6316; 1.3813] 0.7347	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Breast Symptoms						
Age at randomization						0.6402
<65 years of age	31 / 302 (10.3)	NE [25.6; NE]	44 / 297 (14.8)	NE [NE; NE]	0.5550 [0.3469; 0.8772] 0.0113	
>=65 years of age	12 / 134 (9.0)	NE [NE; NE]	17 / 133 (12.8)	NE [19.4; NE]	0.6770 [0.3140; 1.4140] 0.3019	
Race						0.6121
Asian	19 / 154 (12.3)	NE [NE; NE]	27 / 151 (17.9)	NE [NE; NE]	0.5485 [0.2990; 0.9858] 0.0439	
White	22 / 231 (9.5)	NE [21.4; NE]	30 / 230 (13.0)	NE [19.4; NE]	0.6696 [0.3813; 1.1575] 0.1516	
Other	2 / 51 (3.9)	NE [NE; NE]	4 / 49 (8.2)	NE [5.6; NE]	0.3918 [0.0541; 2.0175] 0.2702	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.9448
Asia	19 / 149 (12.8)	NE [25.6; NE]	27 / 147 (18.4)	NE [NE; NE]	0.5528 [0.3016; 0.9932] 0.0467	
Europe	19 / 227 (8.4)	NE [21.4; NE]	27 / 213 (12.7)	NE [19.4; NE]	0.6004 [0.3286; 1.0752] 0.0859	
Rest of the World	5 / 60 (8.3)	NE [14.5; NE]	7 / 70 (10.0)	NE [11.7; NE]	0.6783 [0.1971; 2.1657] 0.5124	
HER2 IHC expression						0.3904
IHC 1+	22 / 239 (9.2)	NE [25.6; NE]	35 / 234 (15.0)	NE [NE; NE]	0.5192 [0.2992; 0.8819] 0.0150	
IHC 2+/ISH-	12 / 117 (10.3)	NE [21.4; NE]	19 / 118 (16.1)	NE [11.2; NE]	0.5215 [0.2449; 1.0675] 0.0749	
IHC >0 <1+	9 / 76 (11.8)	NE [NE; NE]	7 / 76 (9.2)	NE [19.4; NE]	1.0627 [0.3954; 2.9790] 0.9006	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0058
Yes	32 / 394 (8.1)	NE [NE; NE]	56 / 389 (14.4)	NE [NE; NE]	0.4661 [0.2981; 0.7164] 0.0005	
No	11 / 42 (26.2)	19.3 [12.4; NE]	5 / 41 (12.2)	NE [11.7; NE]	2.0436 [0.7415; 6.4998] 0.1769	
Prior Taxane Use In The Non-Metastatic Setting						0.1362
Yes	13 / 179 (7.3)	NE [NE; NE]	26 / 177 (14.7)	NE [NE; NE]	0.3839 [0.1891; 0.7420] 0.0041	
No	30 / 257 (11.7)	NE [25.6; NE]	35 / 253 (13.8)	NE [NE; NE]	0.7374 [0.4498; 1.2014] 0.2205	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5943
1	7 / 65 (10.8)	NE [NE; NE]	7 / 82 (8.5)	NE [13.1; NE]	0.8849 [0.3005; 2.6061] 0.8208	
2	26 / 295 (8.8)	NE [25.6; NE]	44 / 288 (15.3)	NE [NE; NE]	0.5048 [0.3063; 0.8154] 0.0051	
>=3	10 / 75 (13.3)	NE [17.9; NE]	10 / 58 (17.2)	NE [13.8; NE]	0.7098 [0.2892; 1.7406] 0.4448	
ER/PR status I						0.1119
ER+, PR+	21 / 253 (8.3)	NE [NE; NE]	38 / 237 (16.0)	NE [NE; NE]	0.4432 [0.2554; 0.7484] 0.0022	
ER+, PR-	21 / 167 (12.6)	NE [21.4; NE]	21 / 181 (11.6)	NE [19.4; NE]	0.7903 [0.4258; 1.4659] 0.4516	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2900
ER <=10%	1 / 21 (4.8)	NE [8.9; NE]	2 / 14 (14.3)	NE [12.4; NE]	0.2925 [0.0133; 3.1433] 0.2943	
ER >10%	37 / 364 (10.2)	NE [25.6; NE]	46 / 355 (13.0)	NE [NE; NE]	0.6842 [0.4409; 1.0547] 0.0852	
Positive	5 / 51 (9.8)	NE [16.6; NE]	13 / 61 (21.3)	NE [8.4; NE]	0.3228 [0.1029; 0.8631] 0.0249	
Endocrine Resistance						0.7573
Primary	13 / 128 (10.2)	NE [NE; NE]	21 / 140 (15.0)	NE [15.9; NE]	0.5387 [0.2615; 1.0685] 0.0772	
Secondary	30 / 308 (9.7)	NE [25.6; NE]	40 / 288 (13.9)	NE [NE; NE]	0.6102 [0.3766; 0.9784] 0.0398	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.5887
Capecitabine	25 / 266 (9.4)	NE [25.6; NE]	39 / 257 (15.2)	NE [NE; NE]	0.5186 [0.3095; 0.8531] 0.0095	
Nab-Paclitaxel	13 / 103 (12.6)	NE [19.3; NE]	16 / 105 (15.2)	NE [15.9; NE]	0.7911 [0.3731; 1.6461] 0.5294	
Paclitaxel	5 / 67 (7.5)	NE [20.0; NE]	6 / 68 (8.8)	NE [11.2; NE]	0.4610 [0.1174; 1.6225] 0.2210	
Prior anthracycline use						0.9536
Yes	19 / 199 (9.5)	NE [25.6; NE]	27 / 208 (13.0)	NE [NE; NE]	0.5883 [0.3200; 1.0599] 0.0773	
No	24 / 237 (10.1)	NE [NE; NE]	34 / 222 (15.3)	NE [19.4; NE]	0.5843 [0.3424; 0.9815] 0.0417	
Liver metastases						0.9020
Yes	27 / 296 (9.1)	NE [NE; NE]	36 / 283 (12.7)	NE [NE; NE]	0.6074 [0.3638; 1.0018] 0.0501	
No	16 / 140 (11.4)	NE [19.4; NE]	25 / 147 (17.0)	NE [19.4; NE]	0.5749 [0.3005; 1.0685] 0.0808	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.6838
0	25 / 252 (9.9)	NE [NE; NE]	40 / 257 (15.6)	NE [NE; NE]	0.5443 [0.3256; 0.8928] 0.0158	
>=1	17 / 179 (9.5)	NE [20.0; NE]	20 / 164 (12.2)	NE [NE; NE]	0.6171 [0.3170; 1.1870] 0.1446	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Systemic Therapy Side Effects						
Age at randomization						0.4374
<65 years of age	118 / 302 (39.1)	6.2 [4.1; 9.0]	99 / 297 (33.3)	7.5 [4.8; 15.2]	1.1793 [0.9037; 1.5437] 0.2269	
>=65 years of age	45 / 134 (33.6)	11.0 [5.6; 15.3]	48 / 133 (36.1)	4.9 [3.6; 22.1]	0.9487 [0.6290; 1.4283] 0.8091	
Race						0.8256
Asian	78 / 154 (50.6)	8.9 [6.2; 15.3]	63 / 151 (41.7)	9.6 [4.8; NE]	1.0913 [0.7829; 1.5276] 0.6039	
White	73 / 231 (31.6)	5.7 [2.9; 9.0]	76 / 230 (33.0)	4.9 [3.4; 8.3]	1.1121 [0.8050; 1.5342] 0.5204	
Other	12 / 51 (23.5)	3.7 [1.4; 11.7]	8 / 49 (16.3)	3.5 [2.1; NE]	1.4615 [0.6029; 3.7400] 0.4013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.9040
Asia	77 / 149 (51.7)	8.3 [5.6; 15.3]	63 / 147 (42.9)	9.6 [4.8; NE]	1.0852 [0.7780; 1.5201] 0.6260	
Europe	68 / 227 (30.0)	6.3 [2.9; 9.7]	62 / 213 (29.1)	6.1 [3.5; 15.9]	1.1945 [0.8457; 1.6898] 0.3108	
Rest of the World	18 / 60 (30.0)	4.1 [1.4; 11.7]	22 / 70 (31.4)	4.9 [2.2; 10.5]	1.0112 [0.5298; 1.9030] 0.9762	
HER2 IHC expression						0.3461
IHC 1+	88 / 239 (36.8)	8.3 [4.8; 11.8]	88 / 234 (37.6)	6.2 [4.2; 9.9]	0.9813 [0.7289; 1.3211] 0.9021	
IHC 2+/ISH-	46 / 117 (39.3)	4.2 [2.1; 11.7]	35 / 118 (29.7)	10.5 [3.7; NE]	1.4451 [0.9321; 2.2605] 0.1002	
IHC >0 <1+	28 / 76 (36.8)	8.3 [2.7; NE]	22 / 76 (28.9)	9.6 [4.1; NE]	1.2462 [0.7140; 2.2027] 0.4440	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9203
Yes	144 / 394 (36.5)	6.9 [4.2; 9.7]	131 / 389 (33.7)	6.4 [4.2; 12.4]	1.1162 [0.8810; 1.4157] 0.3594	
No	19 / 42 (45.2)	10.3 [2.1; NE]	16 / 41 (39.0)	7.7 [4.1; NE]	1.0520 [0.5382; 2.0818] 0.8849	
Prior Taxane Use In The Non-Metastatic Setting						0.9944
Yes	67 / 179 (37.4)	4.8 [2.9; 11.8]	64 / 177 (36.2)	4.8 [3.4; 15.2]	1.1168 [0.7911; 1.5775] 0.5269	
No	96 / 257 (37.4)	8.3 [6.2; 11.0]	83 / 253 (32.8)	7.5 [4.9; 15.9]	1.1087 [0.8261; 1.4914] 0.4918	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1663
1	27 / 65 (41.5)	3.3 [1.4; 11.7]	18 / 82 (22.0)	NE [3.6; NE]	1.8393 [1.0183; 3.4012] 0.0429	
2	104 / 295 (35.3)	8.3 [4.2; 11.1]	106 / 288 (36.8)	6.2 [4.2; 9.6]	0.9894 [0.7539; 1.2980] 0.9428	
>=3	31 / 75 (41.3)	7.6 [4.1; 12.4]	22 / 58 (37.9)	9.2 [3.6; NE]	1.1553 [0.6683; 2.0287] 0.6083	
ER/PR status I						0.9699
ER+, PR+	92 / 253 (36.4)	8.3 [4.2; 12.4]	79 / 237 (33.3)	8.3 [4.9; 15.2]	1.1020 [0.8163; 1.4917] 0.5253	
ER+, PR-	69 / 167 (41.3)	6.3 [3.0; 9.7]	63 / 181 (34.8)	4.9 [3.4; 21.3]	1.1105 [0.7857; 1.5711] 0.5534	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3024
ER <=10%	8 / 21 (38.1)	4.1 [1.4; NE]	6 / 14 (42.9)	4.2 [0.7; NE]	0.6759 [0.2300; 2.0921] 0.4755	
ER >10%	134 / 364 (36.8)	7.1 [4.2; 11.0]	120 / 355 (33.8)	6.9 [4.3; 10.5]	1.0922 [0.8532; 1.3999] 0.4836	
Positive	21 / 51 (41.2)	8.9 [3.4; 27.6]	21 / 61 (34.4)	21.3 [2.7; NE]	1.2810 [0.6949; 2.3616] 0.4207	
Endocrine Resistance						0.1825
Primary	52 / 128 (40.6)	4.2 [1.4; 10.3]	44 / 140 (31.4)	7.1 [3.7; NE]	1.3844 [0.9271; 2.0764] 0.1077	
Secondary	111 / 308 (36.0)	8.3 [6.2; 11.0]	102 / 288 (35.4)	6.9 [4.2; 10.5]	0.9989 [0.7630; 1.3090] 0.9924	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0129
Capecitabine	95 / 266 (35.7)	8.9 [4.2; 11.8]	79 / 257 (30.7)	10.5 [7.1; 22.1]	1.3589 [1.0088; 1.8355] 0.0437	
Nab-Paclitaxel	42 / 103 (40.8)	6.9 [2.8; 20.0]	41 / 105 (39.0)	4.8 [2.9; NE]	0.9487 [0.6151; 1.4641] 0.8159	
Paclitaxel	26 / 67 (38.8)	6.3 [2.1; 10.3]	27 / 68 (39.7)	1.8 [0.8; 3.4]	0.5395 [0.3099; 0.9375] 0.0263	
Prior anthracycline use						0.2697
Yes	81 / 199 (40.7)	4.1 [2.8; 8.9]	73 / 208 (35.1)	5.6 [3.6; 15.2]	1.2605 [0.9176; 1.7344] 0.1507	
No	82 / 237 (34.6)	9.0 [6.9; 11.7]	74 / 222 (33.3)	7.5 [4.2; 15.9]	0.9795 [0.7144; 1.3449] 0.8984	
Liver metastases						0.4779
Yes	108 / 296 (36.5)	4.2 [2.9; 8.3]	95 / 283 (33.6)	6.4 [4.2; 12.4]	1.1937 [0.9061; 1.5753] 0.2095	
No	55 / 140 (39.3)	11.1 [6.9; 16.5]	52 / 147 (35.4)	8.3 [4.2; NE]	0.9833 [0.6723; 1.4402] 0.9407	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.5091
0	98 / 252 (38.9)	4.3 [3.5; 8.3]	90 / 257 (35.0)	6.9 [4.2; 12.4]	1.1870 [0.8905; 1.5829] 0.2430	
>=1	64 / 179 (35.8)	11.0 [6.2; 12.5]	55 / 164 (33.5)	7.5 [4.2; 21.3]	1.0015 [0.6983; 1.4410] 0.9931	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Endocrine Therapy Symptoms						
Age at randomization						0.5168
<65 years of age	59 / 302 (19.5)	26.3 [18.7; NE]	71 / 297 (23.9)	20.8 [10.5; NE]	0.6432 [0.4528; 0.9104] 0.0124	
>=65 years of age	22 / 134 (16.4)	24.8 [20.0; NE]	37 / 133 (27.8)	15.1 [9.0; 22.8]	0.4918 [0.2804; 0.8395] 0.0094	
Race						0.2516
Asian	37 / 154 (24.0)	27.6 [20.0; NE]	50 / 151 (33.1)	20.8 [11.1; NE]	0.5434 [0.3504; 0.8346] 0.0050	
White	39 / 231 (16.9)	24.8 [14.5; NE]	49 / 230 (21.3)	15.1 [9.7; NE]	0.7260 [0.4719; 1.1083] 0.1390	
Other	5 / 51 (9.8)	20.0 [6.2; NE]	9 / 49 (18.4)	8.4 [2.8; NE]	0.2740 [0.0731; 0.8571] 0.0236	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.6021
Asia	35 / 149 (23.5)	27.6 [20.0; NE]	49 / 147 (33.3)	20.8 [11.1; NE]	0.5175 [0.3304; 0.8014] 0.0029	
Europe	37 / 227 (16.3)	24.8 [13.1; NE]	45 / 213 (21.1)	14.5 [9.0; NE]	0.6785 [0.4343; 1.0525] 0.0833	
Rest of the World	9 / 60 (15.0)	NE [14.5; NE]	14 / 70 (20.0)	15.1 [5.5; NE]	0.6614 [0.2739; 1.5175] 0.3331	
HER2 IHC expression						0.5483
IHC 1+	45 / 239 (18.8)	24.8 [18.7; NE]	67 / 234 (28.6)	15.1 [9.1; NE]	0.4997 [0.3359; 0.7352] 0.0004	
IHC 2+/ISH-	22 / 117 (18.8)	34.5 [15.8; NE]	27 / 118 (22.9)	31.7 [6.3; NE]	0.6310 [0.3513; 1.1181] 0.1127	
IHC >0 <1+	13 / 76 (17.1)	NE [NE; NE]	13 / 76 (17.1)	20.8 [13.1; NE]	0.8403 [0.3853; 1.8325] 0.6576	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.7205
Yes	69 / 394 (17.5)	26.3 [24.8; NE]	96 / 389 (24.7)	15.1 [10.5; 22.8]	0.5743 [0.4183; 0.7841] 0.0005	
No	12 / 42 (28.6)	20.0 [15.2; NE]	12 / 41 (29.3)	NE [3.5; NE]	0.7575 [0.3332; 1.7208] 0.4992	
Prior Taxane Use In The Non-Metastatic Setting						0.4143
Yes	26 / 179 (14.5)	27.6 [20.0; NE]	44 / 177 (24.9)	15.1 [9.6; 24.9]	0.5100 [0.3081; 0.8272] 0.0062	
No	55 / 257 (21.4)	24.8 [15.9; NE]	64 / 253 (25.3)	16.6 [10.4; NE]	0.6498 [0.4498; 0.9350] 0.0198	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5792
1	14 / 65 (21.5)	20.0 [11.9; NE]	17 / 82 (20.7)	14.5 [8.9; NE]	0.7680 [0.3611; 1.5941] 0.4759	
2	50 / 295 (16.9)	26.3 [20.0; NE]	74 / 288 (25.7)	15.1 [9.7; NE]	0.5432 [0.3763; 0.7780] 0.0008	
>=3	17 / 75 (22.7)	34.5 [11.0; NE]	16 / 58 (27.6)	16.6 [9.0; NE]	0.7654 [0.3790; 1.5452] 0.4527	
ER/PR status I						0.3197
ER+, PR+	50 / 253 (19.8)	24.8 [20.0; NE]	60 / 237 (25.3)	16.6 [9.6; 24.9]	0.6634 [0.4538; 0.9655] 0.0317	
ER+, PR-	31 / 167 (18.6)	27.6 [18.7; NE]	46 / 181 (25.4)	15.1 [9.0; NE]	0.4948 [0.3043; 0.7918] 0.0031	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7651
ER <=10%	4 / 21 (19.0)	27.6 [5.6; NE]	4 / 14 (28.6)	5.5 [1.4; NE]	0.2368 [0.0436; 1.1527] 0.0556	
ER >10%	67 / 364 (18.4)	24.8 [20.0; NE]	87 / 355 (24.5)	15.1 [11.1; 24.9]	0.6109 [0.4412; 0.8421] 0.0025	
Positive	10 / 51 (19.6)	NE [10.3; NE]	17 / 61 (27.9)	22.8 [6.3; NE]	0.6164 [0.2709; 1.3302] 0.2242	
Endocrine Resistance						0.9465
Primary	25 / 128 (19.5)	26.3 [17.4; NE]	36 / 140 (25.7)	14.4 [8.2; NE]	0.5900 [0.3483; 0.9838] 0.0435	
Secondary	56 / 308 (18.2)	34.5 [20.0; NE]	72 / 288 (25.0)	16.6 [11.1; NE]	0.5948 [0.4159; 0.8458] 0.0037	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 16:55; Program name: T.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.sas; Output name: T.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.7363
Capecitabine	45 / 266 (16.9)	34.5 [24.8; NE]	62 / 257 (24.1)	17.2 [15.1; 24.9]	0.6210 [0.4190; 0.9129] 0.0152	
Nab-Paclitaxel	20 / 103 (19.4)	27.6 [20.0; NE]	31 / 105 (29.5)	14.4 [8.9; NE]	0.5009 [0.2762; 0.8850] 0.0171	
Paclitaxel	16 / 67 (23.9)	15.9 [10.3; NE]	15 / 68 (22.1)	11.1 [3.7; NE]	0.5209 [0.2443; 1.1030] 0.0818	
Prior anthracycline use						0.5353
Yes	33 / 199 (16.6)	27.6 [18.7; NE]	52 / 208 (25.0)	15.1 [9.0; NE]	0.5440 [0.3463; 0.8423] 0.0062	
No	48 / 237 (20.3)	26.3 [15.9; NE]	56 / 222 (25.2)	16.6 [10.4; NE]	0.6434 [0.4339; 0.9497] 0.0257	
Liver metastases						0.2116
Yes	56 / 296 (18.9)	27.6 [20.0; NE]	65 / 283 (23.0)	16.6 [10.5; NE]	0.6912 [0.4797; 0.9925] 0.0447	
No	25 / 140 (17.9)	24.8 [18.7; NE]	43 / 147 (29.3)	15.1 [9.0; NE]	0.4672 [0.2803; 0.7618] 0.0022	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.1242
0	41 / 252 (16.3)	27.6 [24.8; NE]	70 / 257 (27.2)	15.1 [10.5; 20.8]	0.4929 [0.3305; 0.7252] 0.0003	
>=1	39 / 179 (21.8)	20.0 [11.9; NE]	35 / 164 (21.3)	22.8 [9.0; NE]	0.7785 [0.4892; 1.2418] 0.2911	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Skin Mucosis Symptoms						
Age at randomization						0.9849
<65 years of age	81 / 302 (26.8)	17.2 [12.4; 27.6]	133 / 297 (44.8)	2.8 [2.1; 4.2]	0.3644 [0.2736; 0.4822] <.0001	
>=65 years of age	37 / 134 (27.6)	13.8 [7.6; 17.2]	65 / 133 (48.9)	2.0 [1.4; 3.5]	0.3656 [0.2395; 0.5500] <.0001	
Race						0.7913
Asian	57 / 154 (37.0)	16.6 [13.8; 27.6]	89 / 151 (58.9)	3.5 [2.1; 4.8]	0.3405 [0.2410; 0.4769] <.0001	
White	54 / 231 (23.4)	17.2 [6.9; 24.1]	99 / 230 (43.0)	2.1 [1.5; 3.5]	0.3779 [0.2666; 0.5297] <.0001	
Other	7 / 51 (13.7)	11.7 [4.3; NE]	10 / 49 (20.4)	2.8 [0.8; NE]	0.4688 [0.1676; 1.2375] 0.1232	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2292
Asia	58 / 149 (38.9)	15.3 [13.7; 27.6]	86 / 147 (58.5)	3.5 [2.1; 4.9]	0.3659 [0.2591; 0.5128] <.0001	
Europe	52 / 227 (22.9)	12.4 [6.3; 24.1]	87 / 213 (40.8)	2.1 [1.8; 3.5]	0.4214 [0.2953; 0.5955] <.0001	
Rest of the World	8 / 60 (13.3)	NE [9.6; NE]	25 / 70 (35.7)	2.1 [1.4; 4.2]	0.2457 [0.1023; 0.5299] 0.0003	
HER2 IHC expression						0.4096
IHC 1+	64 / 239 (26.8)	16.6 [13.1; 25.6]	111 / 234 (47.4)	2.8 [2.1; 4.2]	0.3997 [0.2911; 0.5444] <.0001	
IHC 2+/ISH-	34 / 117 (29.1)	15.3 [7.6; 27.6]	53 / 118 (44.9)	2.7 [1.5; 4.2]	0.3608 [0.2266; 0.5654] <.0001	
IHC >0 <1+	19 / 76 (25.0)	NE [9.6; NE]	33 / 76 (43.4)	2.1 [1.4; 4.2]	0.2604 [0.1438; 0.4586] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.7592
Yes	107 / 394 (27.2)	14.6 [11.7; 18.8]	180 / 389 (46.3)	2.7 [2.1; 3.5]	0.3743 [0.2925; 0.4767] <.0001	
No	11 / 42 (26.2)	31.0 [10.3; NE]	18 / 41 (43.9)	5.5 [1.5; NE]	0.3090 [0.1345; 0.6701] 0.0024	
Prior Taxane Use In The Non-Metastatic Setting						0.3595
Yes	50 / 179 (27.9)	14.6 [8.4; NE]	84 / 177 (47.5)	2.8 [2.1; 4.2]	0.4398 [0.3060; 0.6254] <.0001	
No	68 / 257 (26.5)	15.3 [12.4; 24.1]	114 / 253 (45.1)	2.2 [2.0; 4.1]	0.3225 [0.2360; 0.4371] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.2342
1	21 / 65 (32.3)	8.4 [3.5; NE]	35 / 82 (42.7)	2.7 [1.4; 3.6]	0.4982 [0.2806; 0.8602] 0.0119	
2	68 / 295 (23.1)	17.2 [14.6; 27.6]	128 / 288 (44.4)	2.8 [2.0; 4.2]	0.3095 [0.2280; 0.4166] <.0001	
>=3	29 / 75 (38.7)	13.1 [4.9; 21.4]	34 / 58 (58.6)	2.2 [1.6; 3.5]	0.4742 [0.2833; 0.7875] 0.0034	
ER/PR status I						0.8674
ER+, PR+	64 / 253 (25.3)	17.2 [13.1; 31.0]	104 / 237 (43.9)	2.8 [2.1; 4.8]	0.3581 [0.2597; 0.4898] <.0001	
ER+, PR-	53 / 167 (31.7)	14.6 [7.6; 21.4]	86 / 181 (47.5)	2.3 [1.5; 3.5]	0.3673 [0.2544; 0.5245] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2751
ER <=10%	4 / 21 (19.0)	NE [1.4; NE]	8 / 14 (57.1)	2.2 [1.0; 5.5]	0.2493 [0.0645; 0.8196] 0.0180	
ER >10%	102 / 364 (28.0)	15.3 [10.3; 18.8]	157 / 355 (44.2)	2.8 [2.1; 4.2]	0.3841 [0.2963; 0.4956] <.0001	
Positive	12 / 51 (23.5)	27.6 [13.1; NE]	33 / 61 (54.1)	1.8 [1.4; 2.8]	0.2888 [0.1419; 0.5495] 0.0001	
Endocrine Resistance						0.7023
Primary	35 / 128 (27.3)	16.9 [8.4; NE]	62 / 140 (44.3)	2.8 [1.6; 4.2]	0.3946 [0.2553; 0.5996] <.0001	
Secondary	83 / 308 (26.9)	15.3 [11.7; 21.4]	136 / 288 (47.2)	2.3 [2.0; 4.1]	0.3484 [0.2626; 0.4593] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1970
Capecitabine	70 / 266 (26.3)	16.9 [13.1; 24.1]	126 / 257 (49.0)	1.7 [1.5; 2.8]	0.3257 [0.2402; 0.4380] <.0001	
Nab-Paclitaxel	29 / 103 (28.2)	16.6 [7.6; NE]	43 / 105 (41.0)	5.5 [4.2; 15.7]	0.4973 [0.3031; 0.8016] 0.0039	
Paclitaxel	19 / 67 (28.4)	8.4 [4.8; NE]	29 / 68 (42.6)	2.1 [1.8; 2.8]	0.3335 [0.1775; 0.6097] 0.0003	
Prior anthracycline use						0.0362
Yes	60 / 199 (30.2)	14.5 [7.6; 25.6]	96 / 208 (46.2)	2.8 [2.1; 4.2]	0.4852 [0.3480; 0.6713] <.0001	
No	58 / 237 (24.5)	16.6 [13.1; 27.6]	102 / 222 (45.9)	2.1 [1.5; 3.5]	0.2860 [0.2044; 0.3965] <.0001	
Liver metastases						0.1794
Yes	73 / 296 (24.7)	14.5 [10.5; 27.6]	132 / 283 (46.6)	2.7 [2.0; 3.5]	0.3132 [0.2316; 0.4200] <.0001	
No	45 / 140 (32.1)	16.6 [12.4; 25.6]	66 / 147 (44.9)	3.4 [2.1; 5.5]	0.4656 [0.3152; 0.6816] 0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.1901
0	65 / 252 (25.8)	17.2 [13.1; 27.6]	121 / 257 (47.1)	2.1 [1.6; 3.4]	0.3333 [0.2430; 0.4528] <.0001	
>=1	52 / 179 (29.1)	13.8 [8.2; 27.6]	73 / 164 (44.5)	3.5 [2.1; 4.8]	0.4088 [0.2832; 0.5858] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 16:55; Program name: T.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.sas; Output name: T.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Endocrine Sexual Symptoms						
Age at randomization						0.5076
<65 years of age	88 / 302 (29.1)	17.2 [10.2; NE]	66 / 297 (22.2)	22.2 [11.8; NE]	1.2910 [0.9390; 1.7836] 0.1167	
>=65 years of age	27 / 134 (20.1)	17.2 [11.7; NE]	21 / 133 (15.8)	NE [17.4; NE]	1.6330 [0.9253; 2.9216] 0.0892	
Race						0.6166
Asian	50 / 154 (32.5)	NE [15.9; NE]	42 / 151 (27.8)	NE [15.9; NE]	1.1858 [0.7877; 1.7955] 0.4155	
White	55 / 231 (23.8)	11.8 [7.6; 22.1]	40 / 230 (17.4)	22.2 [17.4; NE]	1.5338 [1.0225; 2.3210] 0.0388	
Other	10 / 51 (19.6)	4.9 [2.8; NE]	5 / 49 (10.2)	NE [2.8; NE]	1.7009 [0.5972; 5.5028] 0.3297	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.6368
Asia	49 / 149 (32.9)	NE [15.9; NE]	40 / 147 (27.2)	NE [15.9; NE]	1.2480 [0.8228; 1.9039] 0.2990	
Europe	49 / 227 (21.6)	14.8 [9.1; 22.1]	34 / 213 (16.0)	22.2 [17.4; NE]	1.3913 [0.9003; 2.1752] 0.1384	
Rest of the World	17 / 60 (28.3)	2.8 [1.3; NE]	13 / 70 (18.6)	NE [6.2; NE]	2.0264 [0.9806; 4.2822] 0.0539	
HER2 IHC expression						0.6276
IHC 1+	64 / 239 (26.8)	17.2 [11.0; NE]	50 / 234 (21.4)	19.9 [15.9; NE]	1.4020 [0.9685; 2.0407] 0.0739	
IHC 2+/ISH-	30 / 117 (25.6)	17.2 [10.3; NE]	25 / 118 (21.2)	NE [8.5; NE]	1.1471 [0.6749; 1.9678] 0.6153	
IHC >0 <1+	21 / 76 (27.6)	14.8 [5.0; NE]	11 / 76 (14.5)	NE [NE; NE]	1.6435 [0.8078; 3.5368] 0.1822	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1551
Yes	94 / 394 (23.9)	19.3 [12.4; NE]	75 / 389 (19.3)	22.2 [17.4; NE]	1.2622 [0.9323; 1.7146] 0.1327	
No	21 / 42 (50.0)	4.2 [0.9; 17.2]	12 / 41 (29.3)	19.9 [4.2; NE]	2.1856 [1.0861; 4.6074] 0.0282	
Prior Taxane Use In The Non-Metastatic Setting						0.8015
Yes	47 / 179 (26.3)	15.9 [9.1; NE]	35 / 177 (19.8)	NE [11.8; NE]	1.4065 [0.9083; 2.1979] 0.1265	
No	68 / 257 (26.5)	17.2 [11.0; NE]	52 / 253 (20.6)	22.2 [15.9; NE]	1.3282 [0.9273; 1.9135] 0.1224	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6691
1	15 / 65 (23.1)	NE [6.9; NE]	15 / 82 (18.3)	19.9 [6.4; NE]	1.1039 [0.5343; 2.2800] 0.7865	
2	78 / 295 (26.4)	17.2 [11.0; 22.1]	57 / 288 (19.8)	NE [15.9; NE]	1.4647 [1.0423; 2.0708] 0.0279	
>=3	21 / 75 (28.0)	NE [4.8; NE]	15 / 58 (25.9)	17.4 [11.1; NE]	1.3187 [0.6826; 2.6108] 0.4136	
ER/PR status I						0.4482
ER+, PR+	62 / 253 (24.5)	19.3 [12.4; NE]	46 / 237 (19.4)	NE [17.4; NE]	1.2170 [0.8327; 1.7913] 0.3127	
ER+, PR-	51 / 167 (30.5)	14.8 [5.6; NE]	39 / 181 (21.5)	19.9 [11.8; NE]	1.5060 [0.9932; 2.3001] 0.0543	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2635
ER <=10%	4 / 21 (19.0)	NE [1.3; NE]	5 / 14 (35.7)	2.7 [0.7; NE]	0.6019 [0.1482; 2.2883] 0.4434	
ER >10%	97 / 364 (26.6)	17.2 [11.0; 22.1]	69 / 355 (19.4)	19.9 [17.4; NE]	1.4369 [1.0568; 1.9640] 0.0211	
Positive	14 / 51 (27.5)	NE [10.3; NE]	13 / 61 (21.3)	NE [11.1; NE]	1.3139 [0.6134; 2.8345] 0.4796	
Endocrine Resistance						0.4199
Primary	33 / 128 (25.8)	NE [5.5; NE]	24 / 140 (17.1)	19.9 [15.9; NE]	1.6368 [0.9715; 2.7986] 0.0636	
Secondary	82 / 308 (26.6)	17.2 [11.7; NE]	63 / 288 (21.9)	22.2 [14.9; NE]	1.2577 [0.9063; 1.7534] 0.1719	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.5312
Capecitabine	63 / 266 (23.7)	17.2 [12.4; NE]	54 / 257 (21.0)	22.2 [14.9; NE]	1.2059 [0.8389; 1.7403] 0.3112	
Nab-Paclitaxel	37 / 103 (35.9)	8.4 [4.2; NE]	24 / 105 (22.9)	19.9 [15.9; NE]	1.7307 [1.0406; 2.9327] 0.0347	
Paclitaxel	15 / 67 (22.4)	17.3 [4.9; NE]	9 / 68 (13.2)	NE [6.4; NE]	1.3718 [0.5988; 3.3103] 0.4590	
Prior anthracycline use						0.3946
Yes	55 / 199 (27.6)	15.9 [8.4; 19.3]	39 / 208 (18.8)	NE [19.9; NE]	1.5301 [1.0169; 2.3240] 0.0410	
No	60 / 237 (25.3)	22.1 [11.8; NE]	48 / 222 (21.6)	22.2 [15.9; NE]	1.2291 [0.8420; 1.8037] 0.2868	
Liver metastases						0.7045
Yes	74 / 296 (25.0)	19.3 [11.7; NE]	57 / 283 (20.1)	NE [18.7; NE]	1.3364 [0.9469; 1.8958] 0.0995	
No	41 / 140 (29.3)	15.9 [11.0; NE]	30 / 147 (20.4)	22.2 [14.9; NE]	1.4514 [0.9078; 2.3473] 0.1215	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.1263
0	67 / 252 (26.6)	17.2 [11.0; NE]	60 / 257 (23.3)	22.2 [11.8; NE]	1.2177 [0.8587; 1.7299] 0.2698	
>=1	47 / 179 (26.3)	17.2 [10.3; NE]	23 / 164 (14.0)	19.9 [18.7; NE]	1.9129 [1.1745; 3.2066] 0.0096	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Upset by Hair Loss						
Age at randomization						0.4988
<65 years of age	31 / 302 (10.3)	3.4 [1.3; 6.3]	19 / 297 (6.4)	10.3 [2.2; NE]	1.6411 [0.9343; 2.9592] 0.0885	
>=65 years of age	10 / 134 (7.5)	2.2 [1.3; NE]	13 / 133 (9.8)	7.6 [1.3; NE]	1.1460 [0.4881; 2.6115] 0.7369	
Race						0.1820
Asian	27 / 154 (17.5)	1.4 [1.3; 3.5]	17 / 151 (11.3)	10.3 [3.6; NE]	2.1208 [1.1620; 3.9808] 0.0137	
White	13 / 231 (5.6)	4.1 [0.8; NE]	14 / 230 (6.1)	3.4 [0.8; NE]	0.8832 [0.4092; 1.8925] 0.7428	
Other	1 / 51 (2.0)	NE [6.3; NE]	1 / 49 (2.0)	NE [1.4; NE]	0.0000 [NE; 5.8263] 0.3173	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1827
Asia	27 / 149 (18.1)	1.4 [1.3; 3.5]	17 / 147 (11.6)	10.3 [3.6; NE]	2.0804 [1.1393; 3.9064] 0.0165	
Europe	10 / 227 (4.4)	6.3 [1.3; NE]	10 / 213 (4.7)	6.8 [0.8; NE]	0.9409 [0.3838; 2.3058] 0.8831	
Rest of the World	4 / 60 (6.7)	5.6 [0.8; NE]	5 / 70 (7.1)	1.5 [0.6; NE]	0.6985 [0.1711; 2.6700] 0.5689	
HER2 IHC expression						0.5292
IHC 1+	26 / 239 (10.9)	1.8 [0.9; 6.3]	22 / 234 (9.4)	3.6 [1.3; NE]	1.2985 [0.7357; 2.3121] 0.3681	
IHC 2+/ISH-	6 / 117 (5.1)	6.3 [0.8; NE]	7 / 118 (5.9)	NE [1.5; NE]	1.4316 [0.4603; 4.3158] 0.5186	
IHC >0 <1+	9 / 76 (11.8)	4.1 [1.4; NE]	3 / 76 (3.9)	NE [0.8; NE]	3.6444 [1.0069; 17.6493] 0.0561	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 16:55; Program name: T.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.sas; Output name: T.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9742
Yes	35 / 394 (8.9)	2.5 [1.4; 7.1]	27 / 389 (6.9)	10.3 [3.6; NE]	1.4837 [0.8996; 2.4735] 0.1213	
No	6 / 42 (14.3)	2.4 [0.7; NE]	5 / 41 (12.2)	2.8 [0.8; NE]	1.3662 [0.4097; 4.7588] 0.6049	
Prior Taxane Use In The Non-Metastatic Setting						0.3310
Yes	16 / 179 (8.9)	2.5 [0.8; NE]	12 / 177 (6.8)	NE [2.7; NE]	1.9851 [0.9423; 4.2967] 0.0682	
No	25 / 257 (9.7)	2.5 [1.4; 7.1]	20 / 253 (7.9)	5.6 [1.3; NE]	1.2062 [0.6688; 2.2039] 0.5225	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6139
1	4 / 65 (6.2)	NE [0.7; NE]	7 / 82 (8.5)	3.4 [0.8; NE]	0.8672 [0.2256; 2.8979] 0.8083	
2	32 / 295 (10.8)	1.8 [1.3; 4.1]	21 / 288 (7.3)	10.3 [2.7; NE]	1.5940 [0.9244; 2.8071] 0.0968	
>=3	5 / 75 (6.7)	6.3 [0.1; NE]	4 / 58 (6.9)	NE [2.2; NE]	1.6034 [0.4239; 6.4824] 0.4932	
ER/PR status I						0.1477
ER+, PR+	22 / 253 (8.7)	4.1 [1.4; NE]	18 / 237 (7.6)	3.6 [1.5; NE]	1.0957 [0.5882; 2.0693] 0.7692	
ER+, PR-	19 / 167 (11.4)	1.4 [0.9; NE]	13 / 181 (7.2)	12.4 [3.4; NE]	2.1793 [1.0773; 4.5505] 0.0276	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3186
ER <=10%	1 / 21 (4.8)	NE [7.1; NE]	1 / 14 (7.1)	1.3 [NE; NE]	0.0000 [NE; 1.9420] 0.0833	
ER >10%	35 / 364 (9.6)	2.5 [1.4; 6.3]	24 / 355 (6.8)	10.3 [2.2; NE]	1.4839 [0.8865; 2.5258] 0.1344	
Positive	5 / 51 (9.8)	1.4 [0.8; NE]	7 / 61 (11.5)	7.6 [1.3; NE]	1.9507 [0.5728; 6.1676] 0.2509	
Endocrine Resistance						0.6100
Primary	15 / 128 (11.7)	1.3 [0.8; 6.3]	12 / 140 (8.6)	3.4 [1.3; NE]	1.8233 [0.8494; 4.0009] 0.1268	
Secondary	26 / 308 (8.4)	3.4 [1.4; NE]	20 / 288 (6.9)	12.4 [2.7; NE]	1.3811 [0.7731; 2.5043] 0.2766	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0372
Capecitabine	25 / 266 (9.4)	4.1 [1.5; NE]	16 / 257 (6.2)	12.4 [3.4; NE]	1.5734 [0.8464; 3.0109] 0.1575	
Nab-Paclitaxel	11 / 103 (10.7)	1.4 [0.8; NE]	14 / 105 (13.3)	2.7 [0.8; NE]	1.1105 [0.4919; 2.4451] 0.7817	
Paclitaxel	5 / 67 (7.5)	0.8 [0.7; NE]	2 / 68 (2.9)	NE [0.8; NE]	5.0418 [1.0635; 35.7431] 0.0265	
Prior anthracycline use						0.6001
Yes	14 / 199 (7.0)	3.5 [0.8; NE]	12 / 208 (5.8)	NE [2.7; NE]	1.7652 [0.8142; 3.8864] 0.1469	
No	27 / 237 (11.4)	2.2 [1.4; 6.3]	20 / 222 (9.0)	7.6 [1.4; NE]	1.3102 [0.7345; 2.3773] 0.3554	
Liver metastases						0.7586
Yes	30 / 296 (10.1)	3.4 [1.4; 7.1]	19 / 283 (6.7)	10.3 [3.6; NE]	1.5100 [0.8555; 2.7323] 0.1576	
No	11 / 140 (7.9)	1.3 [0.7; 4.1]	13 / 147 (8.8)	2.7 [1.3; NE]	1.6598 [0.7277; 3.7170] 0.2095	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.2 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.9602
0	25 / 252 (9.9)	3.4 [1.4; 7.1]	18 / 257 (7.0)	10.3 [2.9; NE]	1.4657 [0.8021; 2.7321] 0.2161	
>=1	16 / 179 (8.9)	2.1 [0.8; NE]	12 / 164 (7.3)	7.6 [0.8; NE]	1.5025 [0.7120; 3.2585] 0.2940	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Tabelle 2.12.3 EORTC-QLQ-BR45 – Zeit bis zur bestätigten Verschlechterung – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.12.3 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Body Image						
Region						0.0368
Asia	48 / 149 (32.2)	NE [14.6; NE]	60 / 147 (40.8)	9.0 [5.6; NE]	0.6940 [0.4723; 1.0143] 0.0581	
Europe	52 / 227 (22.9)	12.4 [5.7; NE]	57 / 213 (26.8)	9.1 [4.9; 13.2]	0.8868 [0.6069; 1.2928] 0.5294	
Rest of the World	14 / 60 (23.3)	8.9 [1.5; NE]	10 / 70 (14.3)	NE [8.4; NE]	2.1140 [0.9423; 4.9195] 0.0660	
ER/PR status II						0.0312
ER <=10%	7 / 21 (33.3)	8.9 [1.4; NE]	8 / 14 (57.1)	1.4 [0.7; 3.5]	0.1956 [0.0503; 0.6484] 0.0042	
ER >10%	94 / 364 (25.8)	18.6 [8.9; NE]	98 / 355 (27.6)	9.9 [8.3; NE]	0.9296 [0.6995; 1.2346] 0.6091	
Positive	13 / 51 (25.5)	NE [11.7; NE]	21 / 61 (34.4)	10.4 [4.2; NE]	0.6806 [0.3301; 1.3511] 0.2727	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.3 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Future Perspective						
Prior anthracycline use						0.0341
Yes	36 / 199 (18.1)	17.3 [7.7; NE]	37 / 208 (17.8)	NE [11.8; NE]	1.1729 [0.7383; 1.8612] 0.4943	
No	36 / 237 (15.2)	20.7 [15.9; NE]	52 / 222 (23.4)	12.5 [7.6; 22.2]	0.5708 [0.3702; 0.8709] 0.0089	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.12.3 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Breast Symptoms						
Prior CDK4/6 inhibitor use						0.0058
Yes	32 / 394 (8.1)	NE [NE; NE]	56 / 389 (14.4)	NE [NE; NE]	0.4661 [0.2981; 0.7164] 0.0005	
No	11 / 42 (26.2)	19.3 [12.4; NE]	5 / 41 (12.2)	NE [11.7; NE]	2.0436 [0.7415; 6.4998] 0.1769	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.3 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Systemic Therapy Side Effects						
T-DXd vs. each Investigator's choice chemotherapy						0.0129
Capecitabine	95 / 266 (35.7)	8.9 [4.2; 11.8]	79 / 257 (30.7)	10.5 [7.1; 22.1]	1.3589 [1.0088; 1.8355] 0.0437	
Nab-Paclitaxel	42 / 103 (40.8)	6.9 [2.8; 20.0]	41 / 105 (39.0)	4.8 [2.9; NE]	0.9487 [0.6151; 1.4641] 0.8159	
Paclitaxel	26 / 67 (38.8)	6.3 [2.1; 10.3]	27 / 68 (39.7)	1.8 [0.8; 3.4]	0.5395 [0.3099; 0.9375] 0.0263	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.3 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Skin Mucosis Symptoms						
Prior anthracycline use						0.0362
Yes	60 / 199 (30.2)	14.5 [7.6; 25.6]	96 / 208 (46.2)	2.8 [2.1; 4.2]	0.4852 [0.3480; 0.6713] <.0001	
No	58 / 237 (24.5)	16.6 [13.1; 27.6]	102 / 222 (45.9)	2.1 [1.5; 3.5]	0.2860 [0.2044; 0.3965] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 17:08; Program name: T.2.12.3_EORTC_BR45_TTCDet_FAS_SUB_SIG.sas; Output name: T.2.12.3_EORTC_BR45_TTCDet_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

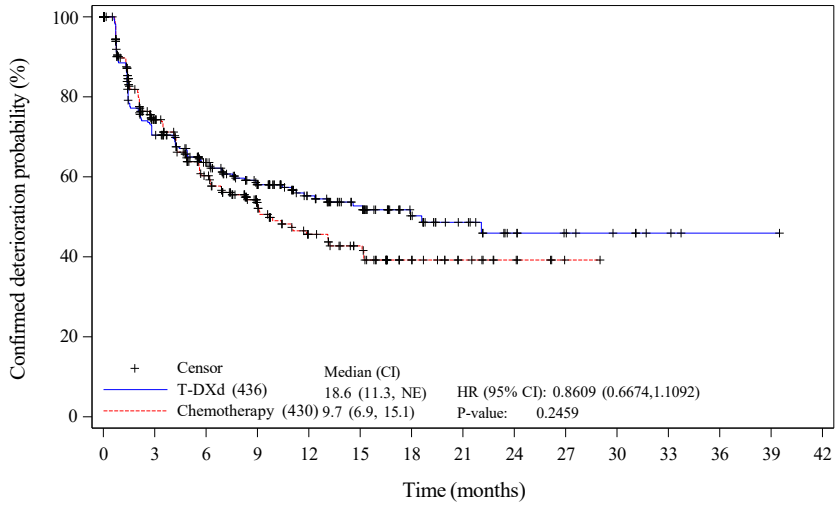
Table 2.12.3 EORTC QLQ-BR45 - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Upset by Hair Loss						
T-DXd vs. each Investigator's choice chemotherapy						0.0372
Capecitabine	25 / 266 (9.4)	4.1 [1.5; NE]	16 / 257 (6.2)	12.4 [3.4; NE]	1.5734 [0.8464; 3.0109] 0.1575	
Nab-Paclitaxel	11 / 103 (10.7)	1.4 [0.8; NE]	14 / 105 (13.3)	2.7 [0.8; NE]	1.1105 [0.4919; 2.4451] 0.7817	
Paclitaxel	5 / 67 (7.5)	0.8 [0.7; NE]	2 / 68 (2.9)	NE [0.8; NE]	5.0418 [1.0635; 35.7431] 0.0265	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Abbildung 2.12.1 EORTC-QLQ-BR45 – Zeit bis zur bestätigten Verschlechterung – Kaplan-Meier-Plot – FAS

Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Body Image



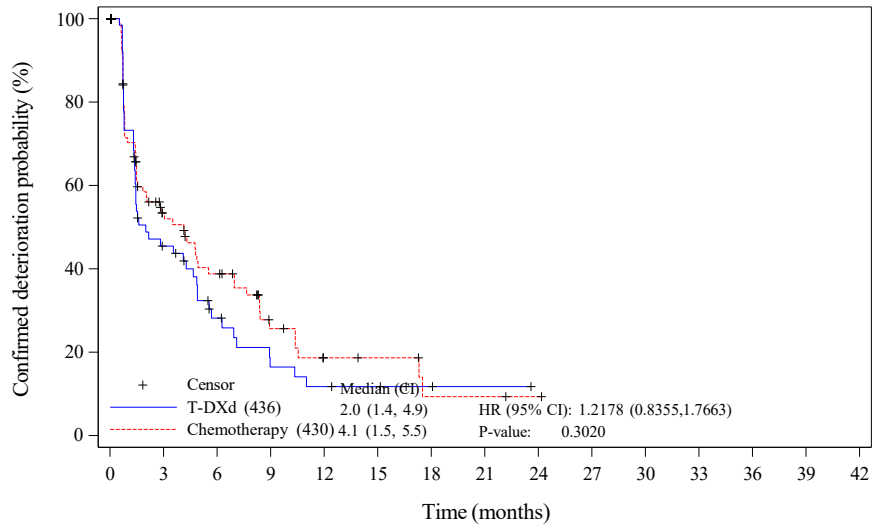
Patients still at risk:

T-DXd(436)	436	177	137	103	73	55	32	21	12	9	6	3	1	1	0
Chemotherapy (430)	430	172	118	73	49	37	19	11	6	1	0				

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10DEC2024 10:32; Program name: F.2.12.1_EORTC_BR45_TTCDet_FAS.sas; Output name: F.2.12.1_EORTC_BR45_TTCDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Sexual Functioning



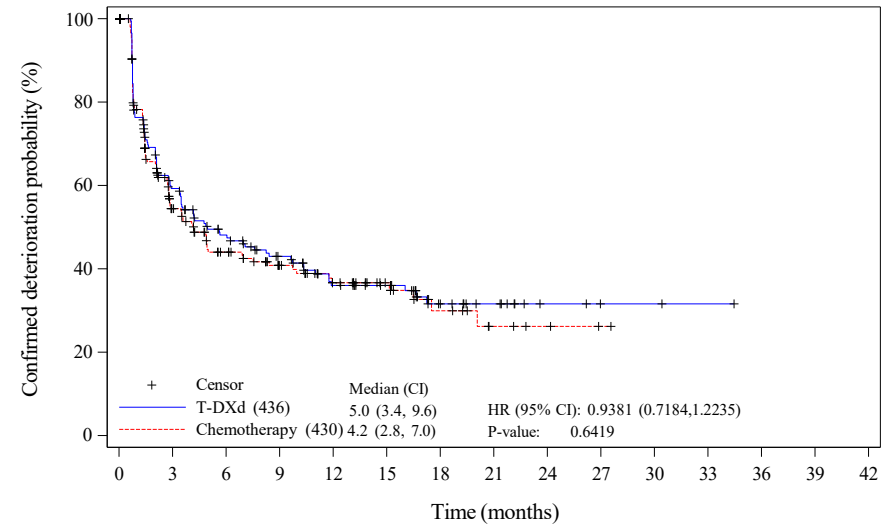
Patients still at risk:

T-DXd(436)	436	26	13	7	5	4	2	1	0
Chemotherapy (430)	430	38	26	12	6	5	2	2	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10DEC2024 10:32; Program name: F.2.12.1_EORTC_BR45_TTCDet_FAS.sas; Output name: F.2.12.1_EORTC_BR45_TTCDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Breast Satisfaction



Patients still at risk:

T-DXd(436)	436	94	69	54	39	32	17	11	4	2	2	1	0
Chemotherapy (430)	430	89	61	43	31	20	11	5	3	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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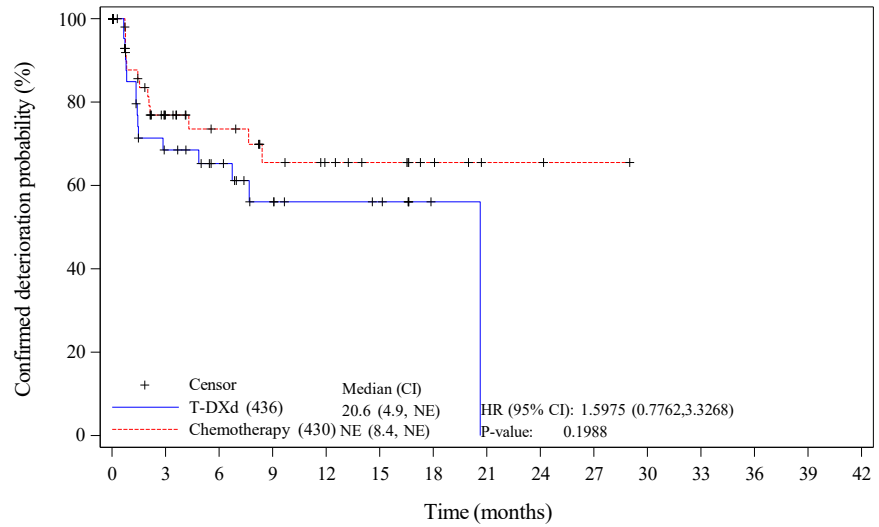
Run date: 10DEC2024 10:32; Program name: F.2.12.1_EORTC_BR45_TTCDet_FAS.sas; Output name: F.2.12.1_EORTC_BR45_TTCDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Sexual Enjoyment



Patients still at risk:

T-DXd(436)	436	23	17	10	7	6	1	0			
Chemotherapy (430)	430	28	21	15	12	9	5	2	2	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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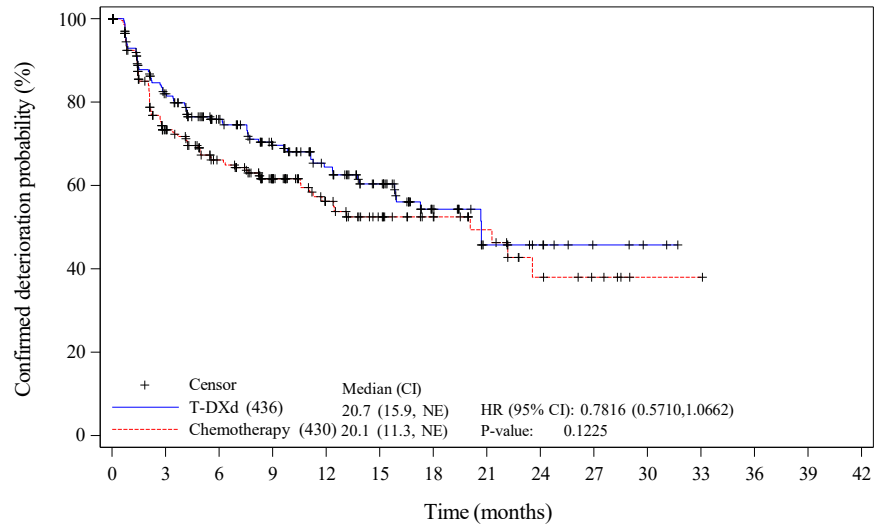
Run date: 10DEC2024 10:32; Program name: F.2.12.1_EORTC_BR45_TTCDet_FAS.sas; Output name: F.2.12.1_EORTC_BR45_TTCDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Future Perspective



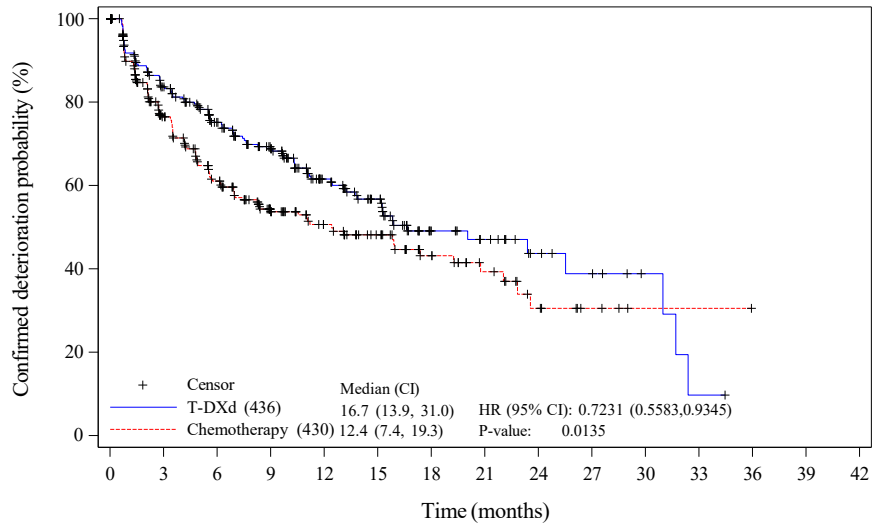
Patients still at risk:

T-DXd(436)	436	153	116	92	69	51	25	13	9	4	2	0
Chemotherapy (430)	430	141	109	76	47	32	23	16	8	5	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10DEC2024 10:32; Program name: F.2.12.1_EORTC_BR45_TTCDet_FAS.sas; Output name: F.2.12.1_EORTC_BR45_TTCDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Arm Symptoms



Patients still at risk:

T-DXd(436)	436	209	162	130	83	60	28	20	11	8	4	1	0
Chemotherapy (430)	430	183	130	85	62	46	28	18	9	4	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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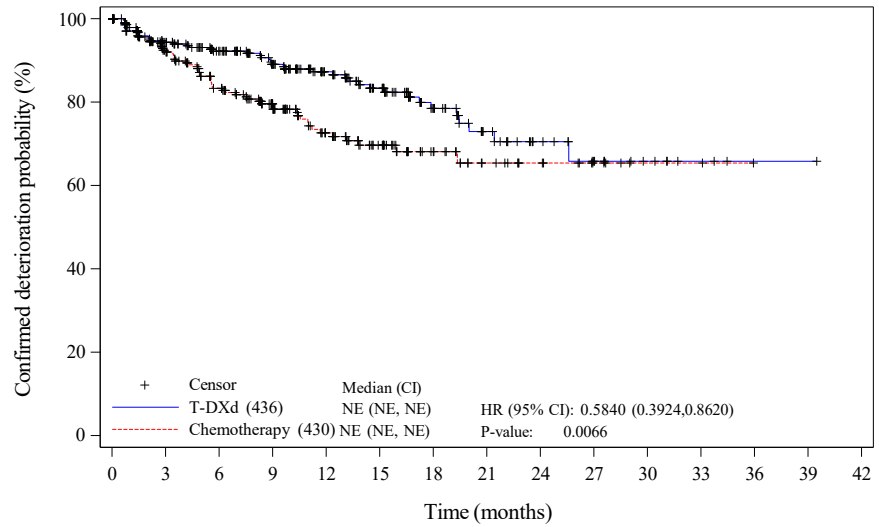
Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Breast Symptoms



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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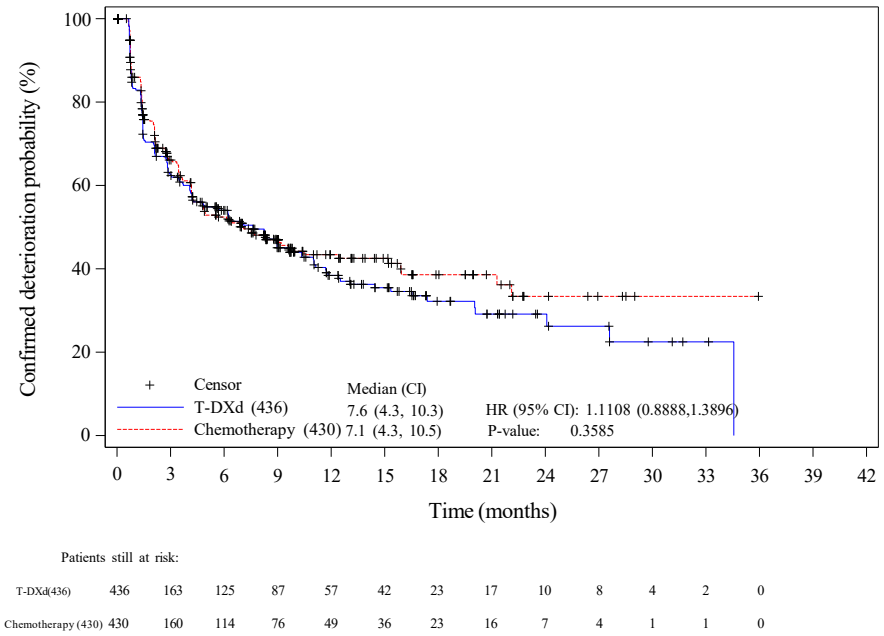
Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Systemic Therapy Side Effects



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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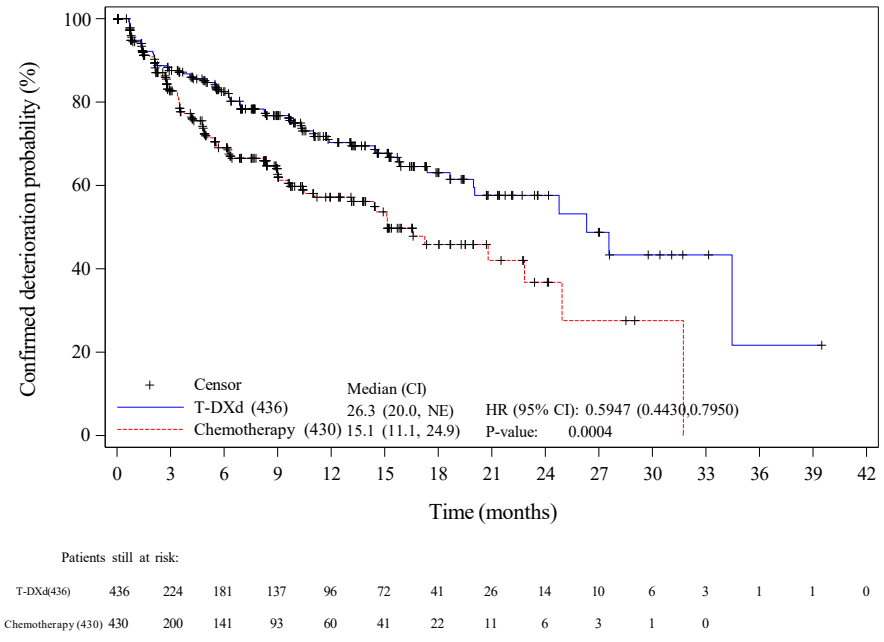
Run date: 10DEC2024 10:32; Program name: F.2.12.1_EORTC_BR45_TTCDet_FAS.sas; Output name: F.2.12.1_EORTC_BR45_TTCDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Endocrine Therapy Symptoms



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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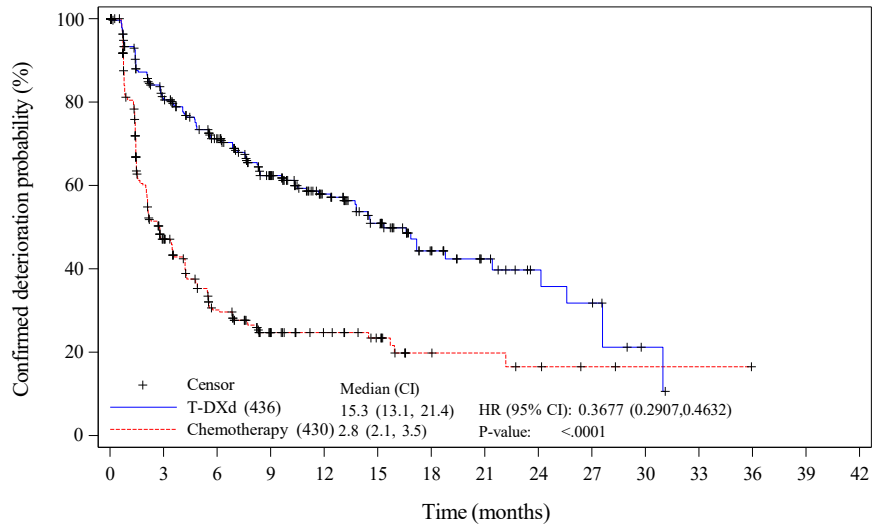
Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Skin Mucosis Symptoms



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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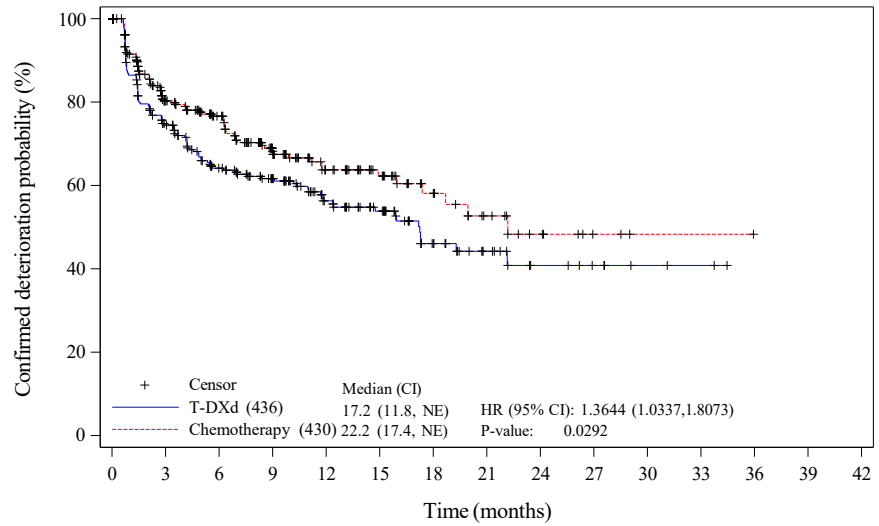
Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Endocrine Sexual Symptoms



Patients still at risk:

T-DXd(436)	436	184	136	110	75	57	30	17	9	6	3	2	0
Chemotherapy (430)	430	187	151	93	62	42	25	15	8	3	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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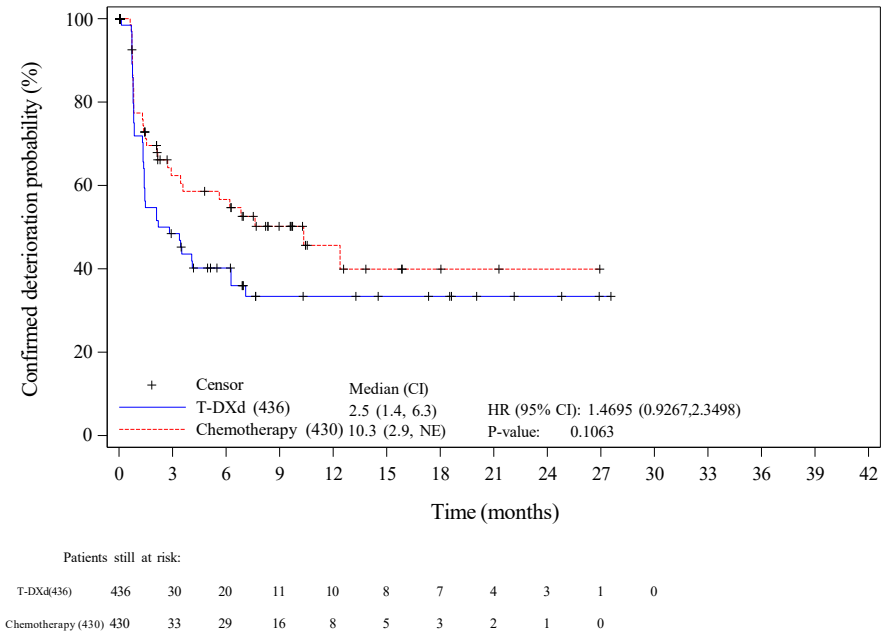
Figure 2.12.1 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Upset by Hair Loss



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Abbildung 2.12.2 EORTC-QLQ-BR45 – Zeit bis zur bestätigten Verschlechterung – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

Daiichi Sankyo Europe GmbH
Data Intelligence - Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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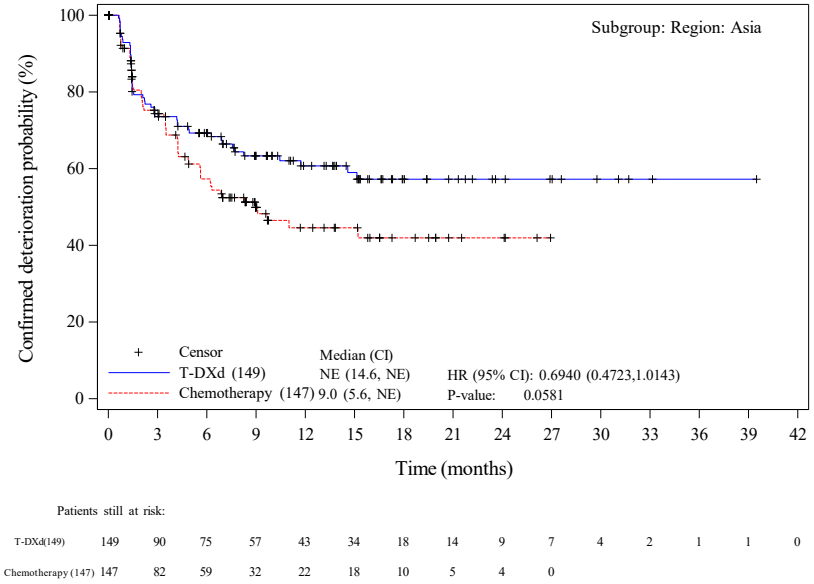
Final
Statistical analyses for AMNOG (HTA Germany)

Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Body Image



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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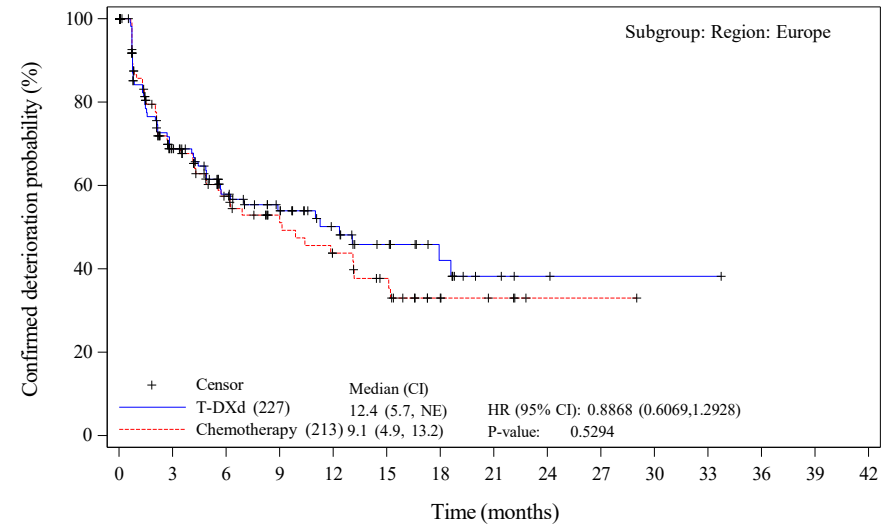
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Body Image



Patients still at risk:

T-DXd(227)	227	71	48	37	25	17	11	4	2	1	1	1	0
Chemotherapy (213)	213	61	40	29	22	16	7	4	1	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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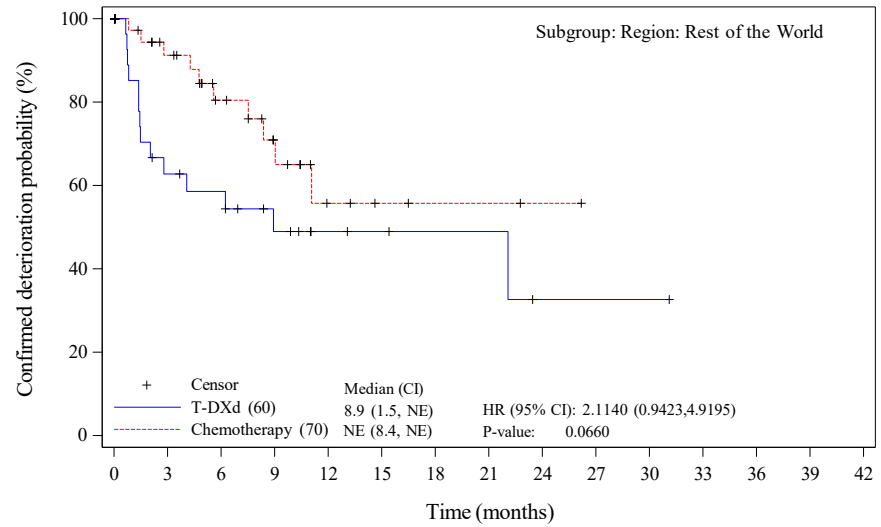
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Body Image



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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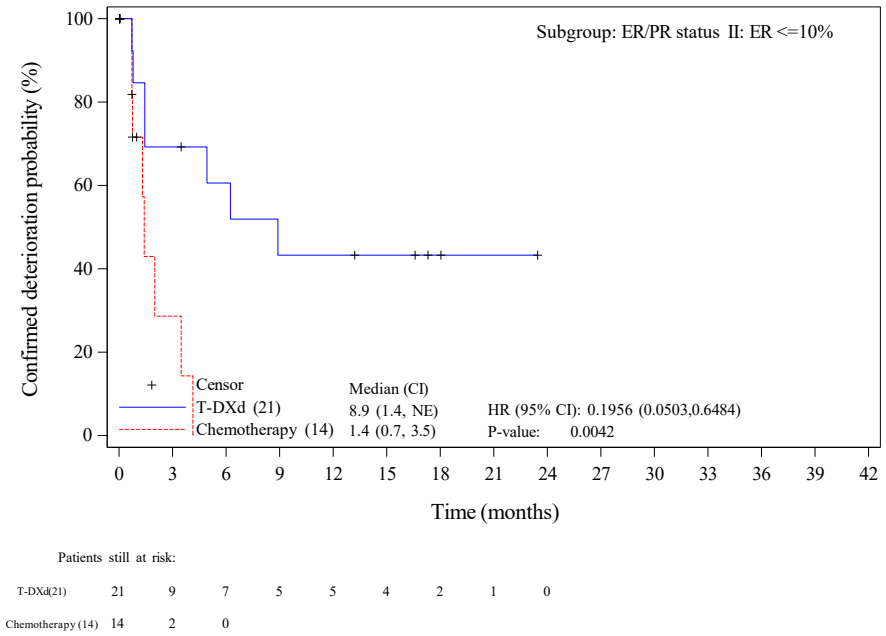
Run date: 05AUG2024 8:12; Program name: F.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.sas; Output name: F.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Body Image



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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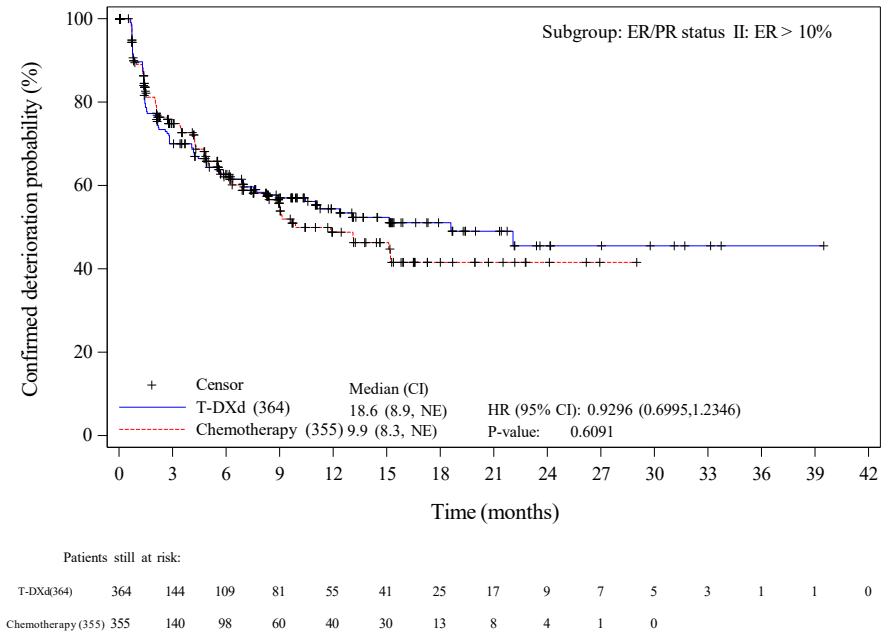
Run date: 05AUG2024 8:12; Program name: F.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.sas; Output name: F.2.12.2_EORTC_BR45_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Body Image



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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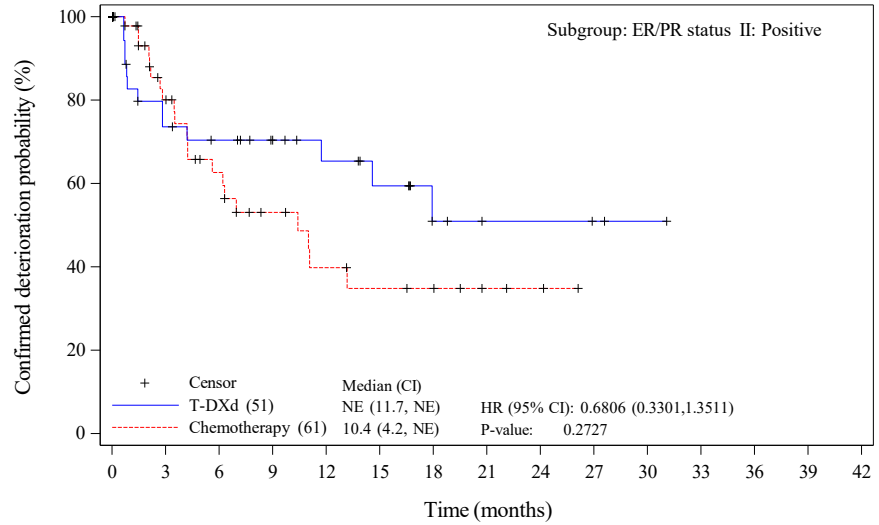
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Body Image



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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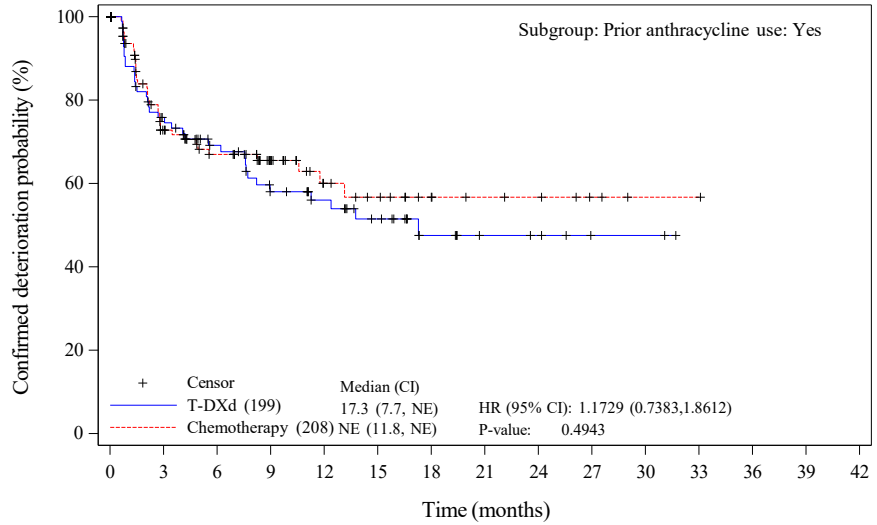
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Future Perspective



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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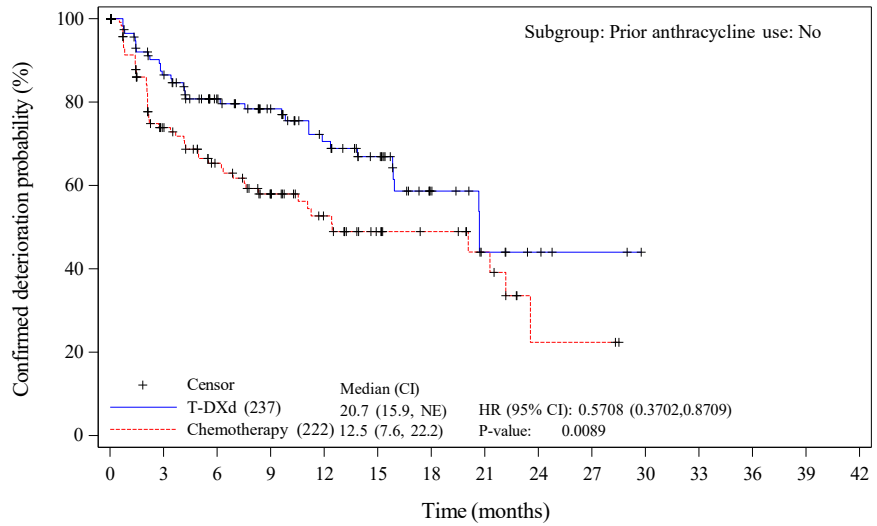
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Future Perspective



Patients still at risk:

T-DXd(237)	237	94	71	58	42	31	15	7	4	2	0
Chemotherapy (222)	222	73	55	41	28	17	13	9	2	2	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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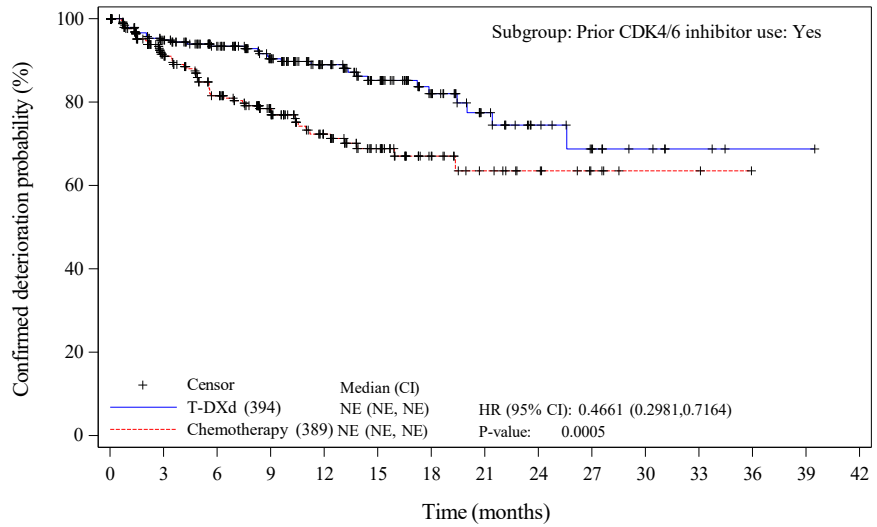
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Breast Symptoms



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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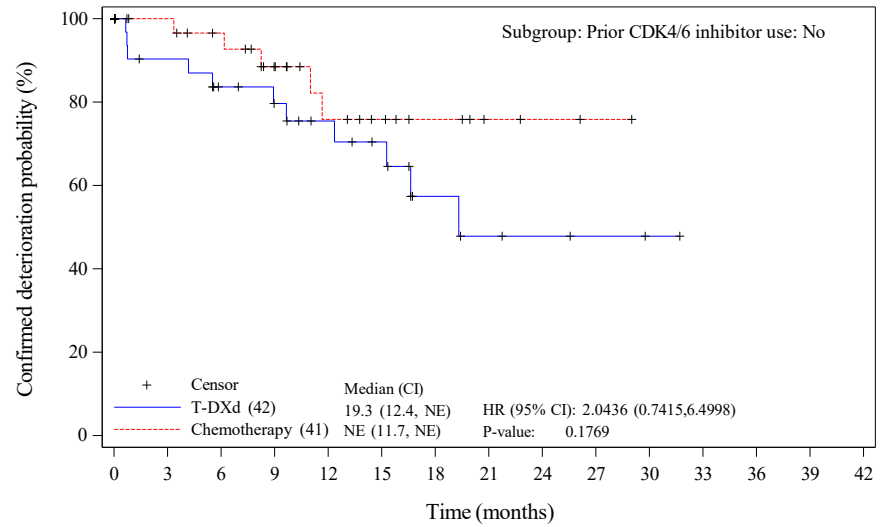
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Breast Symptoms



Patients still at risk:

T-DXd(42)	42	27	22	19	15	12	6	4	3	2	1	0
Chemotherapy (41)	41	29	25	18	12	9	6	3	2	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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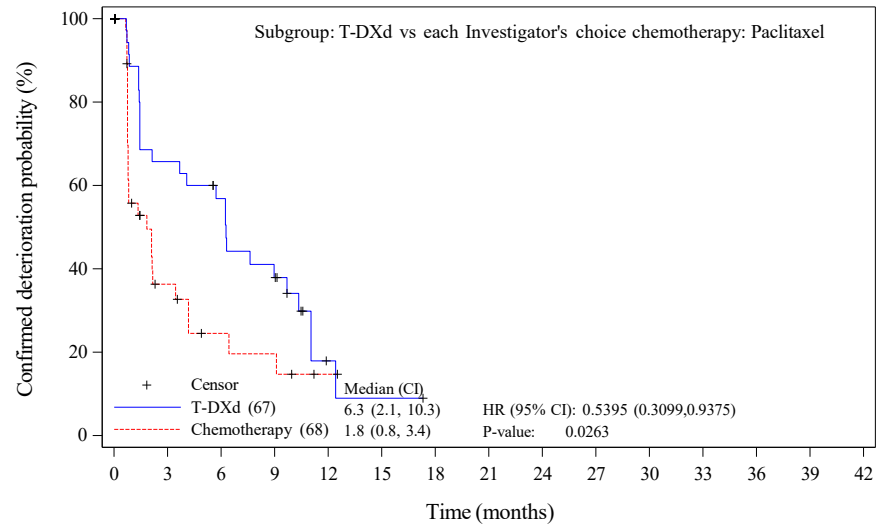
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Systemic Therapy Side Effects



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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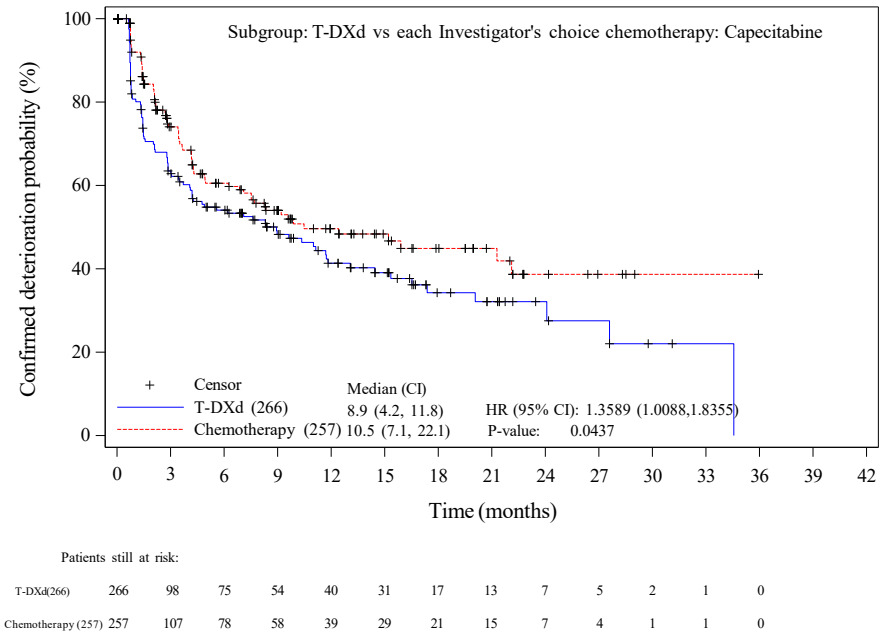
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Systemic Therapy Side Effects



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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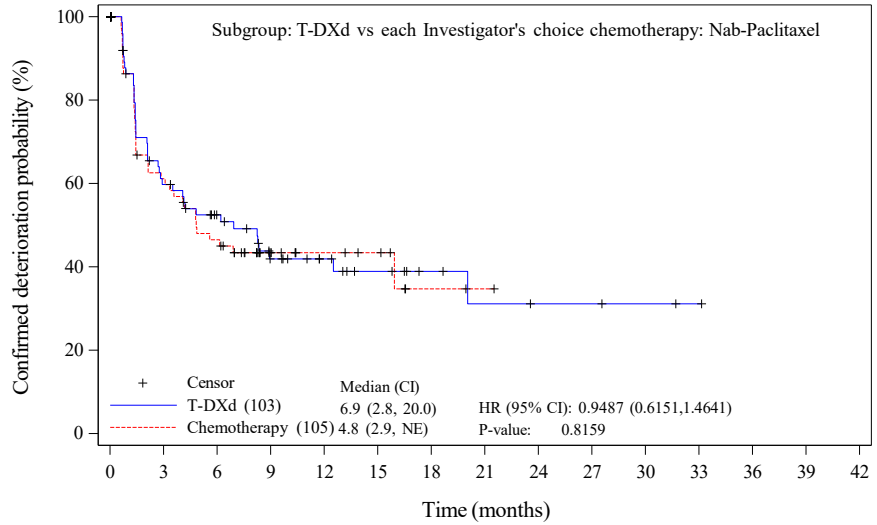
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Systemic Therapy Side Effects



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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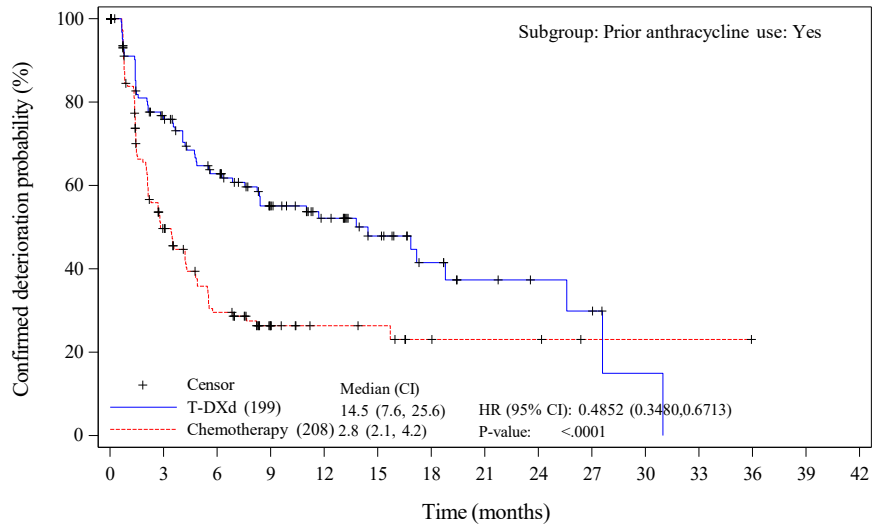
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Skin Mucosis Symptoms



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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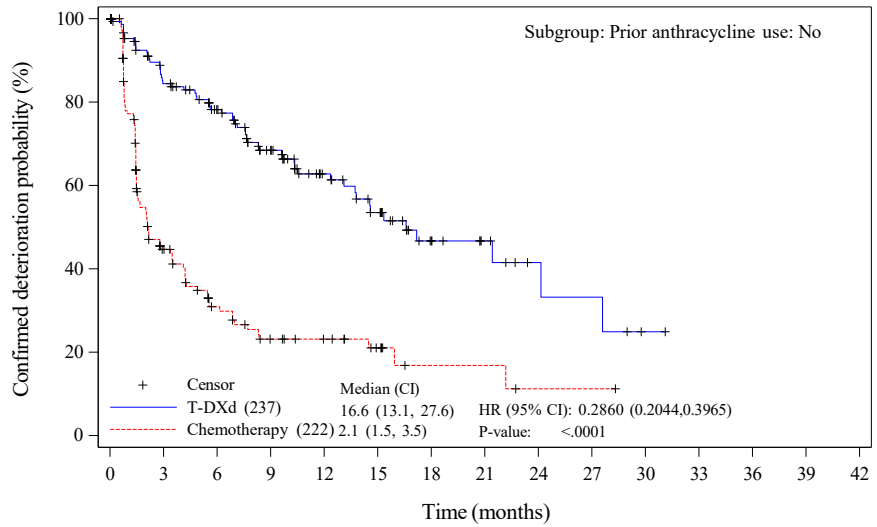
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Skin Mucosis Symptoms



Patients still at risk:

T-DXd(237)	237	115	94	69	44	32	16	10	5	4	1	0
Chemotherapy (222)	222	53	29	18	14	8	3	3	1	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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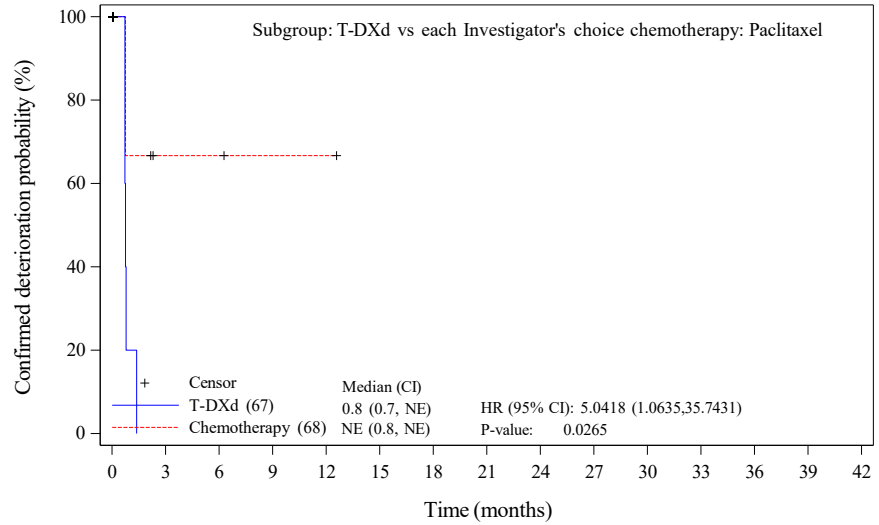
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Upset by Hair Loss



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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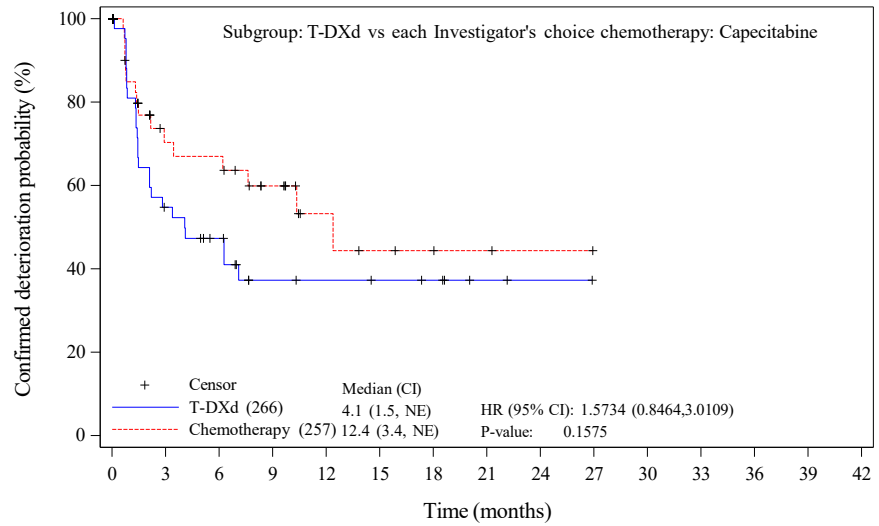
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Upset by Hair Loss



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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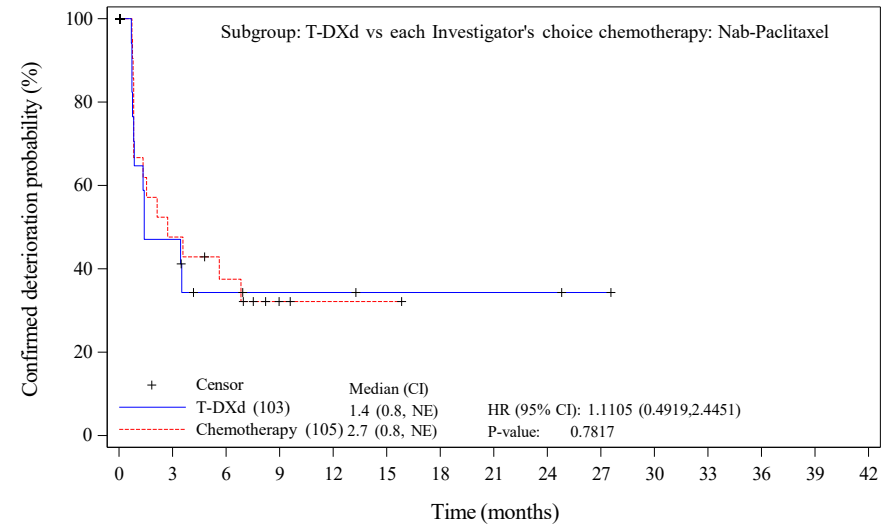
Figure 2.12.2 EORTC-QLQ-BR45 - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Upset by Hair Loss



Patients still at risk:

T-DXd(103)	103	8	4	3	3	2	2	2	2	1	0
Chemotherapy (105)	105	10	7	2	1	1	0				

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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Tabelle 2.12.4 EORTC-QLQ-BR45 – Zeit bis zur bestätigten Verschlechterung – Sensitivitätsanalyse – FAS

Table 2.12.4 EORTC QLQ-BR45 - Time to confirmed deterioration - Sensitivity analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Body Image	104 (23.9)	22.1 [13.1; NE]	112 (26.0)	13.1 [9.1; NE]	0.8982 [0.6866; 1.1739] 0.4321	0.4298
Functional Scales/Sexual Functioning	47 (10.8)	2.0 [1.4; 4.9]	50 (11.6)	4.9 [2.8; 8.9]	1.4113 [0.9450; 2.1041] 0.0905	0.0929
Functional Scales/Breast Satisfaction	94 (21.6)	7.1 [3.5; 16.0]	100 (23.3)	4.9 [3.5; 16.5]	0.9820 [0.7399; 1.3022] 0.8995	0.8974
Functional Scales/Sexual Enjoyment	15 (3.4)	20.6 [6.7; NE]	11 (2.6)	NE [NE; NE]	1.9049 [0.8771; 4.2699] 0.1061	0.1008
Functional Scales/Future Perspective	58 (13.3)	NE [20.7; NE]	76 (17.7)	23.6 [12.5; NE]	0.7383 [0.5223; 1.0382] 0.0827	0.0830
Symptom Scales/Arm Symptoms	94 (21.6)	25.5 [15.3; 32.4]	111 (25.8)	17.4 [11.2; 23.6]	0.7418 [0.5622; 0.9767] 0.0337	0.0340

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Table 2.12.4 EORTC QLQ-BR45 - Time to confirmed deterioration - Sensitivity analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Breast Symptoms	36 (8.3)	NE [NE; NE]	41 (9.5)	NE [NE; NE]	0.7487 [0.4756; 1.1736] 0.2073	0.2061
Symptom Scales/Systemic Therapy Side Effects	147 (33.7)	9.0 [6.2; 11.7]	123 (28.6)	10.5 [6.9; NE]	1.2066 [0.9503; 1.5360] 0.1249	0.1247
Symptom Scales/Endocrine Therapy Symptoms	67 (15.4)	NE [26.3; NE]	86 (20.0)	20.8 [15.1; NE]	0.6342 [0.4583; 0.8739] 0.0056	0.0053
Symptom Scales/Skin Mucosis Symptoms	103 (23.6)	17.2 [13.8; 27.6]	173 (40.2)	3.4 [2.2; 4.2]	0.3751 [0.2915; 0.4801] <.0001	<.0001
Symptom Scales/Endocrine Sexual Symptoms	102 (23.4)	NE [15.9; NE]	70 (16.3)	NE [NE; NE]	1.5256 [1.1277; 2.0758] 0.0066	0.0064
Symptom Scales/Upset by Hair Loss	38 (8.7)	3.4 [1.4; NE]	30 (7.0)	10.3 [3.4; NE]	1.4710 [0.9127; 2.3924] 0.1147	0.1170

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

Tabelle 2.12.9 EORTC-QLQ-BR45 – Zeit bis zur erstmaligen Verschlechterung – FAS

Table 2.12.9 EORTC QLQ-BR45 - Time to first deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Body Image	181 (41.5)	3.5 [2.8; 4.8]	171 (39.8)	4.2 [2.9; 5.6]	1.0296 [0.8345; 1.2707] 0.7856	0.7919
Functional Scales/Sexual Functioning	58 (13.3)	1.4 [1.3; 2.1]	74 (17.2)	1.4 [0.8; 2.1]	1.1534 [0.8118; 1.6318] 0.4218	0.4161
Functional Scales/Breast Satisfaction	141 (32.3)	2.0 [1.4; 2.2]	147 (34.2)	1.5 [1.4; 2.2]	1.0135 [0.8036; 1.2777] 0.9097	0.9170
Functional Scales/Sexual Enjoyment	23 (5.3)	4.0 [2.7; NE]	27 (6.3)	10.4 [2.6; 22.8]	1.2394 [0.6972; 2.1945] 0.4602	0.4579
Functional Scales/Future Perspective	102 (23.4)	10.3 [6.9; 15.5]	119 (27.7)	7.0 [4.2; 12.5]	0.8405 [0.6439; 1.0947] 0.1988	0.2025
Symptom Scales/Arm Symptoms	160 (36.7)	6.4 [4.9; 9.2]	182 (42.3)	3.5 [2.8; 4.9]	0.7585 [0.6119; 0.9392] 0.0114	0.0121

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

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Run date: 04DEC2024 5:53; Program name: T.2.12.9_EORTC_BR45_TTFDet_FAS.sas; Output name: T.2.12.9_EORTC_BR45_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.9 EORTC QLQ-BR45 - Time to first deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Breast Symptoms	86 (19.7)	31.0 [20.0; NE]	105 (24.4)	16.6 [11.7; 32.4]	0.7061 [0.5289; 0.9401] 0.0175	0.0171
Symptom Scales/Systemic Therapy Side Effects	197 (45.2)	2.7 [2.1; 3.4]	193 (44.9)	2.9 [2.2; 4.1]	1.0797 [0.8851; 1.3172] 0.4491	0.4598
Symptom Scales/Endocrine Therapy Symptoms	138 (31.7)	11.4 [9.0; 14.6]	161 (37.4)	5.7 [4.8; 7.6]	0.7059 [0.5605; 0.8878] 0.0030	0.0030
Symptom Scales/Skin Mucosis Symptoms	180 (41.3)	5.6 [4.2; 7.7]	227 (52.8)	2.0 [1.5; 2.1]	0.5275 [0.4316; 0.6437] <.0001	<.0001
Symptom Scales/Endocrine Sexual Symptoms	168 (38.5)	4.1 [3.0; 5.7]	142 (33.0)	6.9 [5.0; 13.7]	1.2463 [0.9970; 1.5609] 0.0539	0.0559
Symptom Scales/Upset by Hair Loss	49 (11.2)	1.5 [1.3; 2.8]	44 (10.2)	2.1 [1.4; 6.9]	1.2053 [0.8009; 1.8181] 0.3704	0.3777

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

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Run date: 04DEC2024 5:53; Program name: T.2.12.9_EORTC_BR45_TTFDet_FAS.sas; Output name: T.2.12.9_EORTC_BR45_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.12.10 EORTC-QLQ-BR45 – Zeit bis zur erstmaligen Verschlechterung – Subgruppenanalyse – FAS

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Body Image						
Age at randomization						0.9070
<65 years of age	129 / 302 (42.7)	2.8 [2.2; 4.2]	116 / 297 (39.1)	4.2 [3.2; 5.7]	1.0377 [0.8068; 1.3361] 0.7726	
>=65 years of age	52 / 134 (38.8)	4.8 [2.8; 5.7]	55 / 133 (41.4)	3.5 [2.2; 6.9]	1.0078 [0.6860; 1.4777] 0.9765	
Race						0.7011
Asian	90 / 154 (58.4)	2.8 [2.1; 4.9]	77 / 151 (51.0)	4.2 [3.2; 6.3]	1.1581 [0.8527; 1.5767] 0.3510	
White	80 / 231 (34.6)	4.2 [2.8; 6.2]	85 / 230 (37.0)	3.7 [2.3; 6.9]	0.9376 [0.6896; 1.2735] 0.6781	
Other	11 / 51 (21.6)	3.5 [1.4; NE]	9 / 49 (18.4)	2.7 [1.4; NE]	1.0063 [0.4142; 2.5075] 0.9737	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0147
Asia	89 / 149 (59.7)	2.8 [2.1; 4.9]	75 / 147 (51.0)	4.3 [3.2; 6.9]	1.1772 [0.8644; 1.6076] 0.3019	
Europe	70 / 227 (30.8)	4.8 [2.8; 7.9]	80 / 213 (37.6)	2.9 [2.2; 4.3]	0.7457 [0.5389; 1.0294] 0.0715	
Rest of the World	22 / 60 (36.7)	2.8 [1.5; 4.9]	16 / 70 (22.9)	15.8 [2.1; NE]	1.9856 [1.0468; 3.8502] 0.0326	
HER2 IHC expression						0.2564
IHC 1+	99 / 239 (41.4)	4.1 [2.2; 5.6]	97 / 234 (41.5)	4.1 [2.8; 6.3]	1.0125 [0.7622; 1.3448] 0.9362	
IHC 2+/ISH-	46 / 117 (39.3)	2.8 [2.1; 6.2]	51 / 118 (43.2)	3.1 [2.1; 4.2]	0.8582 [0.5739; 1.2798] 0.4388	
IHC >0 <1+	35 / 76 (46.1)	3.2 [2.1; 5.6]	23 / 76 (30.3)	7.0 [3.5; NE]	1.4492 [0.8600; 2.4891] 0.1656	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2292
Yes	159 / 394 (40.4)	4.1 [2.8; 4.9]	154 / 389 (39.6)	4.1 [2.9; 4.9]	0.9743 [0.7794; 1.2181] 0.8188	
No	22 / 42 (52.4)	1.8 [1.4; 5.0]	17 / 41 (41.5)	5.6 [1.5; NE]	1.4685 [0.7803; 2.8123] 0.2412	
Prior Taxane Use In The Non-Metastatic Setting						0.6593
Yes	72 / 179 (40.2)	2.8 [2.1; 4.2]	70 / 177 (39.5)	4.2 [2.2; 6.9]	1.0889 [0.7814; 1.5176] 0.6192	
No	109 / 257 (42.4)	4.1 [2.8; 5.7]	101 / 253 (39.9)	4.1 [2.9; 5.6]	0.9860 [0.7511; 1.2954] 0.9195	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5642
1	26 / 65 (40.0)	4.2 [1.5; 5.7]	30 / 82 (36.6)	4.1 [1.5; 8.3]	0.9434 [0.5535; 1.5970] 0.8303	
2	119 / 295 (40.3)	3.5 [2.8; 4.9]	109 / 288 (37.8)	4.3 [3.1; 7.0]	1.1075 [0.8532; 1.4389] 0.4435	
>=3	35 / 75 (46.7)	4.2 [2.0; 8.9]	31 / 58 (53.4)	4.1 [2.0; 6.3]	0.8499 [0.5210; 1.3915] 0.5136	
ER/PR status I						0.6310
ER+, PR+	103 / 253 (40.7)	4.1 [2.8; 5.7]	91 / 237 (38.4)	4.3 [3.2; 6.9]	0.9991 [0.7530; 1.3278] 0.9923	
ER+, PR-	77 / 167 (46.1)	2.9 [2.1; 4.9]	75 / 181 (41.4)	3.7 [2.1; 5.6]	1.1009 [0.7985; 1.5174] 0.5541	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.0514
ER <=10%	10 / 21 (47.6)	4.9 [1.4; 13.8]	8 / 14 (57.1)	1.4 [0.7; 2.0]	0.2140 [0.0615; 0.6778] 0.0050	
ER >10%	148 / 364 (40.7)	2.8 [2.2; 4.2]	138 / 355 (38.9)	4.3 [3.2; 5.6]	1.0753 [0.8517; 1.3583] 0.5470	
Positive	23 / 51 (45.1)	5.6 [3.5; 14.6]	25 / 61 (41.0)	4.2 [2.2; 11.0]	0.9610 [0.5404; 1.7011] 0.8955	
Endocrine Resistance						0.1235
Primary	55 / 128 (43.0)	2.2 [1.5; 4.2]	51 / 140 (36.4)	4.9 [2.8; 10.4]	1.3049 [0.8889; 1.9185] 0.1747	
Secondary	126 / 308 (40.9)	4.1 [2.8; 5.7]	119 / 288 (41.3)	3.5 [2.8; 4.9]	0.9262 [0.7199; 1.1927] 0.5496	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3543
Capecitabine	103 / 266 (38.7)	3.5 [2.8; 5.6]	98 / 257 (38.1)	4.9 [3.7; 9.0]	1.1104 [0.8407; 1.4669] 0.4657	
Nab-Paclitaxel	49 / 103 (47.6)	3.5 [2.1; 6.1]	47 / 105 (44.8)	2.9 [2.0; 6.3]	0.9627 [0.6426; 1.4429] 0.8538	
Paclitaxel	29 / 67 (43.3)	2.9 [1.4; 5.7]	26 / 68 (38.2)	2.1 [0.8; 2.8]	0.7355 [0.4298; 1.2646] 0.2533	
Prior anthracycline use						0.2909
Yes	85 / 199 (42.7)	2.8 [2.1; 4.2]	82 / 208 (39.4)	4.1 [2.7; 6.9]	1.1624 [0.8562; 1.5773] 0.3349	
No	96 / 237 (40.5)	4.8 [2.8; 6.9]	89 / 222 (40.1)	4.2 [2.8; 5.7]	0.9289 [0.6951; 1.2429] 0.6197	
Liver metastases						0.1043
Yes	112 / 296 (37.8)	4.2 [2.8; 6.2]	111 / 283 (39.2)	4.2 [2.8; 5.7]	0.8866 [0.6799; 1.1565] 0.3733	
No	69 / 140 (49.3)	2.2 [1.5; 4.1]	60 / 147 (40.8)	4.3 [2.8; 6.9]	1.3036 [0.9214; 1.8488] 0.1361	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.5099
0	105 / 252 (41.7)	4.1 [2.8; 5.5]	103 / 257 (40.1)	4.2 [2.8; 5.6]	0.9732 [0.7398; 1.2804] 0.8409	
>=1	75 / 179 (41.9)	3.5 [2.2; 5.6]	65 / 164 (39.6)	4.2 [2.8; 7.0]	1.1038 [0.7910; 1.5445] 0.5651	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Sexual Functioning						
Age at randomization						0.1310
<65 years of age	48 / 302 (15.9)	2.0 [1.4; 2.6]	65 / 297 (21.9)	1.4 [0.8; 2.0]	1.0423 [0.7114; 1.5168] 0.7996	
>=65 years of age	10 / 134 (7.5)	0.8 [0.7; 1.4]	9 / 133 (6.8)	2.8 [0.7; NE]	2.2911 [0.8449; 6.5877] 0.0942	
Race						0.3152
Asian	20 / 154 (13.0)	1.4 [0.8; 2.1]	18 / 151 (11.9)	1.5 [0.8; 7.0]	1.3783 [0.7216; 2.6534] 0.3245	
White	32 / 231 (13.9)	2.0 [1.4; 2.6]	52 / 230 (22.6)	1.4 [0.8; 1.8]	0.9942 [0.6282; 1.5525] 0.9903	
Other	6 / 51 (11.8)	0.7 [0.7; NE]	4 / 49 (8.2)	2.8 [0.8; NE]	2.2137 [0.5763; 9.0757] 0.2535	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4002
Asia	20 / 149 (13.4)	1.4 [0.8; 2.8]	16 / 147 (10.9)	1.5 [0.7; 7.0]	1.3513 [0.6959; 2.6682] 0.3713	
Europe	29 / 227 (12.8)	1.6 [1.3; 2.6]	43 / 213 (20.2)	1.0 [0.8; 2.0]	0.9587 [0.5884; 1.5420] 0.8901	
Rest of the World	9 / 60 (15.0)	1.7 [0.7; 2.1]	15 / 70 (21.4)	1.5 [1.4; 5.7]	1.7357 [0.6931; 4.2430] 0.2059	
HER2 IHC expression						0.3465
IHC 1+	27 / 239 (11.3)	1.4 [0.8; 2.1]	41 / 234 (17.5)	0.8 [0.8; 1.5]	0.9052 [0.5485; 1.4711] 0.7019	
IHC 2+/ISH-	18 / 117 (15.4)	2.1 [0.8; 2.6]	22 / 118 (18.6)	2.8 [0.8; 5.7]	1.8483 [0.9433; 3.6282] 0.0662	
IHC >0 <1+	13 / 76 (17.1)	2.0 [0.7; 5.7]	10 / 76 (13.2)	1.5 [0.8; 9.0]	1.5092 [0.6591; 3.5608] 0.3297	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6400
Yes	52 / 394 (13.2)	1.5 [1.4; 2.1]	68 / 389 (17.5)	1.4 [0.8; 2.1]	1.1326 [0.7829; 1.6300] 0.4827	
No	6 / 42 (14.3)	1.1 [0.7; NE]	6 / 41 (14.6)	1.2 [0.6; NE]	1.2693 [0.3774; 4.4543] 0.6853	
Prior Taxane Use In The Non-Metastatic Setting						0.9864
Yes	28 / 179 (15.6)	1.4 [1.3; 2.1]	32 / 177 (18.1)	1.4 [0.8; 3.5]	1.1306 [0.6738; 1.8873] 0.6233	
No	30 / 257 (11.7)	1.5 [0.8; 2.1]	42 / 253 (16.6)	1.5 [0.8; 2.8]	1.1775 [0.7256; 1.8899] 0.4906	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.9586
1	10 / 65 (15.4)	1.3 [0.7; 2.8]	17 / 82 (20.7)	1.4 [0.8; 2.0]	1.2505 [0.5429; 2.7585] 0.5931	
2	34 / 295 (11.5)	2.0 [1.3; 2.6]	47 / 288 (16.3)	1.5 [0.8; 2.9]	1.1364 [0.7239; 1.7657] 0.5651	
>=3	13 / 75 (17.3)	1.4 [0.8; 2.8]	10 / 58 (17.2)	1.5 [0.7; 7.0]	1.2794 [0.5308; 3.2896] 0.5503	
ER/PR status I						0.0495
ER+, PR+	31 / 253 (12.3)	1.4 [1.3; 2.1]	40 / 237 (16.9)	1.5 [0.8; 4.2]	1.6777 [1.0184; 2.7575] 0.0352	
ER+, PR-	27 / 167 (16.2)	1.6 [0.8; 3.5]	33 / 181 (18.2)	0.8 [0.8; 1.5]	0.8046 [0.4795; 1.3387] 0.4165	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4398
ER <=10%	6 / 21 (28.6)	4.4 [0.7; NE]	1 / 14 (7.1)	0.8 [NE; NE]	0.3375 [0.0322; 7.2793] 0.3530	
ER >10%	49 / 364 (13.5)	1.5 [1.3; 2.1]	62 / 355 (17.5)	1.5 [0.8; 2.9]	1.2446 [0.8466; 1.8214] 0.2552	
Positive	3 / 51 (5.9)	1.4 [0.7; NE]	11 / 61 (18.0)	0.8 [0.7; 1.8]	1.6205 [0.3462; 5.9132] 0.5024	
Endocrine Resistance						0.3580
Primary	26 / 128 (20.3)	1.4 [0.8; 2.1]	25 / 140 (17.9)	1.5 [0.8; 3.6]	1.3084 [0.7490; 2.2916] 0.3508	
Secondary	32 / 308 (10.4)	1.5 [1.4; 2.6]	49 / 288 (17.0)	1.4 [0.8; 1.8]	1.0490 [0.6619; 1.6403] 0.8191	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.5918
Capecitabine	35 / 266 (13.2)	1.6 [1.4; 2.1]	52 / 257 (20.2)	1.4 [0.8; 2.1]	1.0095 [0.6506; 1.5484] 0.9583	
Nab-Paclitaxel	21 / 103 (20.4)	1.3 [0.7; 4.1]	12 / 105 (11.4)	0.8 [0.7; 7.5]	1.5248 [0.7457; 3.2697] 0.2382	
Paclitaxel	2 / 67 (3.0)	2.0 [1.4; NE]	10 / 68 (14.7)	2.7 [0.7; 7.0]	0.9344 [0.1387; 3.8934] 0.9328	
Prior anthracycline use						0.9926
Yes	30 / 199 (15.1)	1.4 [1.3; 2.1]	36 / 208 (17.3)	1.5 [0.8; 3.5]	1.1311 [0.6883; 1.8468] 0.6055	
No	28 / 237 (11.8)	1.5 [0.8; 2.1]	38 / 222 (17.1)	1.4 [0.8; 2.8]	1.1681 [0.7071; 1.9085] 0.5299	
Liver metastases						0.7289
Yes	46 / 296 (15.5)	2.0 [1.4; 2.1]	40 / 283 (14.1)	1.5 [0.8; 3.5]	1.1982 [0.7779; 1.8551] 0.3859	
No	12 / 140 (8.6)	0.8 [0.7; 2.0]	34 / 147 (23.1)	1.4 [0.8; 2.8]	1.4264 [0.7046; 2.6966] 0.2947	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.3644
0	37 / 252 (14.7)	2.0 [1.3; 2.8]	52 / 257 (20.2)	1.5 [0.8; 2.8]	1.1357 [0.7319; 1.7492] 0.5528	
>=1	21 / 179 (11.7)	1.4 [0.8; 2.1]	20 / 164 (12.2)	0.8 [0.8; 5.5]	1.3620 [0.7296; 2.5533] 0.3068	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Breast Satisfaction						
Age at randomization						0.5864
<65 years of age	103 / 302 (34.1)	2.0 [1.4; 2.7]	95 / 297 (32.0)	1.5 [1.4; 2.7]	1.0574 [0.7998; 1.3996] 0.6977	
>=65 years of age	38 / 134 (28.4)	1.4 [0.8; 3.5]	52 / 133 (39.1)	1.5 [1.3; 2.2]	0.9168 [0.5966; 1.3949] 0.6916	
Race						0.5738
Asian	66 / 154 (42.9)	0.8 [0.8; 1.5]	61 / 151 (40.4)	1.4 [1.3; 2.2]	1.1688 [0.8239; 1.6601] 0.3833	
White	65 / 231 (28.1)	2.2 [1.6; 3.5]	78 / 230 (33.9)	2.0 [1.4; 2.9]	0.9268 [0.6647; 1.2876] 0.6639	
Other	10 / 51 (19.6)	2.8 [0.8; 4.9]	8 / 49 (16.3)	1.2 [0.7; 4.9]	0.7204 [0.2823; 1.8982] 0.5120	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7881
Asia	65 / 149 (43.6)	0.9 [0.8; 1.5]	60 / 147 (40.8)	1.4 [1.3; 2.2]	1.1167 [0.7851; 1.5908] 0.5409	
Europe	61 / 227 (26.9)	2.2 [1.5; 4.0]	63 / 213 (29.6)	2.1 [1.4; 2.9]	0.9841 [0.6908; 1.4009] 0.9350	
Rest of the World	15 / 60 (25.0)	2.1 [1.4; 6.2]	24 / 70 (34.3)	1.5 [1.3; 4.1]	0.7663 [0.3856; 1.4655] 0.4361	
HER2 IHC expression						0.3183
IHC 1+	79 / 239 (33.1)	1.4 [1.4; 2.2]	84 / 234 (35.9)	1.4 [1.3; 2.1]	0.9214 [0.6767; 1.2534] 0.6082	
IHC 2+/ISH-	36 / 117 (30.8)	2.2 [0.8; 5.1]	40 / 118 (33.9)	1.8 [1.4; 3.5]	0.9307 [0.5888; 1.4655] 0.7323	
IHC >0 <1+	26 / 76 (34.2)	2.1 [0.8; 6.2]	22 / 76 (28.9)	2.9 [1.4; 10.6]	1.5223 [0.8629; 2.7097] 0.1499	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.7747
Yes	126 / 394 (32.0)	2.0 [1.4; 2.2]	129 / 389 (33.2)	1.5 [1.4; 2.2]	1.0152 [0.7934; 1.2987] 0.9027	
No	15 / 42 (35.7)	1.4 [0.7; 4.1]	18 / 41 (43.9)	2.8 [1.3; 3.6]	1.0543 [0.5172; 2.1265] 0.8680	
Prior Taxane Use In The Non-Metastatic Setting						0.6575
Yes	56 / 179 (31.3)	1.6 [1.4; 2.8]	67 / 177 (37.9)	2.1 [1.4; 2.8]	1.0580 [0.7387; 1.5091] 0.7594	
No	85 / 257 (33.1)	2.0 [1.4; 2.8]	80 / 253 (31.6)	1.5 [1.3; 2.2]	0.9769 [0.7193; 1.3280] 0.8803	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.9039
1	24 / 65 (36.9)	2.1 [0.8; 5.5]	23 / 82 (28.0)	2.8 [1.4; 4.9]	1.0657 [0.5939; 1.9148] 0.8506	
2	90 / 295 (30.5)	2.0 [1.4; 2.8]	100 / 288 (34.7)	1.5 [1.4; 2.2]	0.9795 [0.7355; 1.3027] 0.8890	
>=3	27 / 75 (36.0)	1.4 [0.8; 3.4]	24 / 58 (41.4)	1.5 [0.8; 2.9]	1.0041 [0.5787; 1.7527] 0.9946	
ER/PR status I						0.2224
ER+, PR+	79 / 253 (31.2)	1.5 [1.3; 2.2]	90 / 237 (38.0)	1.4 [1.3; 2.1]	0.8868 [0.6527; 1.2015] 0.4289	
ER+, PR-	61 / 167 (36.5)	2.0 [1.4; 3.5]	54 / 181 (29.8)	2.2 [1.4; 2.9]	1.1696 [0.8103; 1.6931] 0.4076	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6755
ER <=10%	9 / 21 (42.9)	0.8 [0.7; 3.4]	5 / 14 (35.7)	0.8 [0.6; NE]	0.9203 [0.2896; 3.1467] 0.8488	
ER >10%	117 / 364 (32.1)	2.0 [1.4; 2.2]	119 / 355 (33.5)	1.5 [1.4; 2.2]	1.0240 [0.7926; 1.3227] 0.8723	
Positive	15 / 51 (29.4)	2.8 [0.8; 11.9]	23 / 61 (37.7)	1.5 [0.8; 2.9]	0.8609 [0.4394; 1.6368] 0.7009	
Endocrine Resistance						0.8760
Primary	43 / 128 (33.6)	2.1 [0.8; 4.1]	46 / 140 (32.9)	1.5 [1.3; 2.8]	0.9762 [0.6413; 1.4831] 0.9200	
Secondary	98 / 308 (31.8)	1.6 [1.4; 2.8]	101 / 288 (35.1)	1.5 [1.4; 2.2]	1.0300 [0.7791; 1.3610] 0.8482	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1599
Capecitabine	92 / 266 (34.6)	2.0 [1.4; 2.2]	92 / 257 (35.8)	1.5 [1.4; 2.2]	1.0858 [0.8124; 1.4507] 0.5738	
Nab-Paclitaxel	39 / 103 (37.9)	0.9 [0.8; 1.4]	35 / 105 (33.3)	1.4 [1.3; 2.7]	1.0860 [0.6865; 1.7246] 0.7442	
Paclitaxel	10 / 67 (14.9)	6.2 [1.4; NE]	20 / 68 (29.4)	1.6 [0.8; 4.8]	0.5475 [0.2438; 1.1532] 0.1316	
Prior anthracycline use						0.3935
Yes	64 / 199 (32.2)	1.6 [1.4; 2.9]	70 / 208 (33.7)	2.2 [1.4; 2.8]	1.1029 [0.7839; 1.5480] 0.5740	
No	77 / 237 (32.5)	2.0 [1.3; 2.7]	77 / 222 (34.7)	1.4 [1.3; 2.1]	0.9175 [0.6667; 1.2625] 0.5806	
Liver metastases						0.3266
Yes	92 / 296 (31.1)	2.1 [1.4; 4.1]	100 / 283 (35.3)	1.5 [1.4; 2.7]	0.9361 [0.7038; 1.2436] 0.6433	
No	49 / 140 (35.0)	1.4 [0.8; 2.0]	47 / 147 (32.0)	1.4 [1.3; 2.2]	1.2115 [0.8109; 1.8119] 0.3546	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.2490
0	84 / 252 (33.3)	2.1 [1.4; 3.5]	93 / 257 (36.2)	1.5 [1.4; 2.2]	0.9002 [0.6684; 1.2103] 0.4861	
>=1	57 / 179 (31.8)	1.4 [0.9; 2.1]	52 / 164 (31.7)	1.5 [1.3; 2.7]	1.1960 [0.8207; 1.7459] 0.3648	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Sexual Enjoyment						
Age at randomization						0.7389
<65 years of age	20 / 302 (6.6)	4.1 [2.8; NE]	24 / 297 (8.1)	8.4 [2.1; 22.8]	1.1943 [0.6448; 2.2006] 0.5606	
>=65 years of age	3 / 134 (2.2)	2.7 [0.7; NE]	3 / 133 (2.3)	10.4 [2.1; NE]	1.4942 [0.2735; 8.1613] 0.6234	
Race						0.6884
Asian	5 / 154 (3.2)	NE [0.8; NE]	6 / 151 (4.0)	19.3 [0.8; NE]	0.9023 [0.2504; 3.2528] 0.8812	
White	17 / 231 (7.4)	3.5 [2.1; NE]	18 / 230 (7.8)	8.4 [2.6; NE]	1.5103 [0.7627; 2.9926] 0.2270	
Other	1 / 51 (2.0)	NE [0.7; NE]	3 / 49 (6.1)	2.8 [2.1; NE]	0.5974 [0.0290; 4.8423] 0.6573	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7871
Asia	6 / 149 (4.0)	4.0 [0.8; NE]	5 / 147 (3.4)	19.3 [0.8; NE]	1.1856 [0.3381; 4.6438] 0.7720	
Europe	15 / 227 (6.6)	3.5 [1.4; NE]	14 / 213 (6.6)	8.4 [2.8; NE]	1.5055 [0.7117; 3.2279] 0.2826	
Rest of the World	2 / 60 (3.3)	NE [0.7; NE]	8 / 70 (11.4)	4.4 [0.8; NE]	0.7918 [0.1187; 3.1993] 0.7836	
HER2 IHC expression						0.5479
IHC 1+	8 / 239 (3.3)	8.4 [1.5; NE]	15 / 234 (6.4)	10.4 [2.0; NE]	0.8918 [0.3523; 2.1162] 0.7953	
IHC 2+/ISH-	10 / 117 (8.5)	2.8 [0.8; NE]	10 / 118 (8.5)	6.1 [2.0; NE]	1.5718 [0.6326; 3.9624] 0.3234	
IHC >0 <1+	5 / 76 (6.6)	11.7 [2.8; NE]	2 / 76 (2.6)	NE [2.6; NE]	2.0030 [0.4258; 14.1143] 0.4013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8903
Yes	22 / 394 (5.6)	4.0 [2.7; NE]	24 / 389 (6.2)	6.2 [2.1; NE]	1.1343 [0.6306; 2.0309] 0.6654	
No	1 / 42 (2.4)	NE [0.8; NE]	3 / 41 (7.3)	19.3 [10.4; NE]	2.4495 [0.0960; 62.4738] 0.5151	
Prior Taxane Use In The Non-Metastatic Setting						0.9943
Yes	13 / 179 (7.3)	3.5 [1.5; NE]	14 / 177 (7.9)	10.4 [0.9; 19.3]	1.1852 [0.5326; 2.6637] 0.6688	
No	10 / 257 (3.9)	8.4 [1.4; NE]	13 / 253 (5.1)	NE [2.1; NE]	1.1849 [0.5048; 2.6991] 0.6782	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3440
1	4 / 65 (6.2)	1.4 [0.7; NE]	7 / 82 (8.5)	10.4 [2.1; NE]	3.3950 [0.8101; 13.4298] 0.0628	
2	13 / 295 (4.4)	8.4 [2.8; NE]	17 / 288 (5.9)	8.4 [2.0; NE]	0.9555 [0.4495; 1.9942] 0.9187	
>=3	6 / 75 (8.0)	4.0 [1.4; NE]	3 / 58 (5.2)	NE [0.8; NE]	1.2439 [0.3258; 5.9288] 0.7659	
ER/PR status I						0.9178
ER+, PR+	10 / 253 (4.0)	8.4 [2.7; NE]	15 / 237 (6.3)	10.4 [3.7; 22.8]	1.2227 [0.5199; 2.7927] 0.6280	
ER+, PR-	13 / 167 (7.8)	2.9 [1.4; NE]	12 / 181 (6.6)	2.6 [0.9; NE]	1.1065 [0.5012; 2.4633] 0.8058	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7676
ER <=10%	2 / 21 (9.5)	3.8 [3.5; NE]	1 / 14 (7.1)	2.1 [NE; NE]	0.0000 [NE; 2.9130] 0.1573	
ER >10%	20 / 364 (5.5)	4.0 [2.1; NE]	21 / 355 (5.9)	12.5 [3.7; NE]	1.3594 [0.7214; 2.5709] 0.3340	
Positive	1 / 51 (2.0)	NE [1.4; NE]	5 / 61 (8.2)	2.6 [0.8; NE]	0.7301 [0.0380; 4.5539] 0.7734	
Endocrine Resistance						0.0608
Primary	12 / 128 (9.4)	2.9 [0.8; 8.4]	11 / 140 (7.9)	19.3 [2.1; NE]	2.3699 [0.9950; 5.8569] 0.0447	
Secondary	11 / 308 (3.6)	NE [2.8; NE]	16 / 288 (5.6)	8.4 [2.1; NE]	0.7515 [0.3385; 1.6084] 0.4713	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.7337
Capecitabine	17 / 266 (6.4)	3.5 [2.1; NE]	22 / 257 (8.6)	4.2 [2.1; 22.8]	1.1726 [0.6094; 2.2243] 0.6223	
Nab-Paclitaxel	4 / 103 (3.9)	NE [0.8; NE]	3 / 105 (2.9)	10.4 [2.0; NE]	1.3571 [0.2624; 9.8563] 0.7249	
Paclitaxel	2 / 67 (3.0)	19.3 [2.1; NE]	2 / 68 (2.9)	NE [0.8; NE]	1.1994 [0.0555; 12.6058] 0.8822	
Prior anthracycline use						0.4477
Yes	16 / 199 (8.0)	2.8 [1.5; 8.4]	16 / 208 (7.7)	8.4 [2.0; 19.3]	1.4984 [0.7180; 3.1757] 0.2754	
No	7 / 237 (3.0)	19.3 [2.9; NE]	11 / 222 (5.0)	NE [2.8; NE]	0.9149 [0.3356; 2.3309] 0.8513	
Liver metastases						0.2106
Yes	18 / 296 (6.1)	4.1 [2.1; NE]	19 / 283 (6.7)	3.7 [1.4; 19.3]	0.9110 [0.4657; 1.7919] 0.7832	
No	5 / 140 (3.6)	4.0 [0.8; NE]	8 / 147 (5.4)	NE [6.2; NE]	1.9519 [0.5883; 5.8688] 0.2335	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.8241
0	17 / 252 (6.7)	3.5 [1.5; NE]	23 / 257 (8.9)	6.2 [2.1; 22.8]	1.2792 [0.6639; 2.4305] 0.4493	
>=1	6 / 179 (3.4)	NE [1.4; NE]	4 / 164 (2.4)	NE [0.8; NE]	1.3791 [0.3929; 5.4077] 0.6011	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Future Perspective						
Age at randomization						0.5045
<65 years of age	70 / 302 (23.2)	10.3 [6.9; 17.2]	77 / 297 (25.9)	7.7 [4.9; 15.2]	0.8865 [0.6398; 1.2260] 0.4677	
>=65 years of age	32 / 134 (23.9)	8.2 [3.5; NE]	42 / 133 (31.6)	3.5 [2.1; 13.8]	0.7361 [0.4610; 1.1643] 0.1924	
Race						0.3966
Asian	50 / 154 (32.5)	14.6 [5.6; NE]	64 / 151 (42.4)	5.6 [3.5; 11.0]	0.7286 [0.4999; 1.0558] 0.0928	
White	46 / 231 (19.9)	7.0 [4.9; 13.8]	49 / 230 (21.3)	7.5 [2.8; NE]	0.9465 [0.6311; 1.4172] 0.7993	
Other	6 / 51 (11.8)	9.0 [1.4; NE]	6 / 49 (12.2)	17.2 [2.0; NE]	1.6474 [0.4946; 5.7337] 0.4054	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4204
Asia	49 / 149 (32.9)	14.6 [5.6; NE]	62 / 147 (42.2)	6.2 [4.1; 11.0]	0.7627 [0.5208; 1.1107] 0.1555	
Europe	39 / 227 (17.2)	8.2 [6.2; NE]	43 / 213 (20.2)	7.5 [2.8; NE]	0.8550 [0.5519; 1.3207] 0.4842	
Rest of the World	14 / 60 (23.3)	6.2 [2.8; 12.4]	14 / 70 (20.0)	17.3 [1.5; NE]	1.2901 [0.6086; 2.7345] 0.4975	
HER2 IHC expression						0.5989
IHC 1+	59 / 239 (24.7)	9.2 [5.6; 17.2]	76 / 234 (32.5)	5.6 [3.5; 10.4]	0.8083 [0.5728; 1.1352] 0.2209	
IHC 2+/ISH-	24 / 117 (20.5)	12.4 [3.6; NE]	29 / 118 (24.6)	7.5 [2.7; 17.2]	0.7855 [0.4534; 1.3484] 0.3829	
IHC >0 <1+	18 / 76 (23.7)	11.8 [4.1; NE]	13 / 76 (17.1)	16.0 [2.1; NE]	1.1766 [0.5793; 2.4568] 0.6446	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6999
Yes	87 / 394 (22.1)	11.1 [6.9; 15.9]	101 / 389 (26.0)	7.5 [4.2; 13.8]	0.8506 [0.6371; 1.1327] 0.2701	
No	15 / 42 (35.7)	4.1 [1.5; NE]	18 / 41 (43.9)	2.2 [1.3; 8.3]	0.7622 [0.3777; 1.5152] 0.4324	
Prior Taxane Use In The Non-Metastatic Setting						0.1416
Yes	43 / 179 (24.0)	7.0 [4.1; 13.8]	46 / 177 (26.0)	7.5 [3.5; NE]	1.0712 [0.7031; 1.6281] 0.7482	
No	59 / 257 (23.0)	12.4 [7.0; NE]	73 / 253 (28.9)	6.9 [3.4; 13.8]	0.7207 [0.5098; 1.0151] 0.0619	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6309
1	13 / 65 (20.0)	8.2 [2.1; NE]	20 / 82 (24.4)	6.9 [2.3; NE]	0.8177 [0.3960; 1.6310] 0.5748	
2	65 / 295 (22.0)	11.3 [6.9; NE]	81 / 288 (28.1)	6.3 [3.1; 17.2]	0.8186 [0.5884; 1.1345] 0.2342	
>=3	24 / 75 (32.0)	7.0 [2.8; 13.8]	17 / 58 (29.3)	9.0 [4.1; 17.3]	1.1328 [0.6115; 2.1456] 0.6917	
ER/PR status I						0.5797
ER+, PR+	62 / 253 (24.5)	9.0 [5.6; 15.9]	69 / 237 (29.1)	6.2 [3.5; 16.0]	0.9018 [0.6383; 1.2712] 0.5525	
ER+, PR-	40 / 167 (24.0)	11.3 [6.2; NE]	47 / 181 (26.0)	7.6 [2.7; 15.2]	0.7647 [0.4989; 1.1672] 0.2177	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7371
ER <=10%	5 / 21 (23.8)	7.0 [2.1; NE]	4 / 14 (28.6)	4.2 [0.7; NE]	0.1792 [0.0238; 0.9680] 0.0373	
ER >10%	81 / 364 (22.3)	11.1 [6.2; NE]	97 / 355 (27.3)	7.6 [3.5; 15.2]	0.8368 [0.6215; 1.1238] 0.2377	
Positive	16 / 51 (31.4)	10.3 [3.6; NE]	18 / 61 (29.5)	7.0 [2.2; NE]	0.8984 [0.4522; 1.7686] 0.7576	
Endocrine Resistance						0.0388
Primary	35 / 128 (27.3)	6.2 [2.2; 11.1]	37 / 140 (26.4)	7.5 [3.4; NE]	1.2761 [0.8007; 2.0296] 0.3026	
Secondary	67 / 308 (21.8)	13.8 [7.6; NE]	81 / 288 (28.1)	6.2 [3.5; 15.2]	0.7097 [0.5119; 0.9808] 0.0385	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.6573
Capecitabine	59 / 266 (22.2)	12.4 [6.2; NE]	68 / 257 (26.5)	10.4 [5.0; 16.0]	0.8381 [0.5896; 1.1875] 0.3211	
Nab-Paclitaxel	29 / 103 (28.2)	7.0 [2.7; NE]	34 / 105 (32.4)	4.2 [2.7; NE]	0.9791 [0.5926; 1.6072] 0.9335	
Paclitaxel	14 / 67 (20.9)	9.2 [2.1; NE]	17 / 68 (25.0)	4.2 [1.4; 7.7]	0.5802 [0.2730; 1.2039] 0.1392	
Prior anthracycline use						0.0309
Yes	49 / 199 (24.6)	7.0 [3.1; 12.4]	53 / 208 (25.5)	9.0 [4.2; NE]	1.1695 [0.7902; 1.7272] 0.4350	
No	53 / 237 (22.4)	12.4 [7.0; NE]	66 / 222 (29.7)	6.2 [2.8; 11.0]	0.6445 [0.4472; 0.9244] 0.0169	
Liver metastases						0.7750
Yes	67 / 296 (22.6)	9.0 [6.2; 13.8]	75 / 283 (26.5)	7.0 [3.4; 15.2]	0.8540 [0.6122; 1.1885] 0.3567	
No	35 / 140 (25.0)	15.5 [4.9; NE]	44 / 147 (29.9)	6.3 [3.5; 17.3]	0.7999 [0.5101; 1.2450] 0.3244	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.8208
0	57 / 252 (22.6)	13.8 [7.6; NE]	67 / 257 (26.1)	10.5 [4.2; 16.0]	0.8370 [0.5856; 1.1914] 0.3237	
>=1	44 / 179 (24.6)	6.9 [4.1; 11.3]	51 / 164 (31.1)	4.2 [2.3; 7.7]	0.7919 [0.5271; 1.1854] 0.2575	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Arm Symptoms						
Age at randomization						0.8046
<65 years of age	114 / 302 (37.7)	6.9 [4.9; 11.0]	122 / 297 (41.1)	4.8 [3.2; 6.2]	0.7721 [0.5961; 0.9990] 0.0496	
>=65 years of age	46 / 134 (34.3)	4.9 [2.2; 10.3]	60 / 133 (45.1)	2.8 [2.2; 3.5]	0.7843 [0.5305; 1.1520] 0.2206	
Race						0.9439
Asian	81 / 154 (52.6)	6.9 [4.2; 13.9]	85 / 151 (56.3)	3.6 [2.7; 5.6]	0.7813 [0.5735; 1.0631] 0.1149	
White	65 / 231 (28.1)	6.3 [4.7; 10.3]	86 / 230 (37.4)	4.1 [2.8; 5.7]	0.7130 [0.5145; 0.9833] 0.0393	
Other	14 / 51 (27.5)	4.9 [1.4; 11.1]	11 / 49 (22.4)	2.1 [0.8; NE]	0.7723 [0.3461; 1.7640] 0.5447	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7835
Asia	79 / 149 (53.0)	6.9 [4.7; 13.9]	83 / 147 (56.5)	4.2 [2.8; 5.6]	0.7739 [0.5658; 1.0572] 0.1060	
Europe	62 / 227 (27.3)	6.4 [4.2; 10.3]	77 / 213 (36.2)	4.1 [2.7; 5.5]	0.6960 [0.4961; 0.9726] 0.0342	
Rest of the World	19 / 60 (31.7)	4.8 [1.4; 16.7]	22 / 70 (31.4)	2.9 [2.0; NE]	0.9453 [0.5035; 1.7573] 0.8587	
HER2 IHC expression						0.7293
IHC 1+	87 / 239 (36.4)	7.0 [4.9; 11.3]	108 / 234 (46.2)	3.4 [2.7; 4.8]	0.6982 [0.5231; 0.9286] 0.0136	
IHC 2+/ISH-	42 / 117 (35.9)	5.6 [2.8; 11.1]	47 / 118 (39.8)	4.8 [2.3; 6.2]	0.8481 [0.5563; 1.2891] 0.4365	
IHC >0 <1+	30 / 76 (39.5)	6.9 [4.7; 15.2]	27 / 76 (35.5)	4.8 [1.4; NE]	0.7839 [0.4650; 1.3281] 0.3654	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2857
Yes	138 / 394 (35.0)	6.3 [4.9; 9.5]	162 / 389 (41.6)	3.4 [2.7; 4.8]	0.7288 [0.5794; 0.9155] 0.0067	
No	22 / 42 (52.4)	7.0 [1.4; 15.1]	20 / 41 (48.8)	6.2 [2.9; 13.1]	0.9831 [0.5283; 1.8341] 0.9450	
Prior Taxane Use In The Non-Metastatic Setting						0.4233
Yes	66 / 179 (36.9)	6.8 [3.5; 13.2]	86 / 177 (48.6)	3.4 [2.1; 4.8]	0.6785 [0.4874; 0.9394] 0.0193	
No	94 / 257 (36.6)	6.3 [4.9; 9.5]	96 / 253 (37.9)	4.2 [2.9; 6.9]	0.8257 [0.6204; 1.0986] 0.1904	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.8636
1	23 / 65 (35.4)	10.3 [2.1; 18.8]	32 / 82 (39.0)	4.9 [2.1; 7.6]	0.7502 [0.4291; 1.2879] 0.2998	
2	105 / 295 (35.6)	6.4 [4.8; 11.0]	120 / 288 (41.7)	3.4 [2.2; 4.3]	0.7433 [0.5700; 0.9677] 0.0281	
>=3	31 / 75 (41.3)	6.8 [3.7; 9.2]	29 / 58 (50.0)	4.9 [2.8; 9.7]	0.8767 [0.5267; 1.4636] 0.6056	
ER/PR status I						0.5633
ER+, PR+	92 / 253 (36.4)	6.6 [4.2; 11.7]	99 / 237 (41.8)	3.4 [2.7; 4.8]	0.7208 [0.5408; 0.9597] 0.0245	
ER+, PR-	67 / 167 (40.1)	6.3 [4.7; 10.3]	78 / 181 (43.1)	4.3 [2.7; 6.2]	0.7935 [0.5695; 1.1018] 0.1674	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3500
ER <=10%	5 / 21 (23.8)	15.9 [4.8; NE]	6 / 14 (42.9)	4.8 [0.7; NE]	0.2903 [0.0817; 0.9874] 0.0359	
ER >10%	135 / 364 (37.1)	5.6 [4.2; 9.2]	148 / 355 (41.7)	3.5 [2.8; 4.9]	0.7852 [0.6200; 0.9934] 0.0434	
Positive	20 / 51 (39.2)	7.0 [2.9; NE]	28 / 61 (45.9)	3.4 [2.1; 18.8]	0.7737 [0.4282; 1.3730] 0.3873	
Endocrine Resistance						0.5467
Primary	49 / 128 (38.3)	6.2 [3.5; 13.9]	64 / 140 (45.7)	2.9 [2.0; 4.9]	0.6876 [0.4689; 1.0011] 0.0520	
Secondary	111 / 308 (36.0)	6.8 [4.9; 9.5]	117 / 288 (40.6)	4.2 [2.9; 5.6]	0.8028 [0.6180; 1.0422] 0.0991	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.8977
Capecitabine	96 / 266 (36.1)	5.6 [4.2; 8.2]	111 / 257 (43.2)	3.4 [2.2; 4.9]	0.7653 [0.5809; 1.0065] 0.0564	
Nab-Paclitaxel	40 / 103 (38.8)	11.7 [4.2; 15.9]	47 / 105 (44.8)	4.9 [3.5; 9.7]	0.7644 [0.4949; 1.1731] 0.2191	
Paclitaxel	24 / 67 (35.8)	6.5 [3.4; 10.3]	24 / 68 (35.3)	3.0 [2.1; 4.9]	0.5870 [0.3266; 1.0525] 0.0693	
Prior anthracycline use						0.2320
Yes	80 / 199 (40.2)	4.9 [2.8; 7.0]	94 / 208 (45.2)	3.6 [2.2; 4.9]	0.8660 [0.6395; 1.1695] 0.3494	
No	80 / 237 (33.8)	9.2 [5.6; 15.1]	88 / 222 (39.6)	3.5 [2.8; 5.9]	0.6864 [0.5056; 0.9305] 0.0151	
Liver metastases						0.6001
Yes	100 / 296 (33.8)	6.8 [4.9; 11.3]	116 / 283 (41.0)	4.2 [2.8; 5.5]	0.7191 [0.5480; 0.9417] 0.0165	
No	60 / 140 (42.9)	5.0 [2.8; 9.5]	66 / 147 (44.9)	3.5 [2.2; 4.9]	0.8324 [0.5853; 1.1822] 0.3057	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.8494
0	87 / 252 (34.5)	6.8 [4.7; 13.9]	109 / 257 (42.4)	4.1 [2.9; 5.5]	0.7439 [0.5590; 0.9868] 0.0402	
>=1	72 / 179 (40.2)	6.4 [4.9; 9.7]	70 / 164 (42.7)	3.5 [2.1; 5.5]	0.7633 [0.5473; 1.0647] 0.1121	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Breast Symptoms						
Age at randomization						0.4588
<65 years of age	60 / 302 (19.9)	31.0 [20.0; NE]	72 / 297 (24.2)	15.9 [10.5; NE]	0.6620 [0.4673; 0.9344] 0.0183	
>=65 years of age	26 / 134 (19.4)	27.6 [11.7; NE]	33 / 133 (24.8)	16.6 [7.6; NE]	0.8244 [0.4885; 1.3767] 0.4617	
Race						0.7639
Asian	42 / 154 (27.3)	31.0 [17.2; NE]	46 / 151 (30.5)	25.6 [13.0; 32.4]	0.7438 [0.4849; 1.1382] 0.1700	
White	39 / 231 (16.9)	20.0 [13.8; NE]	52 / 230 (22.6)	15.9 [9.8; NE]	0.7386 [0.4844; 1.1169] 0.1509	
Other	5 / 51 (9.8)	NE [8.3; NE]	7 / 49 (14.3)	5.6 [4.2; NE]	0.4390 [0.1281; 1.3960] 0.1590	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7376
Asia	43 / 149 (28.9)	27.6 [16.6; NE]	45 / 147 (30.6)	25.6 [13.1; 32.4]	0.7846 [0.5122; 1.2007] 0.2604	
Europe	36 / 227 (15.9)	NE [13.1; NE]	48 / 213 (22.5)	11.2 [7.6; NE]	0.6827 [0.4399; 1.0501] 0.0815	
Rest of the World	7 / 60 (11.7)	NE [13.8; NE]	12 / 70 (17.1)	NE [4.8; NE]	0.5967 [0.2198; 1.4996] 0.2782	
HER2 IHC expression						0.9186
IHC 1+	48 / 239 (20.1)	27.6 [16.6; NE]	62 / 234 (26.5)	15.9 [10.5; NE]	0.6932 [0.4710; 1.0137] 0.0587	
IHC 2+/ISH-	24 / 117 (20.5)	NE [11.9; NE]	29 / 118 (24.6)	12.0 [7.0; NE]	0.7537 [0.4343; 1.2958] 0.3030	
IHC >0 <1+	14 / 76 (18.4)	NE [13.8; NE]	14 / 76 (18.4)	25.6 [9.8; NE]	0.7956 [0.3750; 1.6874] 0.5458	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0346
Yes	70 / 394 (17.8)	31.1 [20.0; NE]	94 / 389 (24.2)	15.9 [11.2; NE]	0.6265 [0.4576; 0.8545] 0.0030	
No	16 / 42 (38.1)	16.6 [4.2; NE]	11 / 41 (26.8)	22.8 [11.0; NE]	1.4149 [0.6499; 3.1748] 0.3844	
Prior Taxane Use In The Non-Metastatic Setting						0.1468
Yes	32 / 179 (17.9)	31.0 [16.6; NE]	48 / 177 (27.1)	13.0 [8.9; NE]	0.5250 [0.3299; 0.8244] 0.0049	
No	54 / 257 (21.0)	27.6 [17.2; NE]	57 / 253 (22.5)	25.6 [12.0; NE]	0.8491 [0.5826; 1.2375] 0.3917	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4416
1	12 / 65 (18.5)	31.0 [11.9; NE]	17 / 82 (20.7)	13.0 [4.9; NE]	0.6123 [0.2773; 1.2971] 0.2035	
2	56 / 295 (19.0)	31.1 [17.2; NE]	75 / 288 (26.0)	15.9 [10.5; NE]	0.6719 [0.4719; 0.9512] 0.0248	
>=3	18 / 75 (24.0)	27.6 [11.7; NE]	13 / 58 (22.4)	25.6 [9.6; NE]	1.0673 [0.5199; 2.2439] 0.8613	
ER/PR status I						0.2343
ER+, PR+	46 / 253 (18.2)	31.0 [31.0; NE]	60 / 237 (25.3)	16.6 [10.4; 25.6]	0.6248 [0.4227; 0.9174] 0.0159	
ER+, PR-	39 / 167 (23.4)	20.0 [14.7; NE]	39 / 181 (21.5)	32.4 [13.0; NE]	0.8876 [0.5627; 1.4011] 0.6062	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.0450
ER <=10%	1 / 21 (4.8)	NE [7.0; NE]	4 / 14 (28.6)	4.7 [2.7; NE]	0.1210 [0.0061; 0.8344] 0.0263	
ER >10%	76 / 364 (20.9)	27.6 [15.9; 31.1]	84 / 355 (23.7)	16.6 [11.7; NE]	0.7994 [0.5843; 1.0927] 0.1585	
Positive	9 / 51 (17.6)	NE [16.6; NE]	17 / 61 (27.9)	NE [4.9; NE]	0.4610 [0.1942; 1.0230] 0.0587	
Endocrine Resistance						0.2965
Primary	24 / 128 (18.8)	31.0 [14.7; NE]	37 / 140 (26.4)	13.0 [8.2; NE]	0.5210 [0.3012; 0.8802] 0.0148	
Secondary	62 / 308 (20.1)	27.6 [17.9; NE]	68 / 288 (23.6)	25.6 [11.7; NE]	0.7797 [0.5507; 1.1019] 0.1566	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.4866
Capecitabine	52 / 266 (19.5)	27.6 [16.6; NE]	65 / 257 (25.3)	16.6 [11.7; NE]	0.6649 [0.4590; 0.9582] 0.0282	
Nab-Paclitaxel	26 / 103 (25.2)	31.0 [12.5; NE]	30 / 105 (28.6)	15.9 [9.6; NE]	0.9420 [0.5503; 1.6038] 0.8244	
Paclitaxel	8 / 67 (11.9)	NE [20.0; NE]	10 / 68 (14.7)	NE [7.4; NE]	0.4632 [0.1671; 1.2150] 0.1138	
Prior anthracycline use						0.1408
Yes	45 / 199 (22.6)	31.0 [13.1; NE]	48 / 208 (23.1)	22.8 [11.2; NE]	0.8764 [0.5802; 1.3214] 0.5272	
No	41 / 237 (17.3)	NE [27.6; NE]	57 / 222 (25.7)	15.9 [10.4; NE]	0.5642 [0.3730; 0.8450] 0.0052	
Liver metastases						0.6001
Yes	56 / 296 (18.9)	31.0 [17.9; NE]	69 / 283 (24.4)	16.6 [11.2; NE]	0.6705 [0.4679; 0.9564] 0.0267	
No	30 / 140 (21.4)	27.6 [16.6; NE]	36 / 147 (24.5)	25.6 [10.5; NE]	0.7572 [0.4627; 1.2301] 0.2600	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.1223
0	45 / 252 (17.9)	31.1 [27.6; NE]	66 / 257 (25.7)	16.6 [10.5; NE]	0.5756 [0.3886; 0.8439] 0.0046	
>=1	40 / 179 (22.3)	31.0 [12.5; NE]	37 / 164 (22.6)	32.4 [9.6; NE]	0.9339 [0.5945; 1.4726] 0.7663	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Systemic Therapy Side Effects						
Age at randomization						0.4968
<65 years of age	142 / 302 (47.0)	2.1 [1.5; 2.8]	129 / 297 (43.4)	2.9 [2.1; 4.9]	1.1299 [0.8904; 1.4354] 0.3199	
>=65 years of age	55 / 134 (41.0)	3.5 [2.1; 4.9]	64 / 133 (48.1)	2.9 [2.1; 4.2]	0.9621 [0.6688; 1.3792] 0.8326	
Race						0.6766
Asian	98 / 154 (63.6)	2.2 [2.1; 3.5]	85 / 151 (56.3)	4.1 [2.7; 6.9]	1.1758 [0.8798; 1.5753] 0.2776	
White	86 / 231 (37.2)	2.8 [1.5; 4.2]	96 / 230 (41.7)	2.7 [2.1; 3.6]	1.0213 [0.7619; 1.3668] 0.8918	
Other	13 / 51 (25.5)	1.6 [1.4; NE]	12 / 49 (24.5)	2.7 [0.8; 4.1]	0.8822 [0.3980; 1.9711] 0.7380	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7793
Asia	97 / 149 (65.1)	2.2 [2.0; 3.5]	85 / 147 (57.8)	3.6 [2.1; 6.9]	1.1551 [0.8636; 1.5483] 0.3331	
Europe	81 / 227 (35.7)	2.8 [1.5; 4.8]	81 / 213 (38.0)	2.7 [2.1; 3.6]	1.0501 [0.7699; 1.4325] 0.7558	
Rest of the World	19 / 60 (31.7)	2.1 [1.3; 11.0]	27 / 70 (38.6)	2.9 [2.1; 5.0]	0.9395 [0.5084; 1.6988] 0.8320	
HER2 IHC expression						0.5350
IHC 1+	104 / 239 (43.5)	2.8 [1.5; 4.1]	112 / 234 (47.9)	3.4 [2.1; 4.9]	1.0215 [0.7813; 1.3345] 0.8777	
IHC 2+/ISH-	55 / 117 (47.0)	2.6 [1.5; 4.1]	47 / 118 (39.8)	3.5 [2.1; 6.4]	1.3164 [0.8903; 1.9551] 0.1692	
IHC >0 <1+	37 / 76 (48.7)	2.4 [1.4; 4.9]	32 / 76 (42.1)	2.7 [1.4; 5.6]	1.0017 [0.6237; 1.6175] 0.9831	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9137
Yes	174 / 394 (44.2)	2.8 [2.1; 3.5]	171 / 389 (44.0)	2.9 [2.2; 4.1]	1.0838 [0.8773; 1.3388] 0.4572	
No	23 / 42 (54.8)	1.7 [1.4; 11.0]	22 / 41 (53.7)	4.1 [2.1; 8.3]	1.0235 [0.5659; 1.8551] 0.9550	
Prior Taxane Use In The Non-Metastatic Setting						0.8193
Yes	83 / 179 (46.4)	2.1 [1.5; 3.5]	87 / 177 (49.2)	2.2 [2.1; 3.5]	1.0550 [0.7799; 1.4258] 0.7336	
No	114 / 257 (44.4)	2.8 [2.1; 4.9]	106 / 253 (41.9)	3.5 [2.3; 5.6]	1.1093 [0.8514; 1.4464] 0.4451	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3330
1	31 / 65 (47.7)	1.5 [1.4; 3.7]	31 / 82 (37.8)	2.9 [1.4; 6.9]	1.2965 [0.7853; 2.1404] 0.3147	
2	127 / 295 (43.1)	2.8 [2.1; 4.1]	135 / 288 (46.9)	2.8 [2.1; 4.1]	0.9792 [0.7677; 1.2482] 0.8591	
>=3	38 / 75 (50.7)	2.9 [1.5; 4.9]	26 / 58 (44.8)	5.0 [2.9; 10.5]	1.3874 [0.8460; 2.3110] 0.1966	
ER/PR status I						0.7333
ER+, PR+	112 / 253 (44.3)	2.8 [2.1; 4.2]	105 / 237 (44.3)	3.4 [2.1; 5.5]	1.0503 [0.8047; 1.3720] 0.7180	
ER+, PR-	83 / 167 (49.7)	2.1 [1.4; 3.4]	82 / 181 (45.3)	2.8 [1.5; 3.6]	1.1286 [0.8308; 1.5327] 0.4438	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1002
ER <=10%	8 / 21 (38.1)	1.5 [1.3; NE]	7 / 14 (50.0)	2.8 [0.7; NE]	0.5791 [0.2042; 1.6794] 0.2902	
ER >10%	161 / 364 (44.2)	2.8 [2.1; 3.7]	155 / 355 (43.7)	2.9 [2.1; 4.1]	1.0601 [0.8501; 1.3225] 0.6050	
Positive	28 / 51 (54.9)	2.1 [1.4; 3.4]	31 / 61 (50.8)	3.4 [2.1; 11.8]	1.5417 [0.9121; 2.6024] 0.1039	
Endocrine Resistance						0.3336
Primary	63 / 128 (49.2)	1.4 [1.4; 2.8]	62 / 140 (44.3)	2.8 [1.5; 4.2]	1.2430 [0.8743; 1.7680] 0.2209	
Secondary	134 / 308 (43.5)	2.8 [2.1; 4.2]	130 / 288 (45.1)	3.4 [2.2; 4.3]	1.0121 [0.7948; 1.2892] 0.9313	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0030
Capecitabine	116 / 266 (43.6)	2.6 [1.6; 3.5]	109 / 257 (42.4)	4.9 [3.4; 7.7]	1.2972 [0.9986; 1.6861] 0.0518	
Nab-Paclitaxel	53 / 103 (51.5)	2.1 [1.4; 3.5]	54 / 105 (51.4)	2.1 [1.4; 3.5]	0.9813 [0.6704; 1.4358] 0.9194	
Paclitaxel	28 / 67 (41.8)	3.7 [1.4; 5.7]	30 / 68 (44.1)	0.9 [0.8; 2.1]	0.4212 [0.2419; 0.7266] 0.0014	
Prior anthracycline use						0.4817
Yes	97 / 199 (48.7)	2.1 [1.4; 2.9]	99 / 208 (47.6)	2.7 [2.1; 3.5]	1.1702 [0.8838; 1.5490] 0.2691	
No	100 / 237 (42.2)	2.8 [2.1; 5.6]	94 / 222 (42.3)	3.6 [2.3; 6.3]	1.0225 [0.7714; 1.3566] 0.8860	
Liver metastases						0.9528
Yes	128 / 296 (43.2)	2.1 [1.5; 2.9]	125 / 283 (44.2)	2.8 [2.1; 4.2]	1.0878 [0.8498; 1.3927] 0.5101	
No	69 / 140 (49.3)	3.5 [2.1; 4.9]	68 / 147 (46.3)	3.5 [2.2; 7.7]	1.0638 [0.7603; 1.4890] 0.7152	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.2547
0	118 / 252 (46.8)	2.1 [1.5; 2.8]	117 / 257 (45.5)	3.4 [2.1; 4.9]	1.1854 [0.9176; 1.5317] 0.1923	
>=1	78 / 179 (43.6)	3.4 [2.1; 4.9]	73 / 164 (44.5)	2.7 [2.1; 3.5]	0.9338 [0.6781; 1.2878] 0.6666	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Endocrine Therapy Symptoms						
Age at randomization						0.1757
<65 years of age	102 / 302 (33.8)	11.1 [8.9; 14.5]	105 / 297 (35.4)	6.9 [4.9; 9.9]	0.7781 [0.5908; 1.0243] 0.0729	
>=65 years of age	36 / 134 (26.9)	13.3 [5.5; NE]	56 / 133 (42.1)	4.2 [2.9; 6.4]	0.5663 [0.3655; 0.8646] 0.0082	
Race						0.5168
Asian	65 / 154 (42.2)	14.6 [9.0; 26.3]	71 / 151 (47.0)	6.9 [4.2; 11.0]	0.6952 [0.4919; 0.9799] 0.0371	
White	62 / 231 (26.8)	9.7 [6.9; 13.1]	78 / 230 (33.9)	5.6 [4.2; 7.0]	0.7578 [0.5407; 1.0576] 0.1028	
Other	11 / 51 (21.6)	13.3 [2.1; NE]	12 / 49 (24.5)	2.1 [0.8; 9.1]	0.4118 [0.1596; 1.0068] 0.0475	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2157
Asia	63 / 149 (42.3)	14.6 [9.7; 26.3]	70 / 147 (47.6)	6.9 [4.2; 11.0]	0.6664 [0.4694; 0.9433] 0.0215	
Europe	56 / 227 (24.7)	10.3 [6.9; 15.9]	72 / 213 (33.8)	5.6 [3.6; 6.9]	0.6519 [0.4573; 0.9245] 0.0162	
Rest of the World	19 / 60 (31.7)	6.9 [2.1; 11.0]	19 / 70 (27.1)	5.0 [3.4; NE]	1.2291 [0.6448; 2.3422] 0.5265	
HER2 IHC expression						0.1333
IHC 1+	73 / 239 (30.5)	11.9 [9.0; 20.0]	98 / 234 (41.9)	4.9 [3.6; 7.0]	0.5773 [0.4221; 0.7856] 0.0004	
IHC 2+/ISH-	37 / 117 (31.6)	9.7 [4.9; NE]	40 / 118 (33.9)	6.2 [3.5; 8.4]	0.8054 [0.5115; 1.2650] 0.3377	
IHC >0 <1+	27 / 76 (35.5)	11.0 [3.4; NE]	22 / 76 (28.9)	13.1 [4.1; 19.4]	1.0994 [0.6270; 1.9498] 0.7372	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9095
Yes	119 / 394 (30.2)	11.7 [9.0; 14.6]	141 / 389 (36.2)	6.2 [4.9; 8.4]	0.6950 [0.5428; 0.8884] 0.0036	
No	19 / 42 (45.2)	9.7 [1.4; 20.0]	20 / 41 (48.8)	4.8 [2.7; 8.9]	0.8236 [0.4316; 1.5646] 0.5364	
Prior Taxane Use In The Non-Metastatic Setting						0.6663
Yes	53 / 179 (29.6)	13.3 [6.9; 20.0]	68 / 177 (38.4)	5.6 [3.5; 8.9]	0.6752 [0.4669; 0.9706] 0.0332	
No	85 / 257 (33.1)	11.0 [7.8; 15.9]	93 / 253 (36.8)	6.0 [4.8; 9.1]	0.7371 [0.5474; 0.9911] 0.0436	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.9341
1	22 / 65 (33.8)	13.3 [6.2; 20.0]	26 / 82 (31.7)	7.6 [3.4; 9.9]	0.7772 [0.4287; 1.3913] 0.3938	
2	92 / 295 (31.2)	11.0 [6.9; 14.6]	110 / 288 (38.2)	5.6 [4.2; 8.4]	0.7089 [0.5353; 0.9366] 0.0153	
>=3	24 / 75 (32.0)	13.9 [5.6; NE]	24 / 58 (41.4)	5.0 [3.5; 19.4]	0.6723 [0.3766; 1.1974] 0.1700	
ER/PR status I						0.4329
ER+, PR+	77 / 253 (30.4)	13.3 [9.0; 20.0]	89 / 237 (37.6)	6.2 [4.9; 8.4]	0.6469 [0.4750; 0.8790] 0.0051	
ER+, PR-	61 / 167 (36.5)	9.6 [5.0; 13.7]	68 / 181 (37.6)	4.2 [3.4; 9.0]	0.7912 [0.5531; 1.1269] 0.1920	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2852
ER <=10%	5 / 21 (23.8)	27.6 [5.6; NE]	5 / 14 (35.7)	2.8 [1.4; NE]	0.3215 [0.0773; 1.2481] 0.0862	
ER >10%	119 / 364 (32.7)	11.0 [6.9; 13.9]	131 / 355 (36.9)	5.7 [4.8; 8.3]	0.7619 [0.5926; 0.9786] 0.0327	
Positive	14 / 51 (27.5)	15.9 [9.7; NE]	25 / 61 (41.0)	4.9 [2.2; NE]	0.5454 [0.2750; 1.0388] 0.0675	
Endocrine Resistance						0.5633
Primary	42 / 128 (32.8)	11.9 [6.9; 19.4]	53 / 140 (37.9)	5.6 [3.7; 9.0]	0.5999 [0.3935; 0.9073] 0.0152	
Secondary	96 / 308 (31.2)	10.3 [6.9; 20.0]	107 / 288 (37.2)	6.2 [4.9; 9.1]	0.7547 [0.5712; 0.9959] 0.0461	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.7177
Capecitabine	81 / 266 (30.5)	11.8 [6.9; 15.9]	95 / 257 (37.0)	6.2 [4.9; 9.1]	0.7607 [0.5641; 1.0242] 0.0719	
Nab-Paclitaxel	37 / 103 (35.9)	11.0 [3.5; 27.6]	45 / 105 (42.9)	5.6 [3.4; 9.9]	0.6955 [0.4420; 1.0856] 0.1082	
Paclitaxel	20 / 67 (29.9)	11.9 [8.3; 20.0]	21 / 68 (30.9)	4.8 [2.8; 9.8]	0.4697 [0.2442; 0.8941] 0.0187	
Prior anthracycline use						0.2811
Yes	58 / 199 (29.1)	13.9 [8.9; 20.0]	80 / 208 (38.5)	5.0 [3.7; 7.6]	0.6220 [0.4388; 0.8758] 0.0064	
No	80 / 237 (33.8)	9.8 [6.9; 13.7]	81 / 222 (36.5)	6.4 [4.8; 10.5]	0.7942 [0.5818; 1.0840] 0.1472	
Liver metastases						0.8918
Yes	94 / 296 (31.8)	11.1 [6.9; 13.9]	103 / 283 (36.4)	5.0 [3.6; 7.6]	0.7067 [0.5317; 0.9382] 0.0163	
No	44 / 140 (31.4)	15.9 [6.9; NE]	58 / 147 (39.5)	6.3 [4.8; 9.8]	0.7089 [0.4763; 1.0478] 0.0822	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.7331
0	77 / 252 (30.6)	13.1 [8.2; 15.9]	101 / 257 (39.3)	6.0 [4.1; 9.8]	0.6713 [0.4964; 0.9042] 0.0086	
>=1	60 / 179 (33.5)	9.8 [6.2; 20.0]	57 / 164 (34.8)	5.6 [4.2; 8.9]	0.7491 [0.5188; 1.0823] 0.1228	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Skin Mucosis Symptoms						
Age at randomization						0.5103
<65 years of age	126 / 302 (41.7)	6.9 [4.9; 9.6]	153 / 297 (51.5)	2.1 [1.5; 2.2]	0.5058 [0.3964; 0.6441] <.0001	
>=65 years of age	54 / 134 (40.3)	4.1 [2.4; 5.6]	74 / 133 (55.6)	1.5 [1.4; 2.2]	0.5877 [0.4106; 0.8360] 0.0031	
Race						0.9665
Asian	90 / 154 (58.4)	7.7 [5.6; 11.1]	98 / 151 (64.9)	2.2 [1.5; 2.8]	0.5347 [0.3981; 0.7171] <.0001	
White	77 / 231 (33.3)	4.7 [2.8; 6.2]	115 / 230 (50.0)	1.5 [1.4; 2.1]	0.5308 [0.3941; 0.7104] <.0001	
Other	13 / 51 (25.5)	4.2 [2.1; 9.1]	14 / 49 (28.6)	2.1 [0.8; 2.8]	0.3778 [0.1593; 0.8632] 0.0194	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7746
Asia	89 / 149 (59.7)	7.7 [5.6; 11.1]	96 / 147 (65.3)	2.2 [1.5; 2.8]	0.5386 [0.4002; 0.7240] <.0001	
Europe	73 / 227 (32.2)	3.9 [2.2; 5.6]	102 / 213 (47.9)	1.7 [1.5; 2.1]	0.5449 [0.3995; 0.7395] 0.0001	
Rest of the World	18 / 60 (30.0)	6.2 [3.0; 9.7]	29 / 70 (41.4)	1.5 [1.3; 2.2]	0.4283 [0.2311; 0.7729] 0.0043	
HER2 IHC expression						0.3437
IHC 1+	98 / 239 (41.0)	5.6 [3.9; 9.7]	125 / 234 (53.4)	2.1 [1.7; 2.8]	0.5938 [0.4527; 0.7765] 0.0001	
IHC 2+/ISH-	47 / 117 (40.2)	6.2 [2.8; 8.3]	64 / 118 (54.2)	2.0 [1.4; 2.7]	0.4472 [0.3014; 0.6586] <.0001	
IHC >0 <1+	34 / 76 (44.7)	6.2 [3.4; 9.1]	37 / 76 (48.7)	1.4 [1.3; 2.1]	0.4063 [0.2501; 0.6570] 0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3238
Yes	158 / 394 (40.1)	5.6 [4.2; 7.7]	204 / 389 (52.4)	2.0 [1.5; 2.1]	0.5103 [0.4124; 0.6303] <.0001	
No	22 / 42 (52.4)	9.0 [2.1; 13.9]	23 / 41 (56.1)	2.9 [1.5; 5.5]	0.6432 [0.3450; 1.1893] 0.1500	
Prior Taxane Use In The Non-Metastatic Setting						0.5645
Yes	77 / 179 (43.0)	4.1 [2.8; 9.6]	100 / 177 (56.5)	2.1 [1.5; 2.8]	0.5722 [0.4196; 0.7767] 0.0003	
No	103 / 257 (40.1)	6.2 [4.9; 8.3]	127 / 253 (50.2)	1.7 [1.5; 2.1]	0.5039 [0.3861; 0.6560] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.2575
1	27 / 65 (41.5)	4.8 [1.6; 10.3]	43 / 82 (52.4)	1.5 [1.4; 2.7]	0.4006 [0.2362; 0.6636] 0.0003	
2	112 / 295 (38.0)	6.2 [4.2; 9.6]	145 / 288 (50.3)	2.0 [1.5; 2.1]	0.5155 [0.3999; 0.6628] <.0001	
>=3	41 / 75 (54.7)	4.8 [2.1; 8.3]	38 / 58 (65.5)	2.1 [1.4; 2.9]	0.7031 [0.4494; 1.1025] 0.1204	
ER/PR status I						0.2232
ER+, PR+	105 / 253 (41.5)	6.2 [4.2; 9.0]	116 / 237 (48.9)	2.1 [1.5; 2.7]	0.5913 [0.4517; 0.7730] 0.0001	
ER+, PR-	74 / 167 (44.3)	5.6 [3.4; 7.7]	103 / 181 (56.9)	1.5 [1.4; 2.1]	0.4525 [0.3300; 0.6168] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.0865
ER <=10%	5 / 21 (23.8)	NE [1.4; NE]	8 / 14 (57.1)	2.2 [1.0; 5.5]	0.2977 [0.0878; 0.9151] 0.0280	
ER >10%	152 / 364 (41.8)	4.9 [3.6; 6.9]	181 / 355 (51.0)	2.1 [1.5; 2.3]	0.5822 [0.4670; 0.7248] <.0001	
Positive	23 / 51 (45.1)	11.1 [4.8; 13.9]	38 / 61 (62.3)	1.5 [1.4; 2.1]	0.3944 [0.2279; 0.6680] 0.0005	
Endocrine Resistance						0.9319
Primary	56 / 128 (43.8)	4.8 [3.4; 8.9]	75 / 140 (53.6)	2.1 [1.4; 2.7]	0.5091 [0.3549; 0.7256] 0.0002	
Secondary	124 / 308 (40.3)	6.2 [4.2; 8.3]	151 / 288 (52.4)	2.0 [1.5; 2.1]	0.5322 [0.4172; 0.6776] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0624
Capecitabine	109 / 266 (41.0)	5.6 [4.1; 7.9]	147 / 257 (57.2)	1.5 [1.4; 1.7]	0.4365 [0.3376; 0.5626] <.0001	
Nab-Paclitaxel	44 / 103 (42.7)	5.6 [2.8; 14.5]	50 / 105 (47.6)	3.5 [2.7; 5.5]	0.7549 [0.4947; 1.1449] 0.1838	
Paclitaxel	27 / 67 (40.3)	6.2 [3.0; 8.9]	30 / 68 (44.1)	2.1 [1.0; 2.8]	0.4352 [0.2480; 0.7563] 0.0025	
Prior anthracycline use						0.0959
Yes	87 / 199 (43.7)	3.9 [2.8; 6.8]	113 / 208 (54.3)	2.1 [2.0; 2.8]	0.6432 [0.4818; 0.8549] 0.0023	
No	93 / 237 (39.2)	6.9 [5.6; 8.9]	114 / 222 (51.4)	1.5 [1.4; 2.1]	0.4529 [0.3418; 0.5985] <.0001	
Liver metastases						0.0326
Yes	111 / 296 (37.5)	6.2 [4.3; 8.9]	151 / 283 (53.4)	1.7 [1.5; 2.1]	0.4282 [0.3314; 0.5513] <.0001	
No	69 / 140 (49.3)	4.9 [2.8; 8.2]	76 / 147 (51.7)	2.2 [1.5; 3.4]	0.7170 [0.5148; 0.9969] 0.0469	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0810
0	103 / 252 (40.9)	6.2 [4.7; 9.0]	141 / 257 (54.9)	1.5 [1.4; 2.1]	0.4647 [0.3569; 0.6030] <.0001	
>=1	76 / 179 (42.5)	5.6 [3.4; 7.7]	81 / 164 (49.4)	2.3 [2.1; 3.4]	0.6405 [0.4660; 0.8793] 0.0055	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Endocrine Sexual Symptoms						
Age at randomization						0.1414
<65 years of age	122 / 302 (40.4)	4.1 [2.9; 7.0]	104 / 297 (35.0)	5.6 [3.7; 7.7]	1.1263 [0.8667; 1.4672] 0.3776	
>=65 years of age	46 / 134 (34.3)	4.2 [2.8; 11.0]	38 / 133 (28.6)	15.9 [6.3; 20.1]	1.6250 [1.0575; 2.5117] 0.0262	
Race						0.7022
Asian	74 / 154 (48.1)	7.1 [2.8; 17.2]	66 / 151 (43.7)	8.3 [4.9; 15.9]	1.1331 [0.8122; 1.5842] 0.4724	
White	81 / 231 (35.1)	3.6 [2.8; 5.5]	68 / 230 (29.6)	6.4 [3.5; 15.9]	1.3749 [0.9964; 1.9030] 0.0525	
Other	13 / 51 (25.5)	4.2 [1.4; NE]	8 / 49 (16.3)	2.8 [0.8; NE]	1.1436 [0.4786; 2.9066] 0.7367	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7562
Asia	74 / 149 (49.7)	4.9 [2.8; 17.2]	64 / 147 (43.5)	8.3 [4.9; 15.9]	1.1831 [0.8463; 1.6590] 0.3332	
Europe	71 / 227 (31.3)	4.8 [3.5; 9.0]	55 / 213 (25.8)	9.1 [3.7; 19.3]	1.2819 [0.9023; 1.8307] 0.1647	
Rest of the World	23 / 60 (38.3)	1.5 [0.8; 2.8]	23 / 70 (32.9)	2.2 [1.4; 6.9]	1.5325 [0.8553; 2.7459] 0.1435	
HER2 IHC expression						0.7725
IHC 1+	95 / 239 (39.7)	4.2 [2.8; 7.6]	79 / 234 (33.8)	6.9 [5.0; 13.8]	1.3430 [0.9954; 1.8155] 0.0537	
IHC 2+/ISH-	43 / 117 (36.8)	3.5 [2.1; 10.3]	39 / 118 (33.1)	7.4 [2.2; NE]	1.1289 [0.7313; 1.7482] 0.5867	
IHC >0 <1+	30 / 76 (39.5)	4.2 [2.1; 11.7]	22 / 76 (28.9)	6.2 [2.2; NE]	1.2110 [0.7014; 2.1236] 0.5119	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4749
Yes	145 / 394 (36.8)	4.2 [3.5; 7.1]	124 / 389 (31.9)	7.7 [5.1; 13.8]	1.2107 [0.9526; 1.5416] 0.1182	
No	23 / 42 (54.8)	1.5 [0.8; 10.3]	18 / 41 (43.9)	4.9 [2.1; NE]	1.5013 [0.8112; 2.8217] 0.2002	
Prior Taxane Use In The Non-Metastatic Setting						0.3901
Yes	63 / 179 (35.2)	4.1 [2.8; 13.1]	60 / 177 (33.9)	6.4 [4.1; NE]	1.1243 [0.7875; 1.6061] 0.5219	
No	105 / 257 (40.9)	4.2 [2.9; 7.0]	82 / 253 (32.4)	6.9 [4.9; 15.9]	1.3429 [1.0069; 1.7972] 0.0451	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6992
1	21 / 65 (32.3)	4.8 [1.5; NE]	22 / 82 (26.8)	6.9 [2.7; NE]	1.0289 [0.5605; 1.8830] 0.9315	
2	112 / 295 (38.0)	4.1 [2.9; 7.6]	96 / 288 (33.3)	7.7 [5.5; 15.9]	1.2923 [0.9837; 1.6998] 0.0656	
>=3	34 / 75 (45.3)	4.1 [2.1; 10.2]	24 / 58 (41.4)	4.9 [2.9; NE]	1.3041 [0.7763; 2.2251] 0.3174	
ER/PR status I						0.6924
ER+, PR+	101 / 253 (39.9)	4.3 [3.5; 8.3]	75 / 237 (31.6)	8.3 [4.1; 20.1]	1.2747 [0.9466; 1.7241] 0.1096	
ER+, PR-	65 / 167 (38.9)	3.5 [2.1; 9.0]	64 / 181 (35.4)	6.9 [4.9; 13.7]	1.1571 [0.8170; 1.6390] 0.4157	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2948
ER <=10%	7 / 21 (33.3)	5.7 [1.3; NE]	5 / 14 (35.7)	2.2 [0.7; NE]	0.9954 [0.3153; 3.3855] 0.9891	
ER >10%	141 / 364 (38.7)	3.6 [2.8; 5.0]	111 / 355 (31.3)	7.7 [5.1; 15.9]	1.3617 [1.0620; 1.7502] 0.0150	
Positive	20 / 51 (39.2)	9.0 [2.8; NE]	26 / 61 (42.6)	6.2 [2.2; 19.3]	0.8519 [0.4685; 1.5263] 0.5893	
Endocrine Resistance						0.4094
Primary	48 / 128 (37.5)	3.6 [2.8; 9.0]	40 / 140 (28.6)	9.1 [4.9; NE]	1.4545 [0.9567; 2.2232] 0.0785	
Secondary	120 / 308 (39.0)	4.3 [2.9; 7.6]	102 / 288 (35.4)	5.7 [3.7; 13.7]	1.1622 [0.8927; 1.5168] 0.2659	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1456
Capecitabine	96 / 266 (36.1)	4.9 [3.5; 11.0]	91 / 257 (35.4)	6.2 [4.9; 11.9]	1.0835 [0.8128; 1.4452] 0.5885	
Nab-Paclitaxel	48 / 103 (46.6)	2.9 [1.5; 5.5]	33 / 105 (31.4)	15.9 [4.9; NE]	1.8014 [1.1583; 2.8352] 0.0086	
Paclitaxel	24 / 67 (35.8)	4.2 [2.1; 10.3]	18 / 68 (26.5)	4.2 [2.1; NE]	1.0687 [0.5761; 2.0135] 0.8393	
Prior anthracycline use						0.7629
Yes	73 / 199 (36.7)	3.6 [2.8; 9.0]	68 / 208 (32.7)	6.2 [3.5; 20.1]	1.2060 [0.8657; 1.6822] 0.2708	
No	95 / 237 (40.1)	4.3 [2.9; 7.1]	74 / 222 (33.3)	7.4 [5.0; 13.8]	1.2854 [0.9494; 1.7470] 0.1045	
Liver metastases						0.5016
Yes	109 / 296 (36.8)	4.1 [2.9; 5.7]	94 / 283 (33.2)	6.3 [3.7; 13.7]	1.1839 [0.8984; 1.5637] 0.2281	
No	59 / 140 (42.1)	4.2 [2.1; 10.3]	48 / 147 (32.7)	9.6 [5.5; 15.9]	1.3560 [0.9269; 1.9938] 0.1209	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.1378
0	92 / 252 (36.5)	4.3 [3.0; 10.3]	90 / 257 (35.0)	6.2 [4.2; 11.9]	1.1022 [0.8230; 1.4762] 0.5137	
>=1	75 / 179 (41.9)	3.6 [2.8; 5.5]	48 / 164 (29.3)	9.6 [5.5; NE]	1.5367 [1.0725; 2.2230] 0.0195	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Upset by Hair Loss						
Age at randomization						0.7373
<65 years of age	37 / 302 (12.3)	1.4 [0.9; 3.0]	27 / 297 (9.1)	2.1 [1.3; 6.9]	1.2586 [0.7687; 2.0874] 0.3618	
>=65 years of age	12 / 134 (9.0)	2.1 [1.3; 19.3]	17 / 133 (12.8)	2.9 [0.8; NE]	0.9948 [0.4518; 2.1011] 0.9967	
Race						0.4117
Asian	32 / 154 (20.8)	1.4 [1.3; 2.1]	25 / 151 (16.6)	2.1 [1.3; 10.3]	1.4710 [0.8717; 2.5099] 0.1470	
White	15 / 231 (6.5)	2.9 [0.8; NE]	17 / 230 (7.4)	2.8 [0.8; 7.0]	0.8617 [0.4233; 1.7357] 0.6674	
Other	2 / 51 (3.9)	6.3 [0.7; NE]	2 / 49 (4.1)	1.4 [0.8; NE]	0.5688 [0.0263; 5.9905] 0.6419	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4801
Asia	32 / 149 (21.5)	1.4 [1.3; 2.1]	25 / 147 (17.0)	2.1 [1.3; 10.3]	1.4390 [0.8527; 2.4560] 0.1716	
Europe	12 / 227 (5.3)	4.1 [0.8; NE]	13 / 213 (6.1)	2.8 [0.8; 12.4]	0.8134 [0.3614; 1.8141] 0.5891	
Rest of the World	5 / 60 (8.3)	1.9 [0.7; NE]	6 / 70 (8.6)	1.8 [0.6; NE]	1.0389 [0.2963; 3.4854] 0.9767	
HER2 IHC expression						0.1587
IHC 1+	31 / 239 (13.0)	1.4 [0.8; 2.1]	30 / 234 (12.8)	1.4 [0.8; 2.2]	1.0593 [0.6362; 1.7637] 0.8337	
IHC 2+/ISH-	7 / 117 (6.0)	1.5 [0.8; NE]	11 / 118 (9.3)	2.8 [0.8; NE]	1.0707 [0.3935; 2.7225] 0.8800	
IHC >0 <1+	11 / 76 (14.5)	2.2 [1.4; NE]	3 / 76 (3.9)	NE [0.8; NE]	4.3952 [1.2805; 20.6393] 0.0220	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.7092
Yes	41 / 394 (10.4)	1.5 [1.3; 2.8]	38 / 389 (9.8)	2.2 [1.3; 7.0]	1.1840 [0.7606; 1.8468] 0.4566	
No	8 / 42 (19.0)	1.5 [0.7; 3.4]	6 / 41 (14.6)	1.8 [0.8; NE]	1.2670 [0.4187; 3.9548] 0.6696	
Prior Taxane Use In The Non-Metastatic Setting						0.4660
Yes	20 / 179 (11.2)	1.4 [0.8; 4.4]	19 / 177 (10.7)	2.8 [1.3; NE]	1.4177 [0.7451; 2.6973] 0.2794	
No	29 / 257 (11.3)	1.5 [1.3; 3.0]	25 / 253 (9.9)	1.5 [0.8; 7.0]	1.0573 [0.6185; 1.8208] 0.8251	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.7660
1	6 / 65 (9.2)	1.1 [0.7; NE]	9 / 82 (11.0)	2.1 [0.8; 2.8]	0.7496 [0.2230; 2.2356] 0.5684	
2	35 / 295 (11.9)	1.5 [1.3; 3.0]	27 / 288 (9.4)	2.9 [1.3; 10.3]	1.2266 [0.7410; 2.0507] 0.4372	
>=3	8 / 75 (10.7)	1.5 [0.1; 6.3]	8 / 58 (13.8)	2.1 [0.8; NE]	1.4312 [0.5251; 3.9012] 0.4636	
ER/PR status I						0.5176
ER+, PR+	28 / 253 (11.1)	1.8 [1.3; 3.4]	24 / 237 (10.1)	2.1 [0.8; 7.0]	1.0752 [0.6221; 1.8725] 0.7825	
ER+, PR-	21 / 167 (12.6)	1.4 [0.8; 3.4]	19 / 181 (10.5)	2.9 [1.3; NE]	1.3647 [0.7320; 2.5605] 0.3198	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4949
ER <=10%	2 / 21 (9.5)	3.0 [0.7; NE]	1 / 14 (7.1)	1.3 [NE; NE]	0.5774 [0.0227; 14.6561] 0.6949	
ER >10%	41 / 364 (11.3)	1.5 [1.3; 3.4]	34 / 355 (9.6)	2.2 [1.3; 6.9]	1.1602 [0.7363; 1.8400] 0.5227	
Positive	6 / 51 (11.8)	1.3 [0.7; 2.2]	9 / 61 (14.8)	1.8 [0.8; NE]	1.8138 [0.6051; 5.0595] 0.2460	
Endocrine Resistance						0.4044
Primary	19 / 128 (14.8)	1.1 [0.7; 2.2]	15 / 140 (10.7)	2.1 [0.8; 2.9]	1.5439 [0.7841; 3.0946] 0.2187	
Secondary	30 / 308 (9.7)	2.1 [1.4; 3.4]	29 / 288 (10.1)	2.9 [1.3; 10.3]	1.0583 [0.6324; 1.7730] 0.8287	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0398
Capecitabine	29 / 266 (10.9)	2.2 [1.4; 4.1]	22 / 257 (8.6)	3.4 [2.1; NE]	1.3202 [0.7603; 2.3249] 0.3253	
Nab-Paclitaxel	15 / 103 (14.6)	1.4 [0.8; 2.2]	19 / 105 (18.1)	1.3 [0.8; 2.8]	0.8734 [0.4288; 1.7364] 0.7170	
Paclitaxel	5 / 67 (7.5)	0.8 [0.7; NE]	3 / 68 (4.4)	NE [0.8; NE]	3.5091 [0.8441; 17.3968] 0.0609	
Prior anthracycline use						0.7309
Yes	18 / 199 (9.0)	1.5 [0.8; 6.3]	19 / 208 (9.1)	2.1 [1.3; 2.9]	1.1219 [0.5752; 2.1700] 0.7342	
No	31 / 237 (13.1)	1.5 [1.3; 2.8]	25 / 222 (11.3)	2.2 [1.3; 10.3]	1.3010 [0.7670; 2.2291] 0.3191	
Liver metastases						0.7157
Yes	36 / 296 (12.2)	1.5 [1.4; 3.4]	27 / 283 (9.5)	2.9 [1.4; 10.3]	1.2227 [0.7444; 2.0324] 0.4297	
No	13 / 140 (9.3)	1.3 [0.7; 2.1]	17 / 147 (11.6)	1.5 [0.8; 12.4]	1.3828 [0.6569; 2.8433] 0.3578	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.12.10 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.7108
0	28 / 252 (11.1)	2.1 [1.4; 4.1]	25 / 257 (9.7)	2.9 [1.3; 10.3]	1.1270 [0.6562; 1.9468] 0.6662	
>=1	21 / 179 (11.7)	1.4 [0.7; 2.2]	17 / 164 (10.4)	1.5 [0.8; 6.9]	1.2970 [0.6782; 2.5077] 0.4430	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 16:29; Program name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: T.2.12.10_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.12.11 EORTC-QLQ-BR45 – Zeit bis zur erstmaligen Verschlechterung – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.12.11 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Body Image						
Region						0.0147
Asia	89 / 149 (59.7)	2.8 [2.1; 4.9]	75 / 147 (51.0)	4.3 [3.2; 6.9]	1.1772 [0.8644; 1.6076] 0.3019	
Europe	70 / 227 (30.8)	4.8 [2.8; 7.9]	80 / 213 (37.6)	2.9 [2.2; 4.3]	0.7457 [0.5389; 1.0294] 0.0715	
Rest of the World	22 / 60 (36.7)	2.8 [1.5; 4.9]	16 / 70 (22.9)	15.8 [2.1; NE]	1.9856 [1.0468; 3.8502] 0.0326	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 16:42; Program name: T.2.12.11_EORTC_BR45_TTFDet_FAS_SUB_SIG.sas; Output name: T.2.12.11_EORTC_BR45_TTFDet_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.12.11 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Sexual Functioning						
ER/PR status I						0.0495
ER+, PR+	31 / 253 (12.3)	1.4 [1.3; 2.1]	40 / 237 (16.9)	1.5 [0.8; 4.2]	1.6777 [1.0184; 2.7575] 0.0352	
ER+, PR-	27 / 167 (16.2)	1.6 [0.8; 3.5]	33 / 181 (18.2)	0.8 [0.8; 1.5]	0.8046 [0.4795; 1.3387] 0.4165	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 04SEP2024 16:42; Program name: T.2.12.11_EORTC_BR45_TTFDet_FAS_SUB_SIG.sas; Output name: T.2.12.11_EORTC_BR45_TTFDet_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.12.11 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Functional Scales/Future Perspective						
Endocrine Resistance						0.0388
Primary	35 / 128 (27.3)	6.2 [2.2; 11.1]	37 / 140 (26.4)	7.5 [3.4; NE]	1.2761 [0.8007; 2.0296] 0.3026	
Secondary	67 / 308 (21.8)	13.8 [7.6; NE]	81 / 288 (28.1)	6.2 [3.5; 15.2]	0.7097 [0.5119; 0.9808] 0.0385	
Prior anthracycline use						0.0309
Yes	49 / 199 (24.6)	7.0 [3.1; 12.4]	53 / 208 (25.5)	9.0 [4.2; NE]	1.1695 [0.7902; 1.7272] 0.4350	
No	53 / 237 (22.4)	12.4 [7.0; NE]	66 / 222 (29.7)	6.2 [2.8; 11.0]	0.6445 [0.4472; 0.9244] 0.0169	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.12.11 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Breast Symptoms						
Prior CDK4/6 inhibitor use						0.0346
Yes	70 / 394 (17.8)	31.1 [20.0; NE]	94 / 389 (24.2)	15.9 [11.2; NE]	0.6265 [0.4576; 0.8545] 0.0030	
No	16 / 42 (38.1)	16.6 [4.2; NE]	11 / 41 (26.8)	22.8 [11.0; NE]	1.4149 [0.6499; 3.1748] 0.3844	
ER/PR status II						0.0450
ER <=10%	1 / 21 (4.8)	NE [7.0; NE]	4 / 14 (28.6)	4.7 [2.7; NE]	0.1210 [0.0061; 0.8344] 0.0263	
ER >10%	76 / 364 (20.9)	27.6 [15.9; 31.1]	84 / 355 (23.7)	16.6 [11.7; NE]	0.7994 [0.5843; 1.0927] 0.1585	
Positive	9 / 51 (17.6)	NE [16.6; NE]	17 / 61 (27.9)	NE [4.9; NE]	0.4610 [0.1942; 1.0230] 0.0587	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.11 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Systemic Therapy Side Effects						
T-DXd vs. each Investigator's choice chemotherapy						0.0030
Capecitabine	116 / 266 (43.6)	2.6 [1.6; 3.5]	109 / 257 (42.4)	4.9 [3.4; 7.7]	1.2972 [0.9986; 1.6861] 0.0518	
Nab-Paclitaxel	53 / 103 (51.5)	2.1 [1.4; 3.5]	54 / 105 (51.4)	2.1 [1.4; 3.5]	0.9813 [0.6704; 1.4358] 0.9194	
Paclitaxel	28 / 67 (41.8)	3.7 [1.4; 5.7]	30 / 68 (44.1)	0.9 [0.8; 2.1]	0.4212 [0.2419; 0.7266] 0.0014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.12.11 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Skin Mucosis Symptoms						
Liver metastases						0.0326
Yes	111 / 296 (37.5)	6.2 [4.3; 8.9]	151 / 283 (53.4)	1.7 [1.5; 2.1]	0.4282 [0.3314; 0.5513] <.0001	
No	69 / 140 (49.3)	4.9 [2.8; 8.2]	76 / 147 (51.7)	2.2 [1.5; 3.4]	0.7170 [0.5148; 0.9969] 0.0469	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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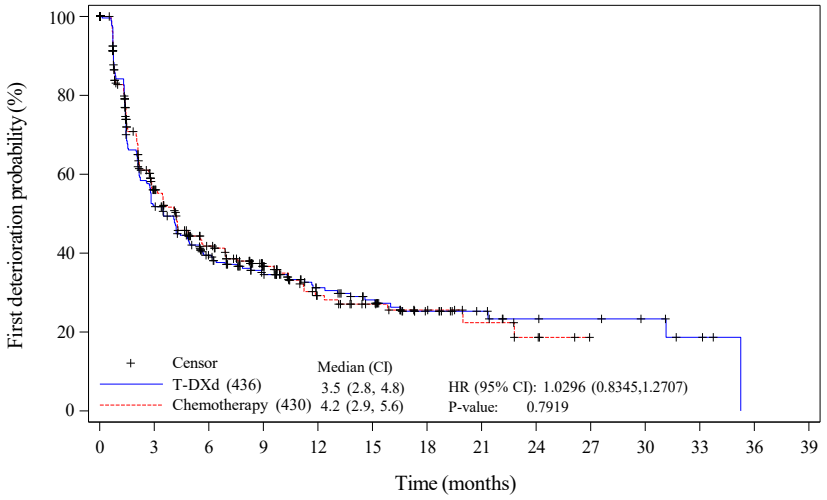
Table 2.12.11 EORTC QLQ-BR45 - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Symptom Scales/Upset by Hair Loss						
T-DXd vs. each Investigator's choice chemotherapy						0.0398
Capecitabine	29 / 266 (10.9)	2.2 [1.4; 4.1]	22 / 257 (8.6)	3.4 [2.1; NE]	1.3202 [0.7603; 2.3249] 0.3253	
Nab-Paclitaxel	15 / 103 (14.6)	1.4 [0.8; 2.2]	19 / 105 (18.1)	1.3 [0.8; 2.8]	0.8734 [0.4288; 1.7364] 0.7170	
Paclitaxel	5 / 67 (7.5)	0.8 [0.7; NE]	3 / 68 (4.4)	NE [0.8; NE]	3.5091 [0.8441; 17.3968] 0.0609	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Abbildung 2.12.5 EORTC-QLQ-BR45 – Zeit bis zur erstmaligen Verschlechterung – Kaplan-Meier-Plot – FAS

Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Body Image



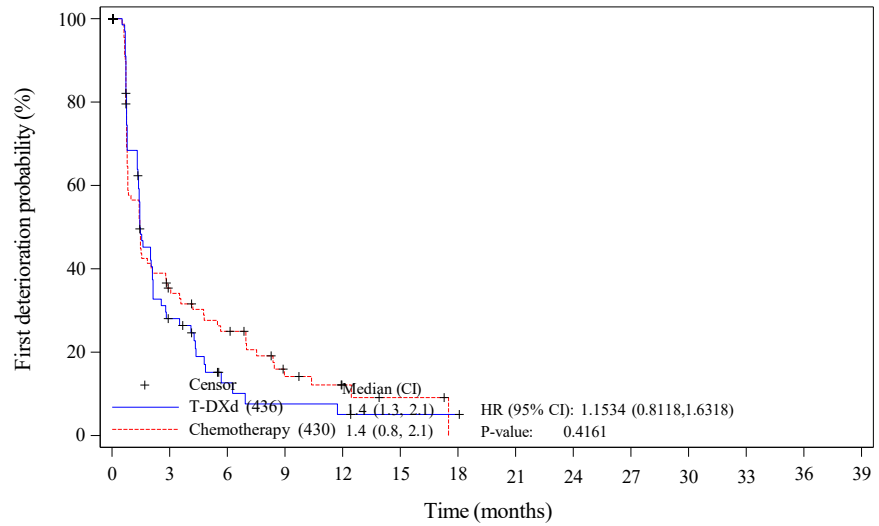
Patients still at risk:

T-DXd(436)	436	133	87	65	43	33	20	14	9	8	6	3	0
Chemotherapy (430)	430	131	81	47	27	19	11	7	4	0			

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10DEC2024 10:34; Program name: F.2.12.5_EORTC_BR45_TTFDet_FAS.sas; Output name: F.2.12.5_EORTC_BR45_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Sexual Functioning



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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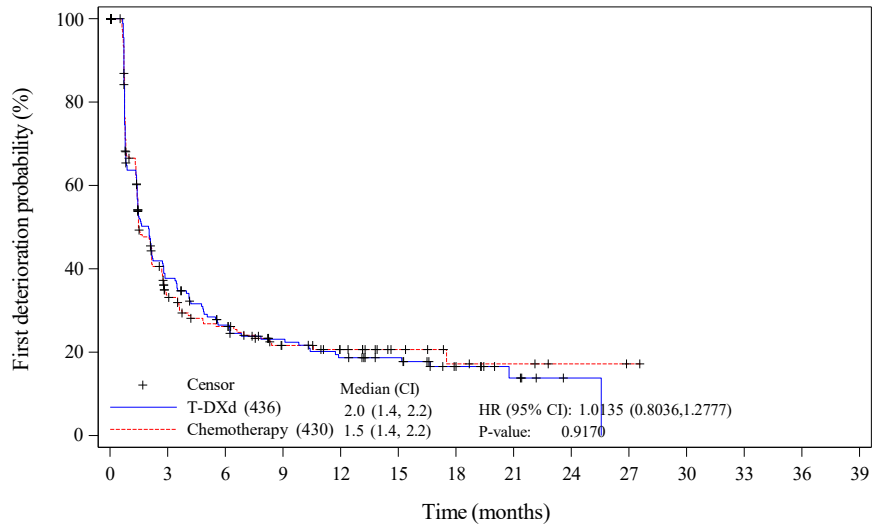
Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Breast Satisfaction



Patients still at risk:

T-DXd(436)	436	63	40	32	25	20	11	5	1	0
Chemotherapy (430)	430	55	40	23	17	9	5	4	2	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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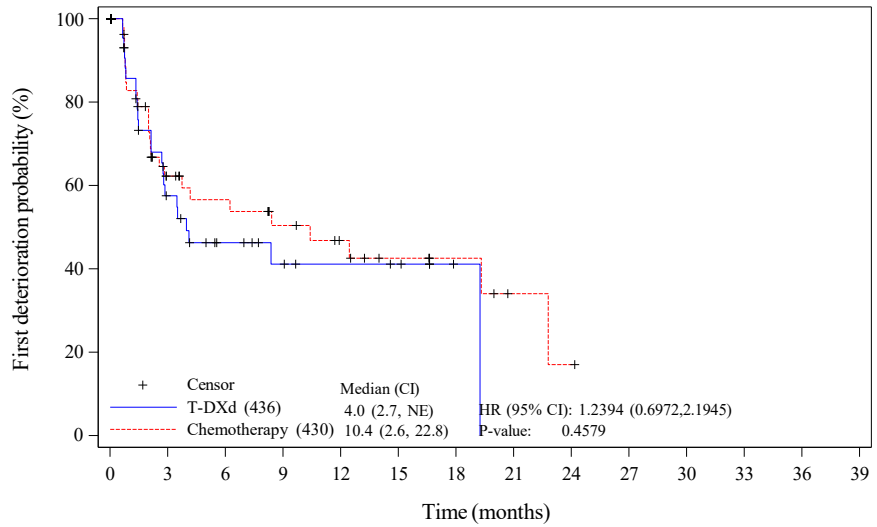
Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Sexual Enjoyment



Patients still at risk:

T-DXd(436)	436	21	12	8	6	5	1	0		
Chemotherapy (430)	430	25	20	15	11	7	5	2	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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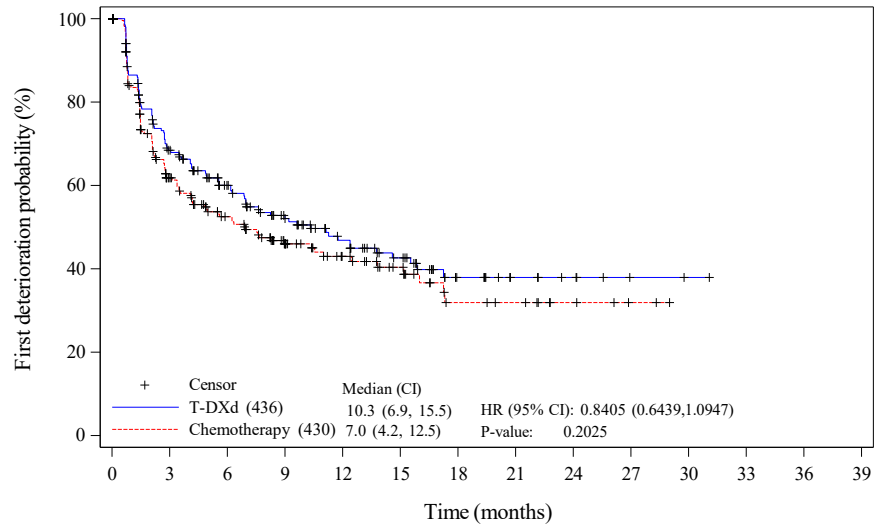
Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Functional Scales/Future Perspective



Patients still at risk:

T-DXd(436)	436	129	95	70	49	35	16	9	6	2	1	0
Chemotherapy (430)	430	119	86	56	36	25	12	10	5	2	0	

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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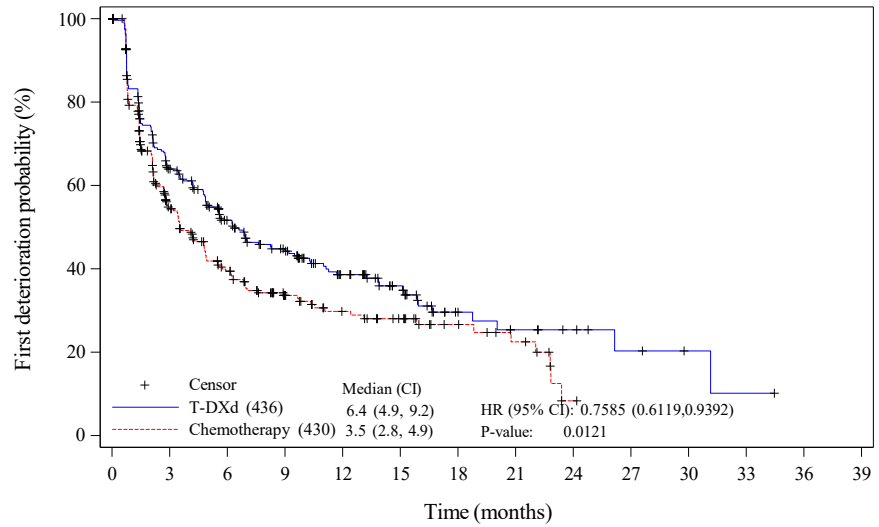
Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Arm Symptoms



Patients still at risk:

T-DXd(436)	436	160	110	82	53	34	15	10	7	4	2	1	0
Chemotherapy (430)	430	128	80	49	34	25	15	10	1	0			

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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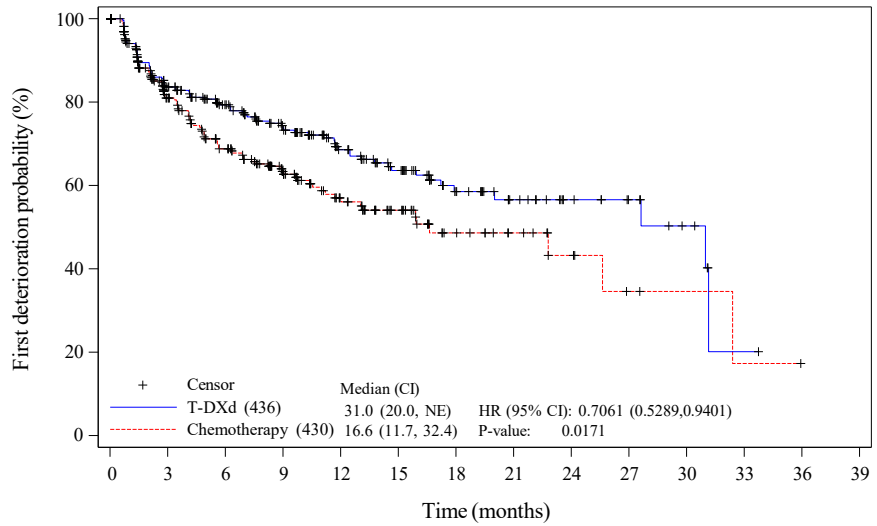
Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Breast Symptoms



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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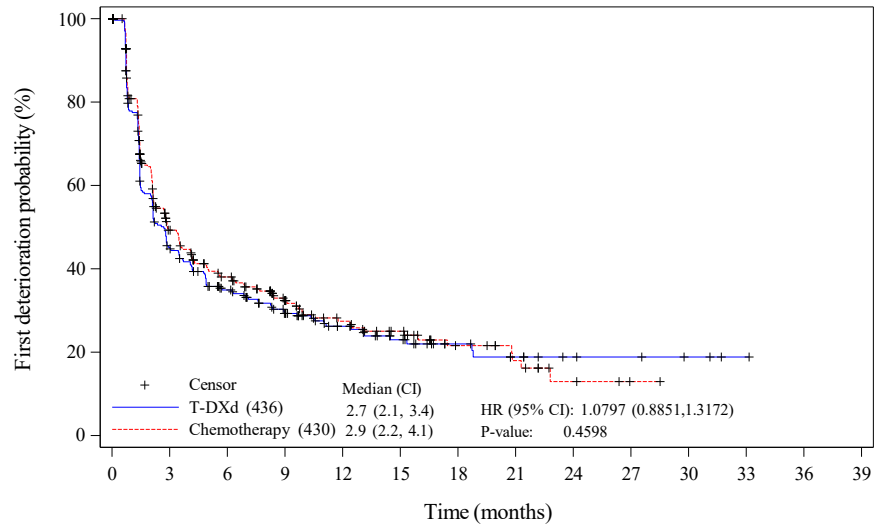
Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Systemic Therapy Side Effects



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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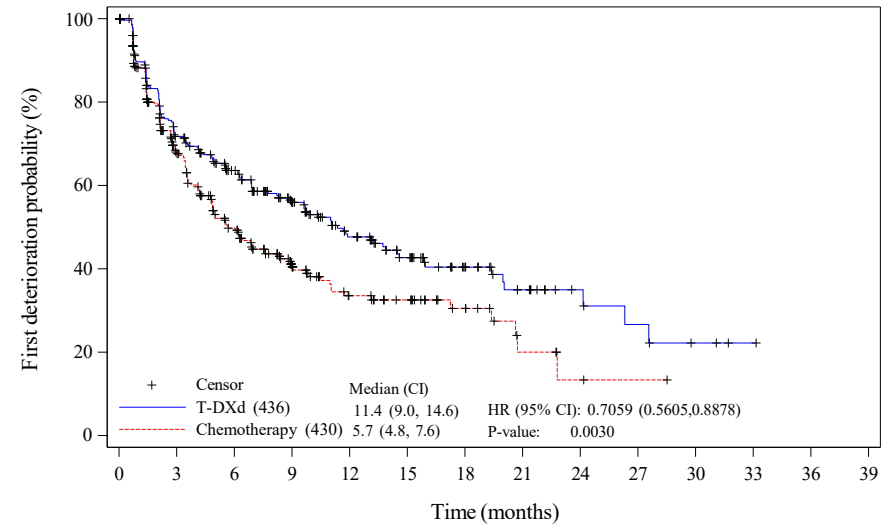
Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Endocrine Therapy Symptoms



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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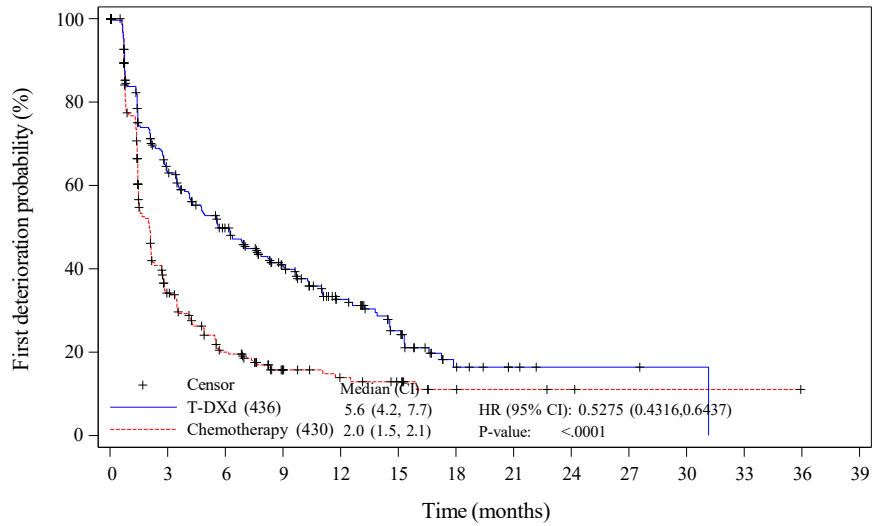
Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Skin Mucosis Symptoms



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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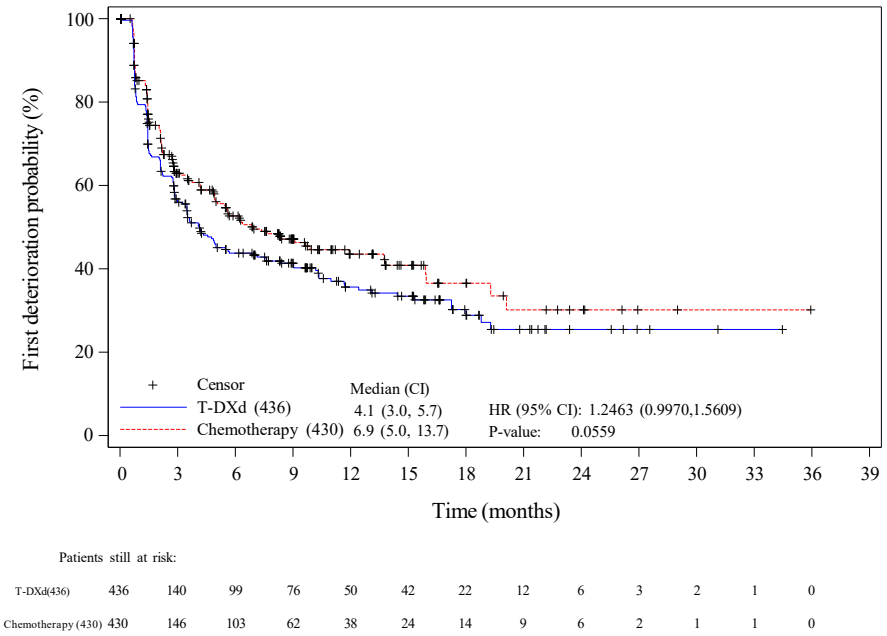
Run date: 10DEC2024 10:34; Program name: F.2.12.5_EORTC_BR45_TTFDet_FAS.sas; Output name: F.2.12.5_EORTC_BR45_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Endocrine Sexual Symptoms



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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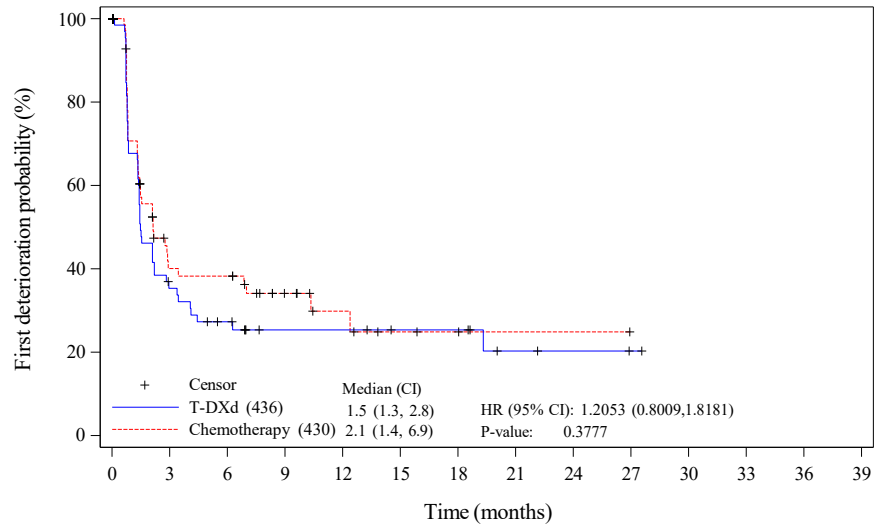
Run date: 10DEC2024 10:34; Program name: F.2.12.5_EORTC_BR45_TTFDet_FAS.sas; Output name: F.2.12.5_EORTC_BR45_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.5 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set
Symptom Scales/Upset by Hair Loss



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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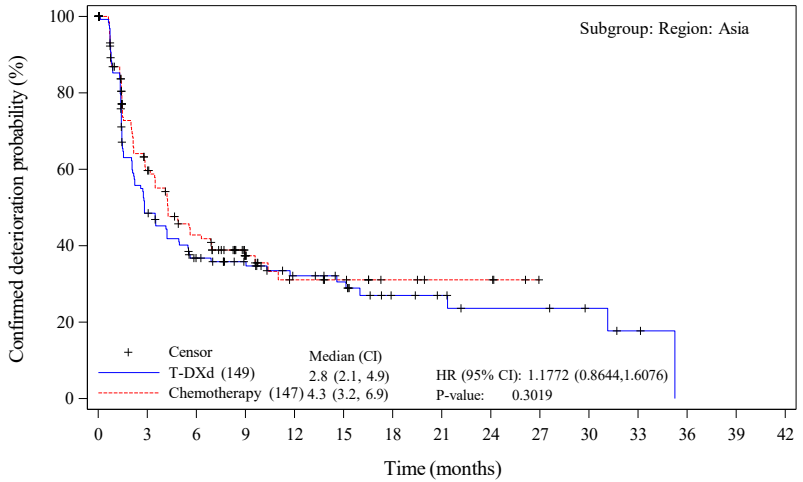
Abbildung 2.12.6 EORTC-QLQ-BR45 – Zeit bis zur erstmaligen Verschlechterung – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Body Image



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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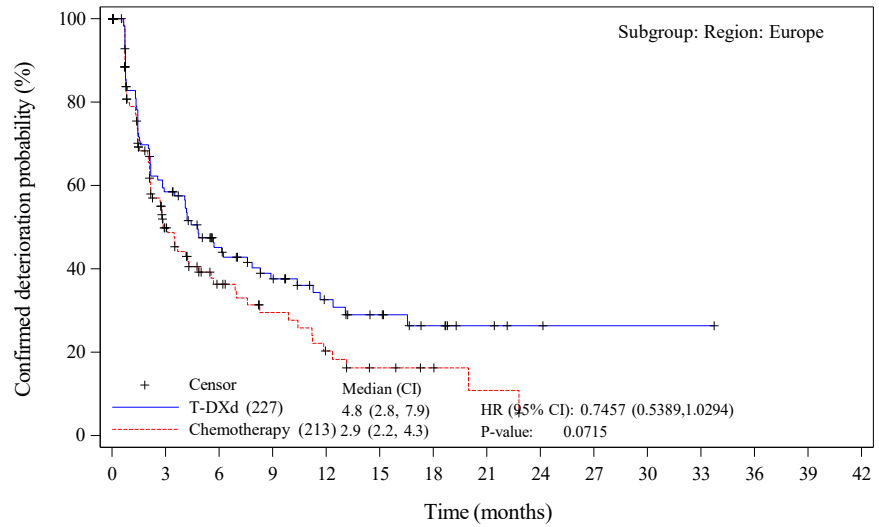
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Body Image



Patients still at risk:

T-DXd(227)	227	62	39	28	18	13	8	4	2	1	1	1	0
Chemotherapy (213)	213	45	24	16	10	6	4	2	0				

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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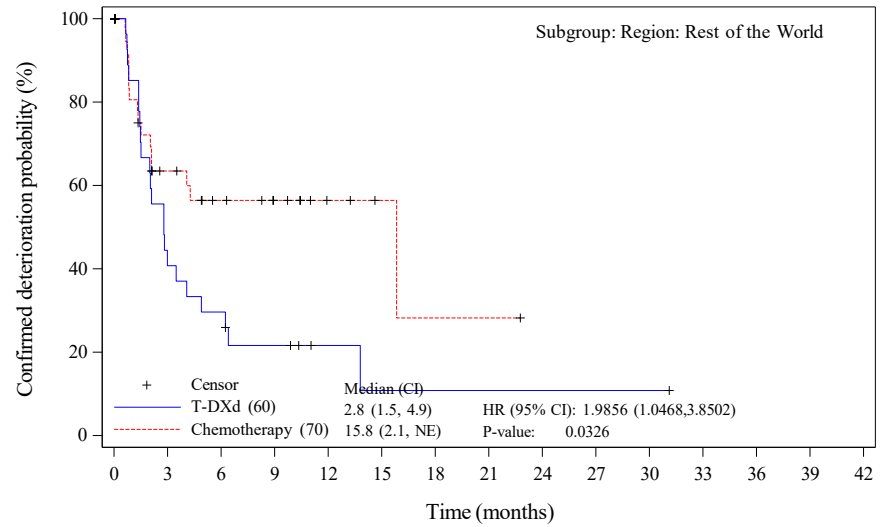
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Body Image



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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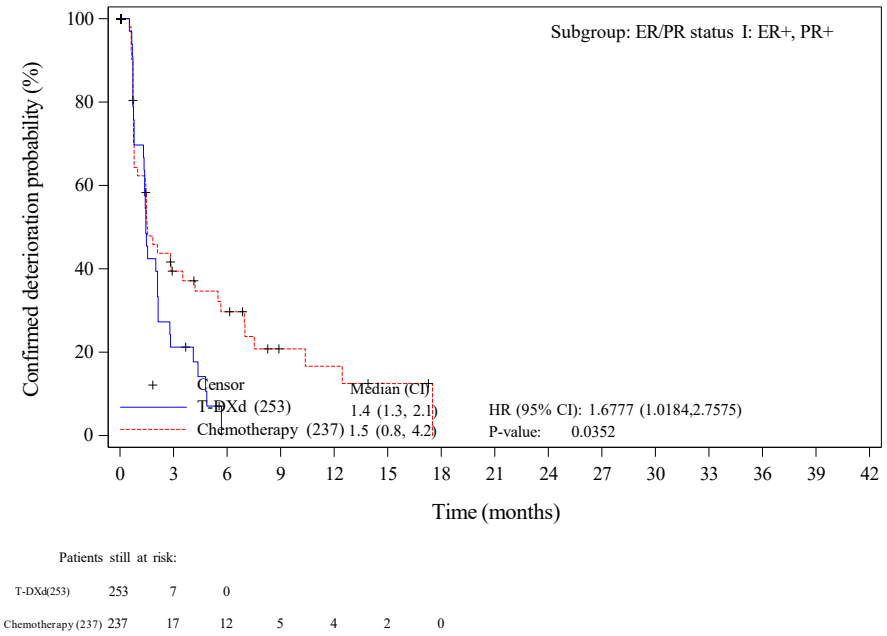
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Sexual Functioning



Patients still at risk:

T-DXd(253)	253	7	0				
Chemotherapy (237)	237	17	12	5	4	2	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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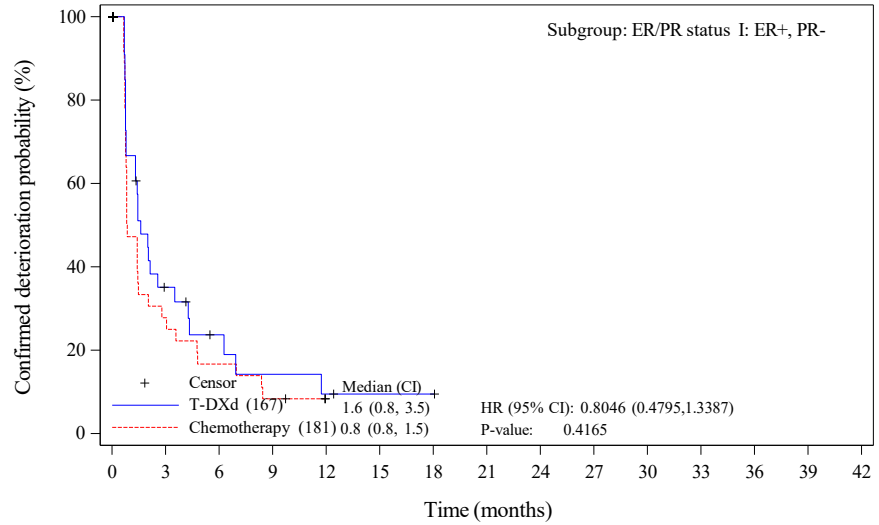
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Sexual Functioning



Patients still at risk:

T-DXd(167)	167	10	5	3	2	1	1	0
Chemotherapy (181)	181	10	6	3	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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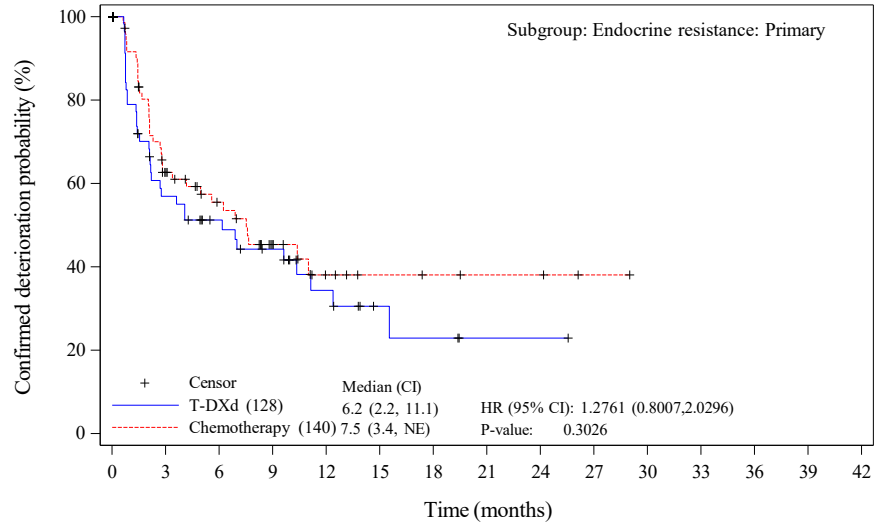
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Future Perspective



Patients still at risk:

T-DXd(128)	128	30	22	17	9	4	3	1	1	0
Chemotherapy (140)	140	40	28	15	8	5	4	3	3	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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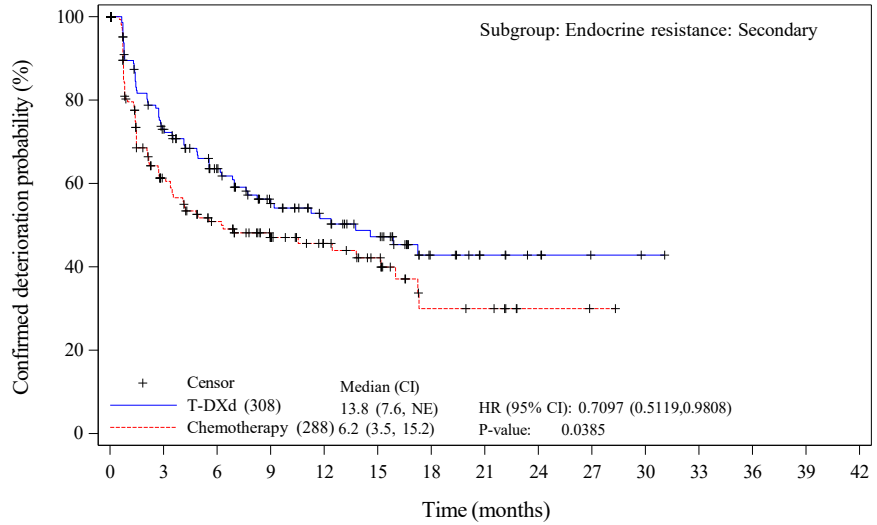
Run date: 05AUG2024 8:00; Program name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Future Perspective



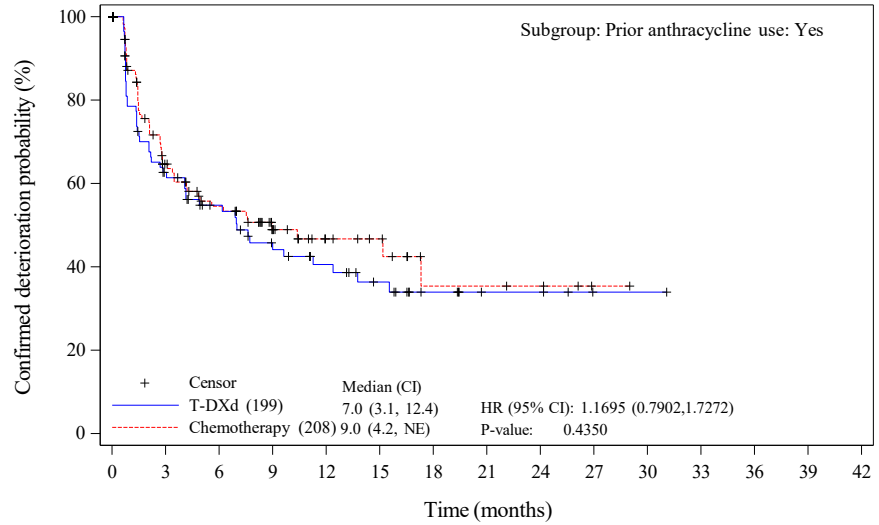
Patients still at risk:

T-DXd(308)	308	99	73	53	40	31	13	8	5	2	1	0
Chemotherapy (288)	288	78	57	41	28	20	8	7	2	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 05AUG2024 8:00; Program name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Future Perspective



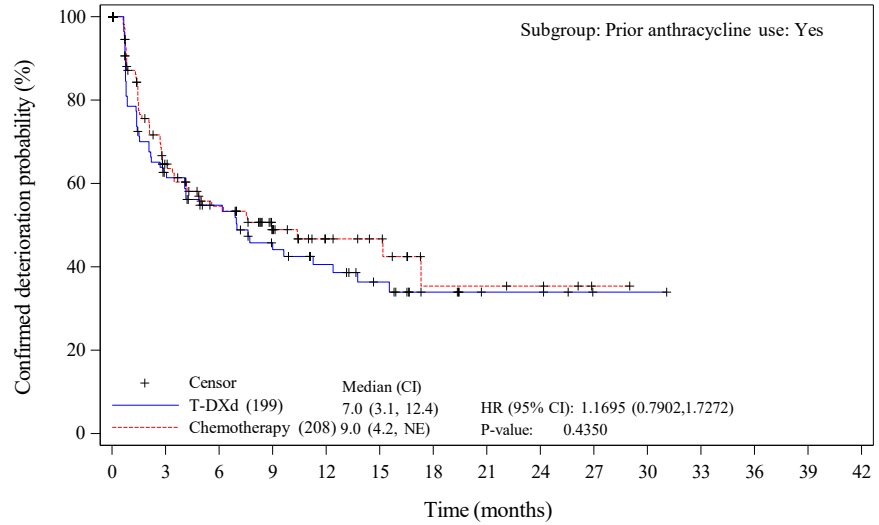
Patients still at risk:

T-DXd(199)	199	49	37	28	21	15	8	4	4	1	1	0
Chemotherapy (208)	208	61	45	26	15	12	5	5	4	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 05AUG2024 8:00; Program name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Functional Scales/Future Perspective



Patients still at risk:

T-DXd(199)	199	49	37	28	21	15	8	4	4	1	1	0
Chemotherapy (208)	208	61	45	26	15	12	5	5	4	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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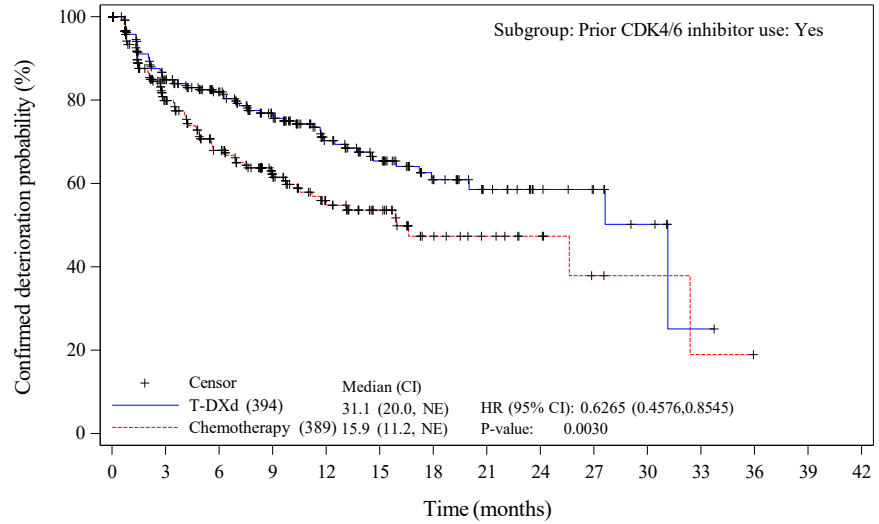
Run date: 05AUG2024 8:00; Program name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Breast Symptoms



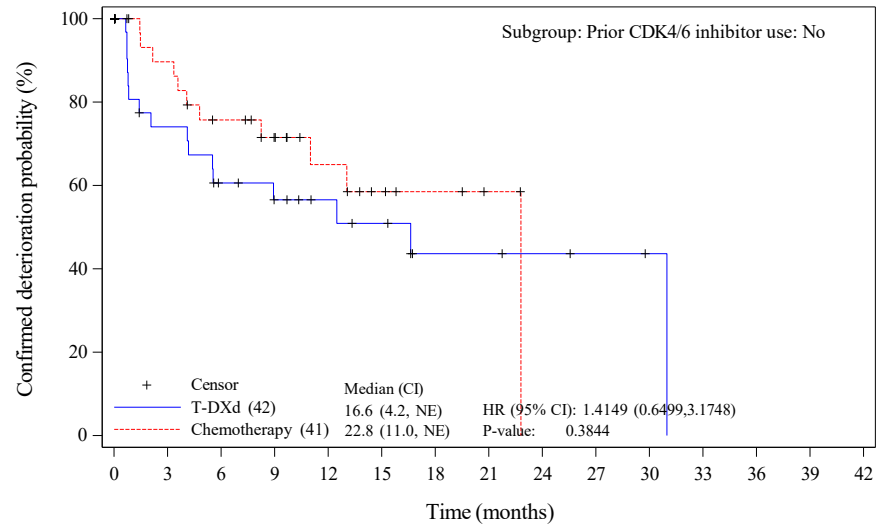
Patients still at risk:

T-DXd(394)	394	187	153	122	82	60	35	21	13	9	5	1	0
Chemotherapy (389)	389	165	122	80	50	34	16	11	7	3	2	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 05AUG2024 8:00; Program name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Breast Symptoms



Patients still at risk:

T-DXd(42)	42	22	16	13	10	8	4	4	3	2	1	0
Chemotherapy (41)	41	26	20	15	10	6	4	2	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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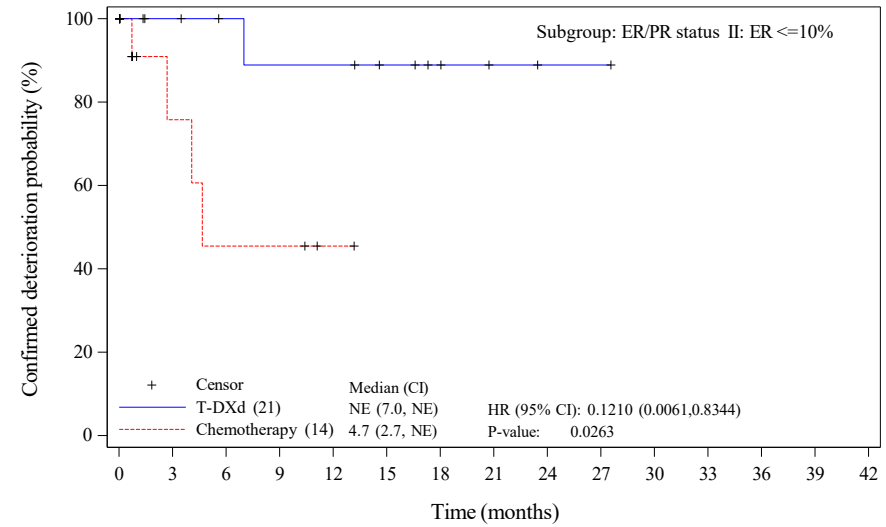
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Breast Symptoms



Patients still at risk:

T-DXd(21)	21	11	9	8	8	6	4	2	1	1	0
Chemotherapy (14)	14	5	3	3	1	0					

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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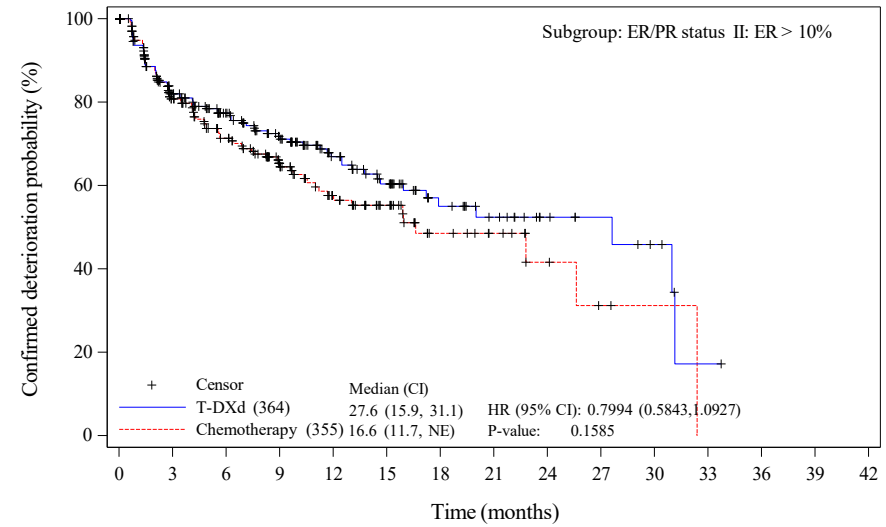
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Breast Symptoms



Patients still at risk:

T-DXd(364)	364	169	134	105	69	50	27	19	11	8	5	1	0
Chemotherapy (355)	355	156	120	79	50	33	16	11	5	2	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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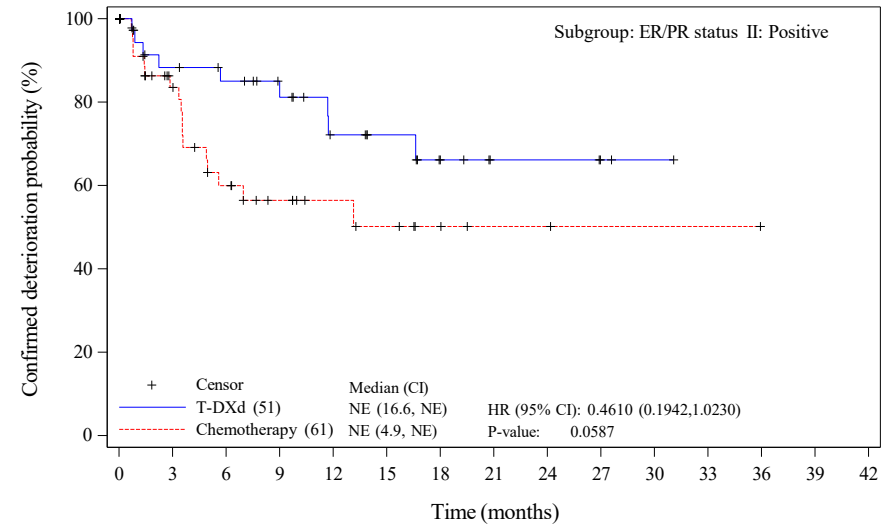
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Breast Symptoms



Patients still at risk:

T-DXd(51)	51	29	26	22	15	12	8	4	4	2	1	0
Chemotherapy (61)	61	30	19	13	9	7	4	2	2	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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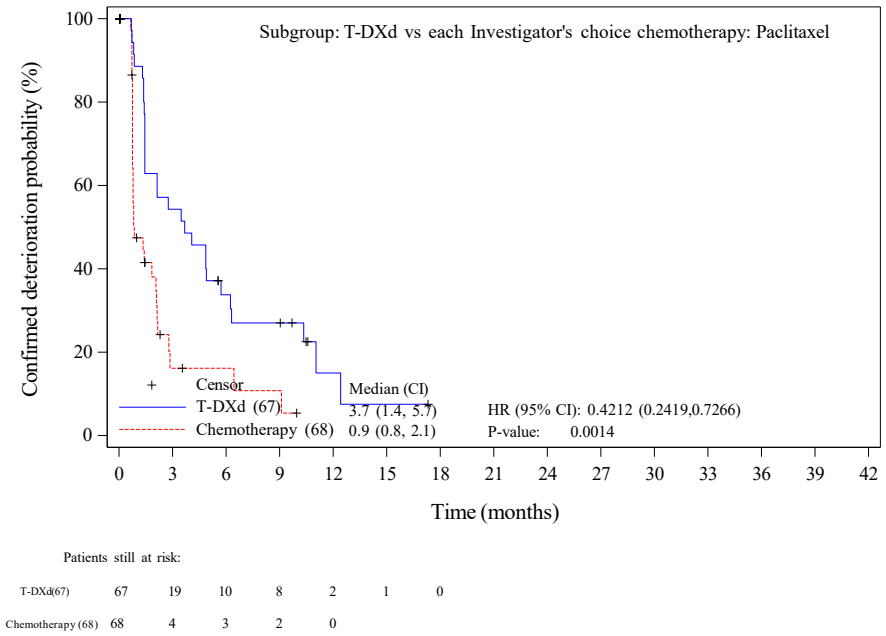
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Systemic Therapy Side Effects



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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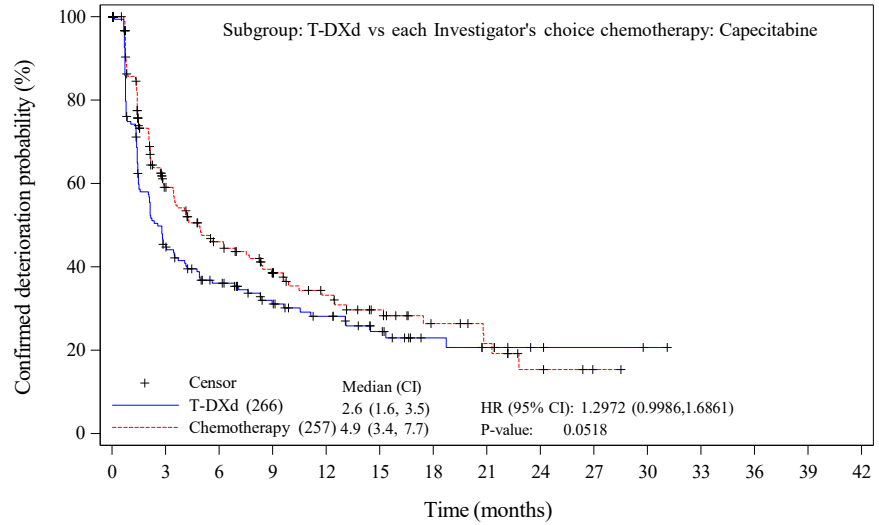
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Systemic Therapy Side Effects



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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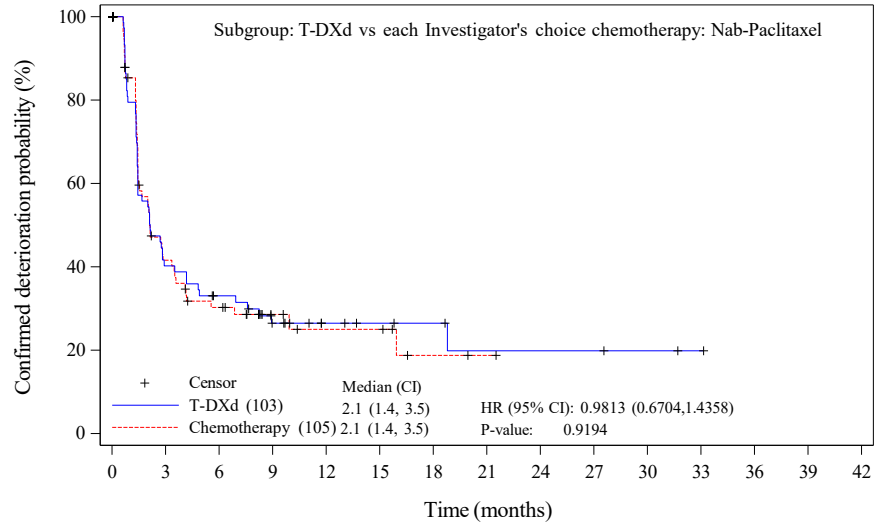
Run date: 05AUG2024 8:00; Program name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Systemic Therapy Side Effects



Patients still at risk:

T-DXd(103)	103	28	21	14	8	6	5	3	3	3	2	1	0
Chemotherapy (105)	105	30	20	9	6	6	2	1	0				

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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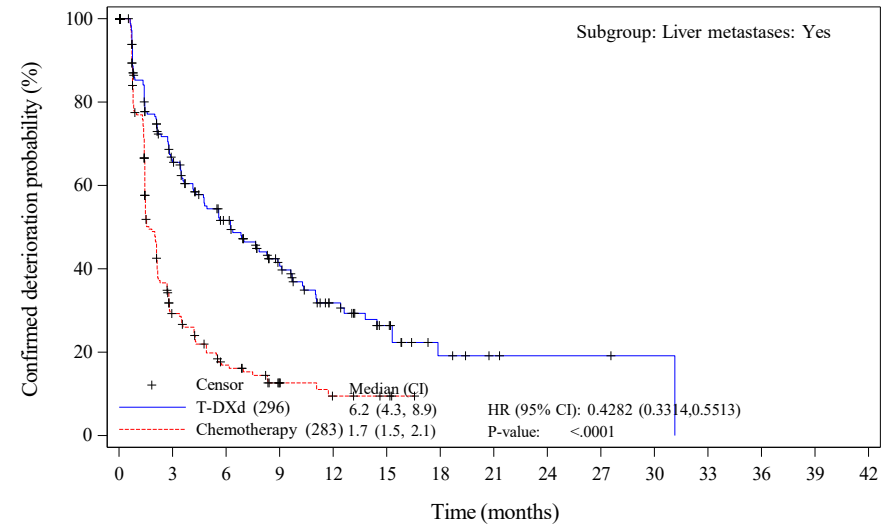
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Skin Mucosis Symptoms



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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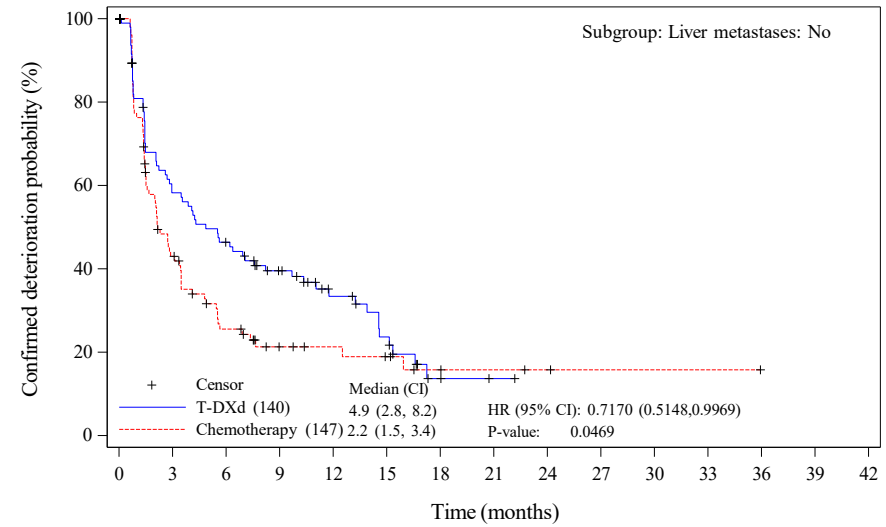
Run date: 05AUG2024 8:00; Program name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Skin Mucosis Symptoms



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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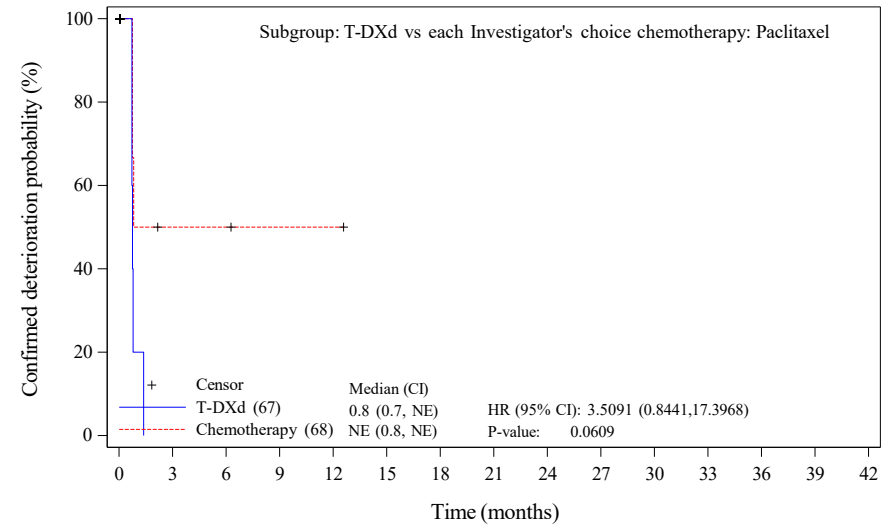
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Upset by Hair Loss



Patients still at risk:

T-DXd(67)	67	0				
Chemotherapy (68)	68	2	2	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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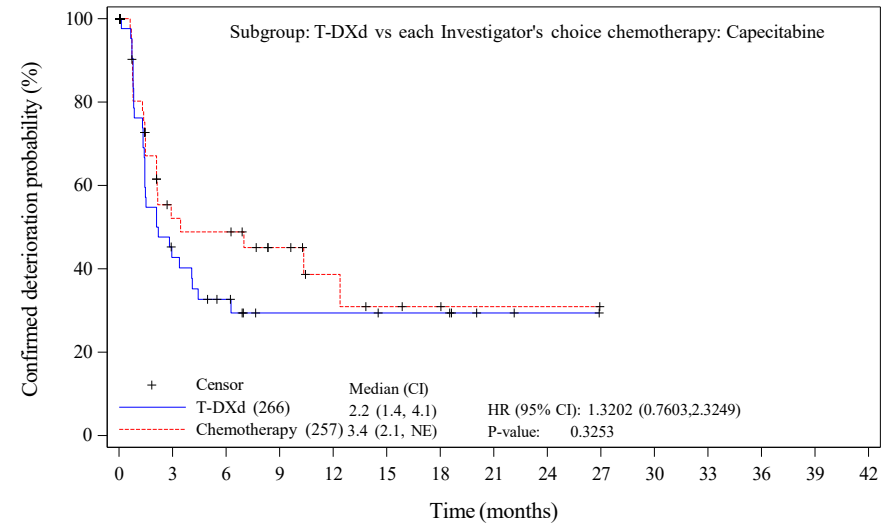
Run date: 05AUG2024 8:00; Program name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Upset by Hair Loss



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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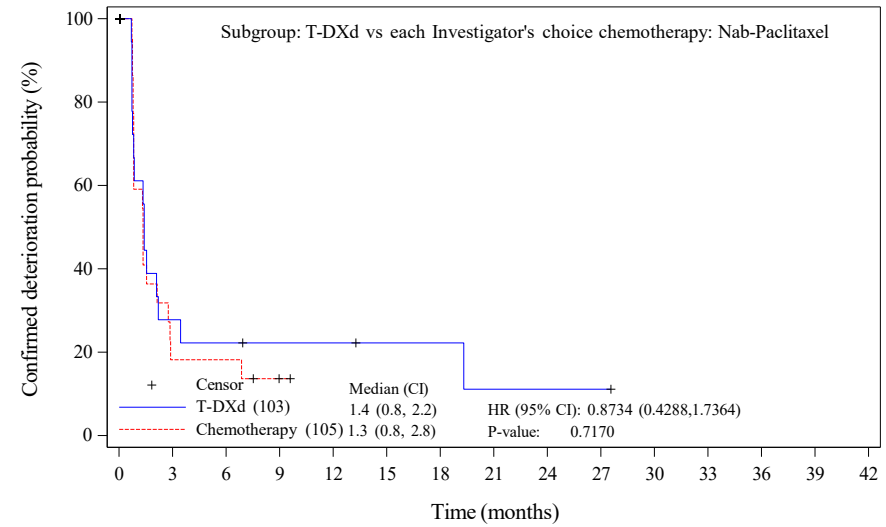
Figure 2.12.6 EORTC-QLQ-BR45 - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set
Symptom Scales/Upset by Hair Loss



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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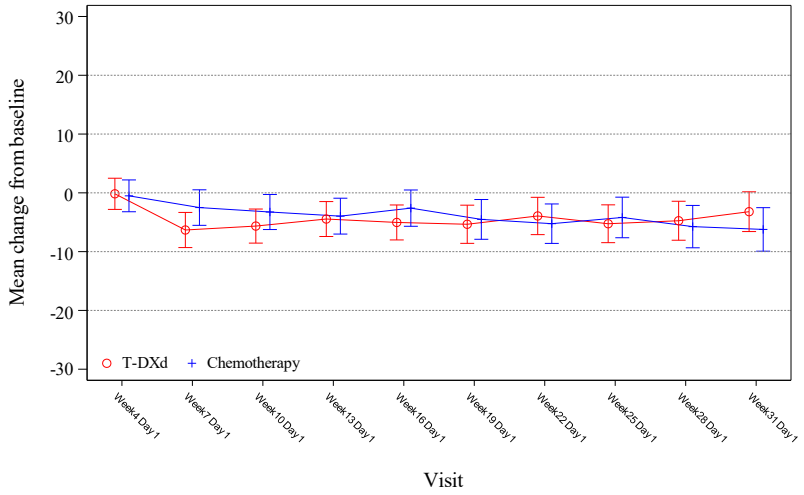
Run date: 05AUG2024 8:00; Program name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.sas; Output name: F.2.12.6_EORTC_BR45_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.12.9 EORTC-QLQ-BR45 – Mean change from baseline-Plot – FAS

Figure 2.12.9 EORTC-QLQ-BR45 - Mean change from baseline- Full Analysis Set
Functional Scales/Body Image
Mean baseline values: T-Dxd:78.9; Chemotherapy:78.1



Number of subjects with an observation:

T-DXd	251	234	234	216	214	206	203	194	183	171
Chemotherapy	254	238	220	206	184	184	166	143	135	118

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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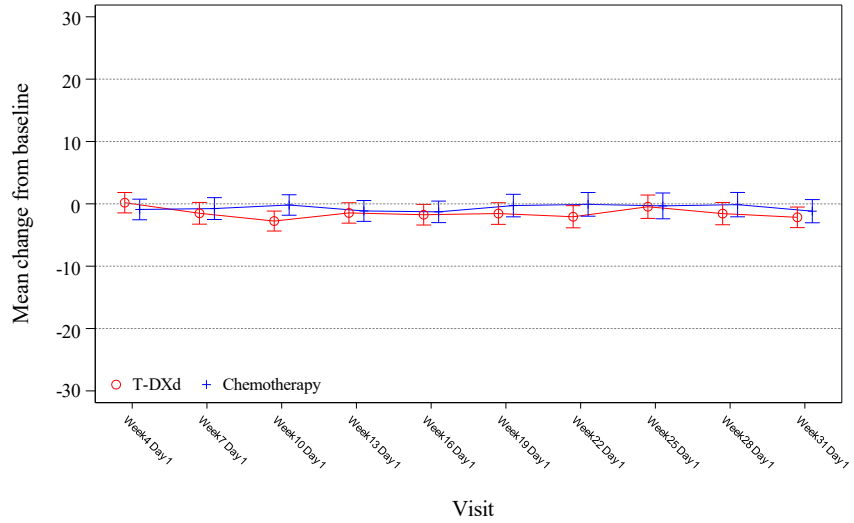
Figure 2.12.9 EORTC-QLQ-BR45 - Mean change from baseline- Full Analysis Set
Functional Scales/Sexual Functioning
Mean baseline values: T-Dxd:7.9; Chemotherapy:9.2



Number of subjects with an observation:

T-DXd	251	233	234	215	213	205	203	194	183	171
Chemotherapy	254	238	220	206	184	184	166	143	135	118

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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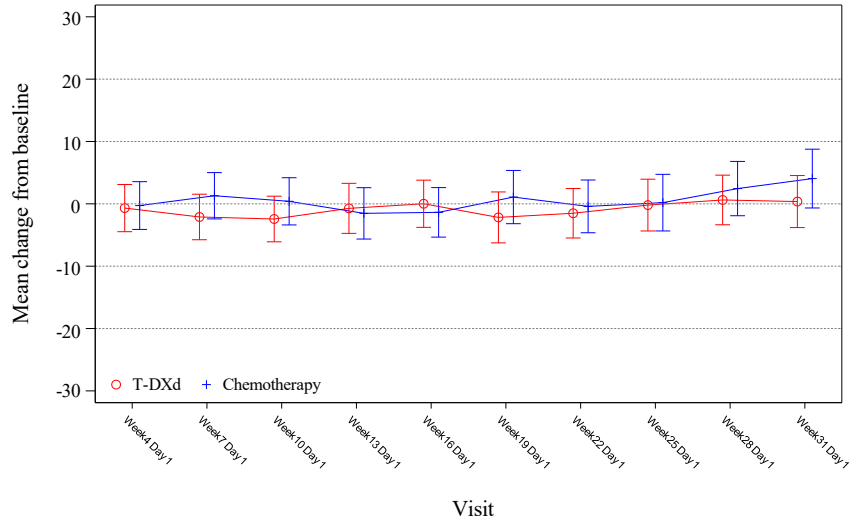
Figure 2.12.9 EORTC-QLQ-BR45 - Mean change from baseline- Full Analysis Set
Functional Scales/Breast Satisfaction
Mean baseline values: T-Dxd:32.7; Chemotherapy:34.2



Number of subjects with an observation:

T-DXd	250	233	234	214	213	205	202	194	183	171
Chemotherapy	253	237	218	204	182	182	164	141	133	117

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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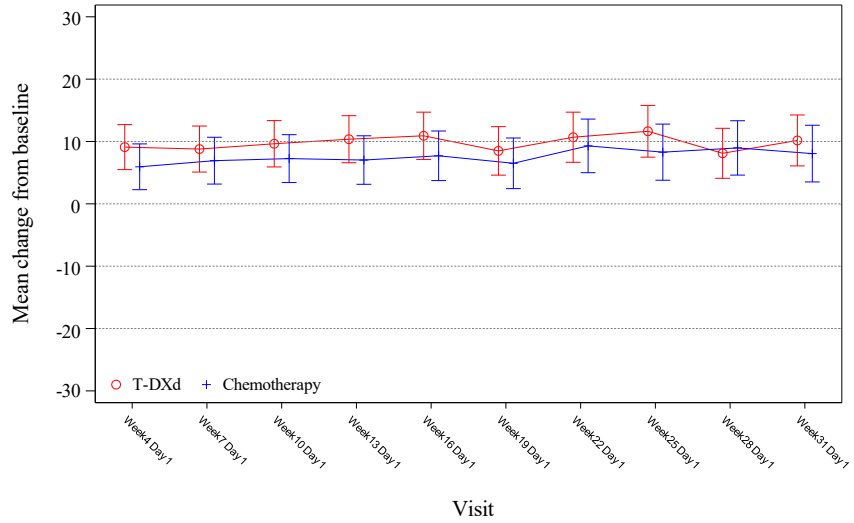
Figure 2.12.9 EORTC-QLQ-BR45 - Mean change from baseline- Full Analysis Set
Functional Scales/Future Perspective
Mean baseline values: T-Dxd:45.2; Chemotherapy:47.6



Number of subjects with an observation:

T-DXd	251	234	234	216	214	206	203	194	183	171
Chemotherapy	254	238	220	206	184	184	166	143	135	118

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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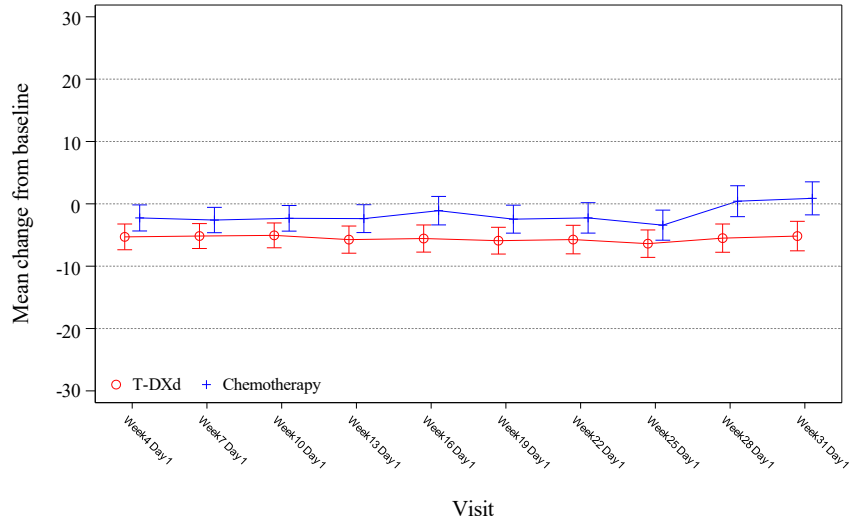
Figure 2.12.9 EORTC-QLQ-BR45 - Mean change from baseline- Full Analysis Set
Symptom Scales/Arm Symptoms
Mean baseline values: T-Dxd:15.1; Chemotherapy:18.4



Number of subjects with an observation:

T-DXd	251	234	234	216	214	206	203	194	183	171
Chemotherapy	254	238	220	206	184	184	166	143	135	118

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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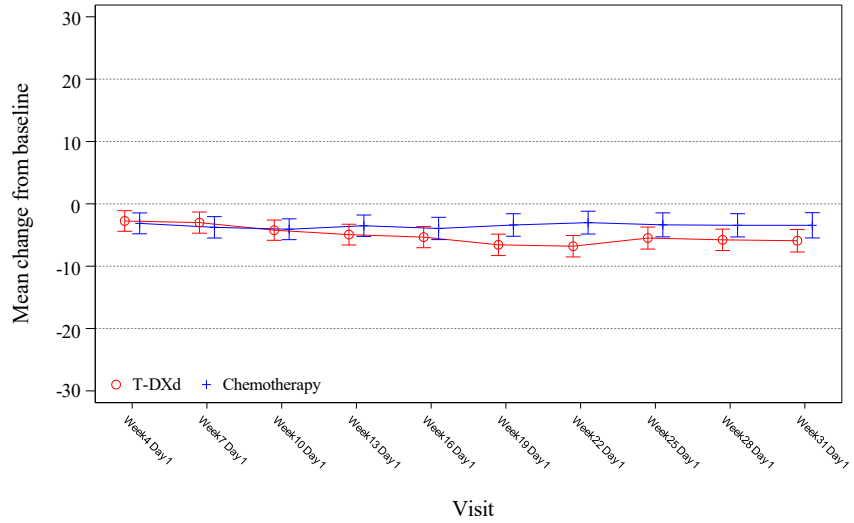
Figure 2.12.9 EORTC-QLQ-BR45 - Mean change from baseline- Full Analysis Set
Symptom Scales/Breast Symptoms
Mean baseline values: T-Dxd:12.3; Chemotherapy:13.6



Number of subjects with an observation:

T-DXd	251	234	234	216	214	206	202	194	183	171
Chemotherapy	254	238	220	206	184	184	166	143	135	118

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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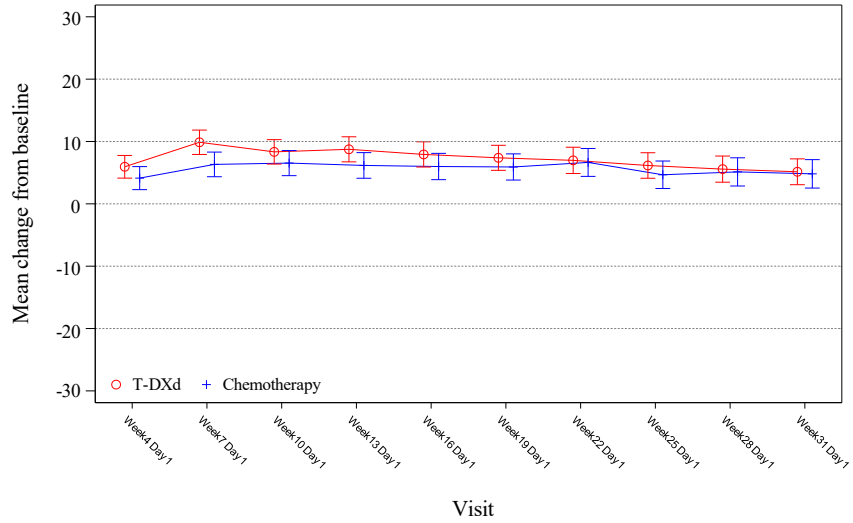
Figure 2.12.9 EORTC-QLQ-BR45 - Mean change from baseline- Full Analysis Set
Symptom Scales/Systemic Therapy Side Effects
Mean baseline values: T-Dxd:14.1; Chemotherapy:14.3



Number of subjects with an observation:

T-DXd	251	234	234	216	214	206	203	194	183	171
Chemotherapy	254	238	220	206	184	184	166	143	135	118

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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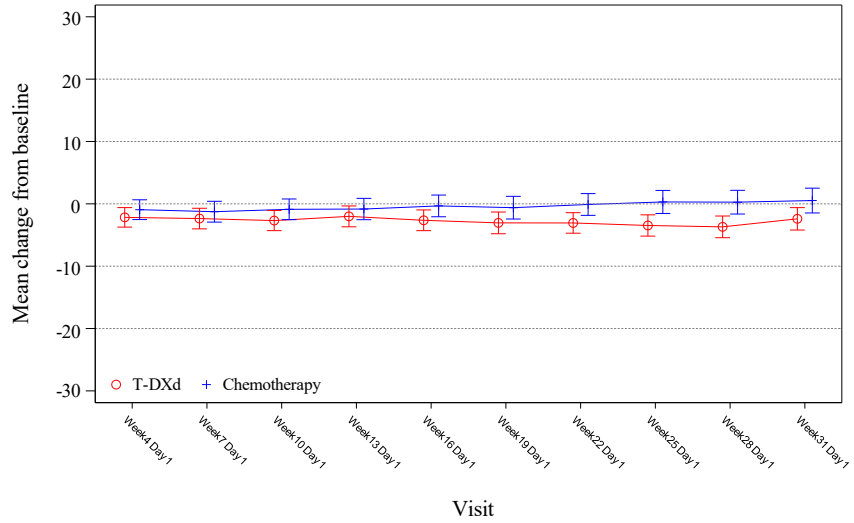
Figure 2.12.9 EORTC-QLQ-BR45 - Mean change from baseline- Full Analysis Set
Symptom Scales/Endocrine Therapy Symptoms
Mean baseline values: T-Dxd:15.3; Chemotherapy:17.8



Number of subjects with an observation:

T-DXd	251	234	234	216	214	206	203	194	183	171
Chemotherapy	254	238	220	206	184	184	166	143	135	118

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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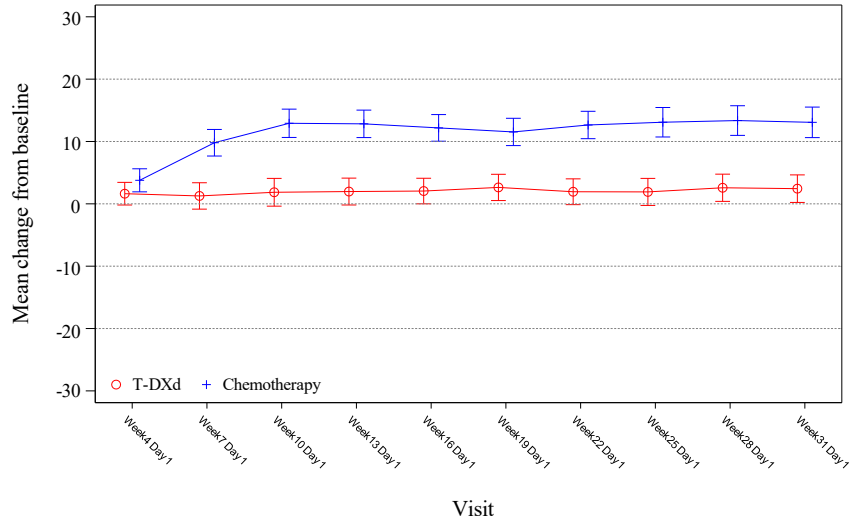
Figure 2.12.9 EORTC-QLQ-BR45 - Mean change from baseline- Full Analysis Set
Symptom Scales/Skin Mucosis Symptoms
Mean baseline values: T-Dxd:6.9; Chemotherapy:7.2



Number of subjects with an observation:

T-DXd	251	234	234	215	214	206	203	194	183	171
Chemotherapy	254	238	220	206	184	184	166	143	135	118

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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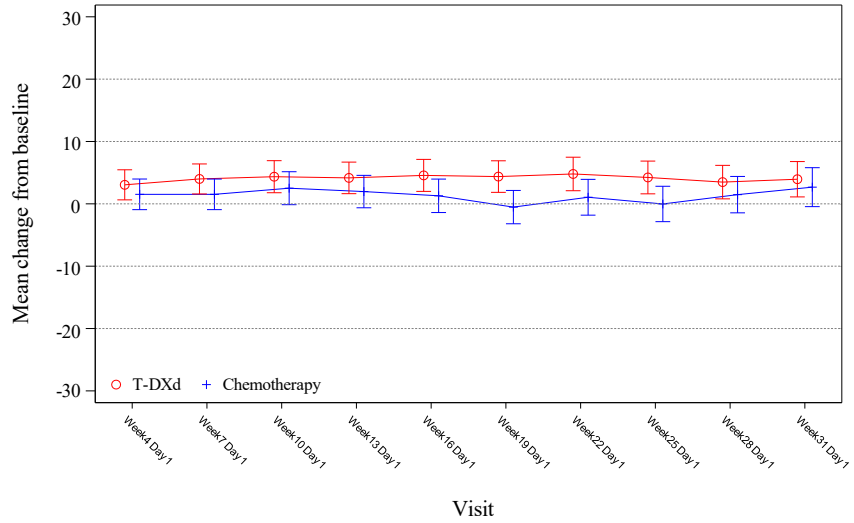
Figure 2.12.9 EORTC-QLQ-BR45 - Mean change from baseline- Full Analysis Set
Symptom Scales/Endocrine Sexual Symptoms
Mean baseline values: T-Dxd:11.8; Chemotherapy:12.6



Number of subjects with an observation:

T-DXd	251	234	234	216	214	206	203	194	183	171
Chemotherapy	253	237	219	205	183	183	165	142	134	117

Mean changes from baseline are estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
LS: least square; MMRM: mixed model for repeated measurement; CI: confidence interval

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Tabelle 2.12.15 EORTC-QLQ-BR45 – Mixed Model for Repeated Measurement – FAS

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Functional Scales/Body Image			
Week 4 Day 1			
Estimated change from baseline [a]			
n	251	254	
LS Means [95% CI]	-0.16 [-2.82; 2.49]	-0.51 [-3.21; 2.20]	
Standard error	1.35	1.38	
Difference of LS Means [95% CI]			0.34 [-2.62; 3.31]
Standard error for difference			1.51
p-value			0.8199
Hedges' g [95% CI]			0.02 [-0.16; 0.19]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	234	238	
LS Means [95% CI]	-6.32 [-9.31; -3.33]	-2.50 [-5.53; 0.52]	
Standard error	1.52	1.54	
Difference of LS Means [95% CI]			-3.82 [-7.36; -0.27]
Standard error for difference			1.81
p-value			0.0351
Hedges' g [95% CI]			-0.16 [-0.34; 0.02]
Week 10 Day 1			
Estimated change from baseline [a]			
n	234	220	
LS Means [95% CI]	-5.65 [-8.55; -2.75]	-3.26 [-6.24; -0.27]	
Standard error	1.48	1.52	
Difference of LS Means [95% CI]			-2.39 [-5.83; 1.04]
Standard error for difference			1.75
p-value			0.1716
Hedges' g [95% CI]			-0.11 [-0.29; 0.08]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	216	206	
LS Means [95% CI]	-4.45 [-7.43; -1.48]	-3.96 [-7.01; -0.91]	
Standard error	1.51	1.55	
Difference of LS Means [95% CI]			-0.49 [-4.05; 3.07]
Standard error for difference			1.81
p-value			0.7860
Hedges' g [95% CI]			-0.02 [-0.21; 0.17]
Week 16 Day 1			
Estimated change from baseline [a]			
n	214	184	
LS Means [95% CI]	-5.04 [-8.01; -2.06]	-2.60 [-5.69; 0.49]	
Standard error	1.51	1.57	
Difference of LS Means [95% CI]			-2.44 [-6.03; 1.16]
Standard error for difference			1.83
p-value			0.1840
Hedges' g [95% CI]			-0.11 [-0.31; 0.09]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.

b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.

CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	206	184	
LS Means [95% CI]	-5.34 [-8.59; -2.10]	-4.52 [-7.90; -1.13]	
Standard error	1.65	1.72	
Difference of LS Means [95% CI]			-0.83 [-4.90; 3.24]
Standard error for difference			2.07
p-value			0.6901
Hedges' g [95% CI]			-0.04 [-0.23; 0.16]
Week 22 Day 1			
Estimated change from baseline [a]			
n	203	166	
LS Means [95% CI]	-3.93 [-7.10; -0.76]	-5.24 [-8.60; -1.89]	
Standard error	1.61	1.71	
Difference of LS Means [95% CI]			1.31 [-2.68; 5.30]
Standard error for difference			2.03
p-value			0.5188
Hedges' g [95% CI]			0.06 [-0.15; 0.26]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	194	143	
LS Means [95% CI]	-5.26 [-8.47; -2.04]	-4.19 [-7.64; -0.74]	
Standard error	1.64	1.76	
Difference of LS Means [95% CI]			-1.07 [-5.18; 3.04]
Standard error for difference			2.09
p-value			0.6090
Hedges' g [95% CI]			-0.05 [-0.26; 0.17]
Week 28 Day 1			
Estimated change from baseline [a]			
n	183	135	
LS Means [95% CI]	-4.74 [-8.06; -1.43]	-5.74 [-9.35; -2.14]	
Standard error	1.69	1.83	
Difference of LS Means [95% CI]			1.00 [-3.31; 5.31]
Standard error for difference			2.19
p-value			0.6491
Hedges' g [95% CI]			0.04 [-0.18; 0.27]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	171	118	
LS Means [95% CI]	-3.20 [-6.59; 0.18]	-6.22 [-9.92; -2.52]	
Standard error	1.72	1.88	
Difference of LS Means [95% CI]			3.02 [-1.42; 7.46]
Standard error for difference			2.26
p-value			0.1821
Hedges' g [95% CI]			0.14 [-0.10; 0.37]
Average [b]			
n	271	291	
LS Means [95% CI]	-4.41 [-7.03; -1.79]	-3.87 [-6.58; -1.17]	
Standard error	1.33	1.38	
Difference of LS Means [95% CI]			-0.54 [-3.49; 2.42]
Standard error for difference			1.50
p-value			0.7217
Hedges' g [95% CI]			-0.02 [-0.19; 0.14]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Functional Scales/Sexual Functioning			
Week 4 Day 1			
Estimated change from baseline [a]			
n	251	254	
LS Means [95% CI]	0.18 [-1.45; 1.82]	-0.90 [-2.56; 0.75]	
Standard error	0.83	0.84	
Difference of LS Means [95% CI]			1.09 [-0.84; 3.01]
Standard error for difference			0.98
p-value			0.2684
Hedges' g [95% CI]			0.08 [-0.09; 0.26]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	233	238	
LS Means [95% CI]	-1.52 [-3.26; 0.22]	-0.76 [-2.51; 1.00]	
Standard error	0.89	0.89	
Difference of LS Means [95% CI]			-0.76 [-2.87; 1.35]
Standard error for difference			1.07
p-value			0.4789
Hedges' g [95% CI]			-0.06 [-0.24; 0.13]
Week 10 Day 1			
Estimated change from baseline [a]			
n	234	220	
LS Means [95% CI]	-2.76 [-4.36; -1.16]	-0.18 [-1.83; 1.46]	
Standard error	0.82	0.84	
Difference of LS Means [95% CI]			-2.58 [-4.47; -0.69]
Standard error for difference			0.96
p-value			0.0077
Hedges' g [95% CI]			-0.21 [-0.39; -0.02]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.

b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.

CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	215	206	
LS Means [95% CI]	-1.46 [-3.09; 0.18]	-1.14 [-2.81; 0.53]	
Standard error	0.83	0.85	
Difference of LS Means [95% CI]			-0.32 [-2.27; 1.63]
Standard error for difference			0.99
p-value			0.7469
Hedges' g [95% CI]			-0.03 [-0.22; 0.16]
Week 16 Day 1			
Estimated change from baseline [a]			
n	213	184	
LS Means [95% CI]	-1.75 [-3.40; -0.10]	-1.28 [-3.01; 0.44]	
Standard error	0.84	0.88	
Difference of LS Means [95% CI]			-0.46 [-2.48; 1.55]
Standard error for difference			1.02
p-value			0.6518
Hedges' g [95% CI]			-0.04 [-0.24; 0.16]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	205	184	
LS Means [95% CI]	-1.56 [-3.29; 0.18]	-0.28 [-2.08; 1.53]	
Standard error	0.88	0.92	
Difference of LS Means [95% CI]			-1.28 [-3.43; 0.87]
Standard error for difference			1.09
p-value			0.2431
Hedges' g [95% CI]			-0.10 [-0.30; 0.10]
Week 22 Day 1			
Estimated change from baseline [a]			
n	203	166	
LS Means [95% CI]	-2.07 [-3.85; -0.29]	-0.08 [-1.98; 1.82]	
Standard error	0.90	0.97	
Difference of LS Means [95% CI]			-1.99 [-4.26; 0.28]
Standard error for difference			1.15
p-value			0.0854
Hedges' g [95% CI]			-0.16 [-0.36; 0.05]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	194	143	
LS Means [95% CI]	-0.46 [-2.34; 1.41]	-0.33 [-2.40; 1.74]	
Standard error	0.96	1.05	
Difference of LS Means [95% CI]			-0.14 [-2.62; 2.35]
Standard error for difference			1.26
p-value			0.9139
Hedges' g [95% CI]			-0.01 [-0.23; 0.21]
Week 28 Day 1			
Estimated change from baseline [a]			
n	183	135	
LS Means [95% CI]	-1.57 [-3.35; 0.22]	-0.13 [-2.08; 1.83]	
Standard error	0.91	0.99	
Difference of LS Means [95% CI]			-1.44 [-3.76; 0.88]
Standard error for difference			1.18
p-value			0.2235
Hedges' g [95% CI]			-0.12 [-0.34; 0.10]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	171	118	
LS Means [95% CI]	-2.16 [-3.82; -0.51]	-1.18 [-3.04; 0.68]	
Standard error	0.84	0.95	
Difference of LS Means [95% CI]			-0.99 [-3.13; 1.15]
Standard error for difference			1.09
p-value			0.3651
Hedges' g [95% CI]			-0.09 [-0.33; 0.14]
Average [b]			
n	271	291	
LS Means [95% CI]	-1.51 [-2.90; -0.12]	-0.63 [-2.07; 0.82]	
Standard error	0.71	0.73	
Difference of LS Means [95% CI]			-0.89 [-2.42; 0.65]
Standard error for difference			0.78
p-value			0.2580
Hedges' g [95% CI]			-0.07 [-0.24; 0.09]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Functional Scales/Breast Satisfaction			
Week 4 Day 1			
Estimated change from baseline [a]			
n	250	253	
LS Means [95% CI]	-0.68 [-4.46; 3.11]	-0.27 [-4.10; 3.56]	
Standard error	1.93	1.95	
Difference of LS Means [95% CI]			-0.40 [-4.90; 4.09]
Standard error for difference			2.29
p-value			0.8596
Hedges' g [95% CI]			-0.01 [-0.19; 0.16]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	233	237	
LS Means [95% CI]	-2.10 [-5.76; 1.55]	1.30 [-2.42; 5.01]	
Standard error	1.86	1.89	
Difference of LS Means [95% CI]			-3.40 [-7.71; 0.90]
Standard error for difference			2.19
p-value			0.1210
Hedges' g [95% CI]			-0.12 [-0.30; 0.06]
Week 10 Day 1			
Estimated change from baseline [a]			
n	234	218	
LS Means [95% CI]	-2.43 [-6.09; 1.22]	0.41 [-3.38; 4.19]	
Standard error	1.86	1.93	
Difference of LS Means [95% CI]			-2.84 [-7.19; 1.52]
Standard error for difference			2.22
p-value			0.2015
Hedges' g [95% CI]			-0.10 [-0.28; 0.09]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	214	204	
LS Means [95% CI]	-0.73 [-4.74; 3.29]	-1.53 [-5.65; 2.60]	
Standard error	2.04	2.10	
Difference of LS Means [95% CI]			0.80 [-4.15; 5.75]
Standard error for difference			2.52
p-value			0.7506
Hedges' g [95% CI]			0.03 [-0.17; 0.22]
Week 16 Day 1			
Estimated change from baseline [a]			
n	213	182	
LS Means [95% CI]	0.01 [-3.77; 3.80]	-1.37 [-5.34; 2.61]	
Standard error	1.93	2.02	
Difference of LS Means [95% CI]			1.38 [-3.26; 6.02]
Standard error for difference			2.36
p-value			0.5597
Hedges' g [95% CI]			0.05 [-0.15; 0.25]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	205	182	
LS Means [95% CI]	-2.17 [-6.26; 1.91]	1.09 [-3.18; 5.36]	
Standard error	2.08	2.17	
Difference of LS Means [95% CI]			-3.26 [-8.40; 1.87]
Standard error for difference			2.61
p-value			0.2123
Hedges' g [95% CI]			-0.11 [-0.31; 0.09]
Week 22 Day 1			
Estimated change from baseline [a]			
n	202	164	
LS Means [95% CI]	-1.51 [-5.48; 2.46]	-0.41 [-4.63; 3.82]	
Standard error	2.02	2.15	
Difference of LS Means [95% CI]			-1.10 [-6.11; 3.91]
Standard error for difference			2.55
p-value			0.6653
Hedges' g [95% CI]			-0.04 [-0.25; 0.17]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	194	141	
LS Means [95% CI]	-0.20 [-4.35; 3.95]	0.19 [-4.35; 4.73]	
Standard error	2.11	2.31	
Difference of LS Means [95% CI]			-0.39 [-5.81; 5.03]
Standard error for difference			2.76
p-value			0.8877
Hedges' g [95% CI]			-0.01 [-0.23; 0.20]
Week 28 Day 1			
Estimated change from baseline [a]			
n	183	133	
LS Means [95% CI]	0.62 [-3.36; 4.60]	2.45 [-1.91; 6.80]	
Standard error	2.03	2.22	
Difference of LS Means [95% CI]			-1.82 [-6.95; 3.31]
Standard error for difference			2.61
p-value			0.4852
Hedges' g [95% CI]			-0.07 [-0.29; 0.16]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	171	117	
LS Means [95% CI]	0.37 [-3.80; 4.54]	4.05 [-0.66; 8.77]	
Standard error	2.12	2.40	
Difference of LS Means [95% CI]			-3.68 [-9.28; 1.91]
Standard error for difference			2.84
p-value			0.1959
Hedges' g [95% CI]			-0.14 [-0.37; 0.10]
Average [b]			
n	270	289	
LS Means [95% CI]	-0.88 [-4.06; 2.30]	0.59 [-2.71; 3.89]	
Standard error	1.62	1.68	
Difference of LS Means [95% CI]			-1.47 [-5.00; 2.05]
Standard error for difference			1.79
p-value			0.4121
Hedges' g [95% CI]			-0.05 [-0.22; 0.11]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Functional Scales/Future Perspective			
Week 4 Day 1			
Estimated change from baseline [a]			
n	251	254	
LS Means [95% CI]	9.10 [5.49; 12.71]	5.94 [2.27; 9.61]	
Standard error	1.84	1.87	
Difference of LS Means [95% CI]			3.16 [-1.05; 7.37]
Standard error for difference			2.14
p-value			0.1408
Hedges' g [95% CI]			0.11 [-0.07; 0.28]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	234	238	
LS Means [95% CI]	8.79 [5.10; 12.48]	6.93 [3.17; 10.68]	
Standard error	1.88	1.91	
Difference of LS Means [95% CI]			1.86 [-2.51; 6.23]
Standard error for difference			2.22
p-value			0.4027
Hedges' g [95% CI]			0.06 [-0.12; 0.24]
Week 10 Day 1			
Estimated change from baseline [a]			
n	234	220	
LS Means [95% CI]	9.64 [5.92; 13.35]	7.26 [3.42; 11.09]	
Standard error	1.89	1.95	
Difference of LS Means [95% CI]			2.38 [-2.08; 6.84]
Standard error for difference			2.27
p-value			0.2945
Hedges' g [95% CI]			0.08 [-0.10; 0.27]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	216	206	
LS Means [95% CI]	10.37 [6.60; 14.14]	7.03 [3.13; 10.92]	
Standard error	1.92	1.98	
Difference of LS Means [95% CI]			3.34 [-1.22; 7.91]
Standard error for difference			2.32
p-value			0.1507
Hedges' g [95% CI]			0.12 [-0.07; 0.31]
Week 16 Day 1			
Estimated change from baseline [a]			
n	214	184	
LS Means [95% CI]	10.91 [7.12; 14.70]	7.71 [3.73; 11.68]	
Standard error	1.93	2.03	
Difference of LS Means [95% CI]			3.21 [-1.45; 7.87]
Standard error for difference			2.37
p-value			0.1770
Hedges' g [95% CI]			0.11 [-0.08; 0.31]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	206	184	
LS Means [95% CI]	8.49 [4.60; 12.38]	6.50 [2.44; 10.56]	
Standard error	1.98	2.07	
Difference of LS Means [95% CI]			1.99 [-2.82; 6.79]
Standard error for difference			2.45
p-value			0.4165
Hedges' g [95% CI]			0.07 [-0.13; 0.27]
Week 22 Day 1			
Estimated change from baseline [a]			
n	203	166	
LS Means [95% CI]	10.68 [6.66; 14.70]	9.30 [5.00; 13.60]	
Standard error	2.05	2.19	
Difference of LS Means [95% CI]			1.39 [-3.73; 6.50]
Standard error for difference			2.60
p-value			0.5946
Hedges' g [95% CI]			0.05 [-0.16; 0.25]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.

b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.

CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	194	143	
LS Means [95% CI]	11.64 [7.49; 15.79]	8.29 [3.79; 12.79]	
Standard error	2.11	2.29	
Difference of LS Means [95% CI]			3.35 [-2.03; 8.73]
Standard error for difference			2.74
p-value			0.2215
Hedges' g [95% CI]			0.12 [-0.10; 0.33]
Week 28 Day 1			
Estimated change from baseline [a]			
n	183	135	
LS Means [95% CI]	8.11 [4.10; 12.12]	8.97 [4.61; 13.33]	
Standard error	2.04	2.22	
Difference of LS Means [95% CI]			-0.86 [-6.02; 4.30]
Standard error for difference			2.62
p-value			0.7425
Hedges' g [95% CI]			-0.03 [-0.25; 0.19]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	171	118	
LS Means [95% CI]	10.17 [6.09; 14.25]	8.06 [3.51; 12.61]	
Standard error	2.08	2.32	
Difference of LS Means [95% CI]			2.11 [-3.27; 7.49]
Standard error for difference			2.74
p-value			0.4409
Hedges' g [95% CI]			0.08 [-0.15; 0.31]
Average [b]			
n	271	291	
LS Means [95% CI]	9.79 [6.59; 12.99]	7.60 [4.28; 10.92]	
Standard error	1.63	1.69	
Difference of LS Means [95% CI]			2.19 [-1.37; 5.75]
Standard error for difference			1.81
p-value			0.2267
Hedges' g [95% CI]			0.08 [-0.09; 0.24]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Symptom Scales/Arm Symptoms			
Week 4 Day 1			
Estimated change from baseline [a]			
n	251	254	
LS Means [95% CI]	-5.30 [-7.36; -3.23]	-2.26 [-4.35; -0.17]	
Standard error	1.05	1.07	
Difference of LS Means [95% CI]			-3.04 [-5.47; -0.61]
Standard error for difference			1.24
p-value			0.0144
Hedges' g [95% CI]			-0.18 [-0.36; -0.01]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	234	238	
LS Means [95% CI]	-5.16 [-7.16; -3.17]	-2.60 [-4.63; -0.57]	
Standard error	1.02	1.03	
Difference of LS Means [95% CI]			-2.57 [-4.90; -0.24]
Standard error for difference			1.18
p-value			0.0307
Hedges' g [95% CI]			-0.16 [-0.34; 0.02]
Week 10 Day 1			
Estimated change from baseline [a]			
n	234	220	
LS Means [95% CI]	-5.06 [-7.05; -3.07]	-2.32 [-4.38; -0.27]	
Standard error	1.01	1.05	
Difference of LS Means [95% CI]			-2.73 [-5.07; -0.40]
Standard error for difference			1.19
p-value			0.0218
Hedges' g [95% CI]			-0.18 [-0.36; 0.01]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	216	206	
LS Means [95% CI]	-5.74 [-7.92; -3.56]	-2.37 [-4.61; -0.14]	
Standard error	1.11	1.14	
Difference of LS Means [95% CI]			-3.37 [-6.02; -0.71]
Standard error for difference			1.35
p-value			0.0132
Hedges' g [95% CI]			-0.21 [-0.40; -0.01]
Week 16 Day 1			
Estimated change from baseline [a]			
n	214	184	
LS Means [95% CI]	-5.56 [-7.74; -3.39]	-1.10 [-3.38; 1.19]	
Standard error	1.11	1.16	
Difference of LS Means [95% CI]			-4.47 [-7.17; -1.77]
Standard error for difference			1.37
p-value			0.0012
Hedges' g [95% CI]			-0.28 [-0.48; -0.08]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	206	184	
LS Means [95% CI]	-5.91 [-8.05; -3.76]	-2.46 [-4.70; -0.21]	
Standard error	1.09	1.14	
Difference of LS Means [95% CI]			-3.45 [-6.10; -0.81]
Standard error for difference			1.34
p-value			0.0106
Hedges' g [95% CI]			-0.22 [-0.42; -0.02]
Week 22 Day 1			
Estimated change from baseline [a]			
n	203	166	
LS Means [95% CI]	-5.73 [-8.02; -3.44]	-2.26 [-4.69; 0.18]	
Standard error	1.17	1.24	
Difference of LS Means [95% CI]			-3.47 [-6.39; -0.56]
Standard error for difference			1.49
p-value			0.0198
Hedges' g [95% CI]			-0.21 [-0.42; -0.01]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	194	143	
LS Means [95% CI]	-6.39 [-8.59; -4.19]	-3.42 [-5.83; -1.01]	
Standard error	1.12	1.23	
Difference of LS Means [95% CI]			-2.97 [-5.80; -0.13]
Standard error for difference			1.44
p-value			0.0402
Hedges' g [95% CI]			-0.19 [-0.41; 0.02]
Week 28 Day 1			
Estimated change from baseline [a]			
n	183	135	
LS Means [95% CI]	-5.50 [-7.77; -3.23]	0.43 [-2.05; 2.90]	
Standard error	1.15	1.26	
Difference of LS Means [95% CI]			-5.93 [-8.87; -2.99]
Standard error for difference			1.50
p-value			<.0001
Hedges' g [95% CI]			-0.39 [-0.61; -0.16]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	171	118	
LS Means [95% CI]	-5.17 [-7.53; -2.80]	0.88 [-1.77; 3.53]	
Standard error	1.20	1.35	
Difference of LS Means [95% CI]			-6.05 [-9.21; -2.89]
Standard error for difference			1.61
p-value			0.0002
Hedges' g [95% CI]			-0.39 [-0.63; -0.16]
Average [b]			
n	271	291	
LS Means [95% CI]	-5.55 [-7.33; -3.78]	-1.75 [-3.59; 0.10]	
Standard error	0.90	0.94	
Difference of LS Means [95% CI]			-3.80 [-5.77; -1.84]
Standard error for difference			1.00
p-value			0.0002
Hedges' g [95% CI]			-0.25 [-0.41; -0.08]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Symptom Scales/Breast Symptoms			
Week 4 Day 1			
Estimated change from baseline [a]			
n	251	254	
LS Means [95% CI]	-2.75 [-4.40; -1.10]	-3.13 [-4.81; -1.46]	
Standard error	0.84	0.85	
Difference of LS Means [95% CI]			0.38 [-1.56; 2.32]
Standard error for difference			0.99
p-value			0.6980
Hedges' g [95% CI]			0.03 [-0.15; 0.20]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	234	238	
LS Means [95% CI]	-3.01 [-4.71; -1.32]	-3.77 [-5.48; -2.05]	
Standard error	0.86	0.87	
Difference of LS Means [95% CI]			0.76 [-1.26; 2.78]
Standard error for difference			1.03
p-value			0.4622
Hedges' g [95% CI]			0.06 [-0.12; 0.24]
Week 10 Day 1			
Estimated change from baseline [a]			
n	234	220	
LS Means [95% CI]	-4.23 [-5.85; -2.60]	-4.07 [-5.75; -2.40]	
Standard error	0.83	0.85	
Difference of LS Means [95% CI]			-0.15 [-2.07; 1.77]
Standard error for difference			0.98
p-value			0.8760
Hedges' g [95% CI]			-0.01 [-0.20; 0.17]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	216	206	
LS Means [95% CI]	-4.93 [-6.60; -3.27]	-3.51 [-5.23; -1.80]	
Standard error	0.85	0.87	
Difference of LS Means [95% CI]			-1.42 [-3.42; 0.57]
Standard error for difference			1.02
p-value			0.1624
Hedges' g [95% CI]			-0.11 [-0.30; 0.08]
Week 16 Day 1			
Estimated change from baseline [a]			
n	214	184	
LS Means [95% CI]	-5.34 [-7.04; -3.64]	-3.95 [-5.73; -2.16]	
Standard error	0.87	0.91	
Difference of LS Means [95% CI]			-1.39 [-3.49; 0.70]
Standard error for difference			1.06
p-value			0.1916
Hedges' g [95% CI]			-0.11 [-0.31; 0.09]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	206	184	
LS Means [95% CI]	-6.57 [-8.29; -4.86]	-3.39 [-5.20; -1.59]	
Standard error	0.87	0.92	
Difference of LS Means [95% CI]			-3.18 [-5.31; -1.06]
Standard error for difference			1.08
p-value			0.0034
Hedges' g [95% CI]			-0.25 [-0.45; -0.05]
Week 22 Day 1			
Estimated change from baseline [a]			
n	202	166	
LS Means [95% CI]	-6.80 [-8.51; -5.08]	-3.01 [-4.85; -1.18]	
Standard error	0.87	0.93	
Difference of LS Means [95% CI]			-3.78 [-5.93; -1.64]
Standard error for difference			1.09
p-value			0.0006
Hedges' g [95% CI]			-0.31 [-0.51; -0.10]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	194	143	
LS Means [95% CI]	-5.49 [-7.25; -3.72]	-3.37 [-5.29; -1.45]	
Standard error	0.90	0.98	
Difference of LS Means [95% CI]			-2.12 [-4.38; 0.15]
Standard error for difference			1.15
p-value			0.0668
Hedges' g [95% CI]			-0.17 [-0.39; 0.04]
Week 28 Day 1			
Estimated change from baseline [a]			
n	183	135	
LS Means [95% CI]	-5.77 [-7.49; -4.06]	-3.44 [-5.30; -1.58]	
Standard error	0.87	0.95	
Difference of LS Means [95% CI]			-2.33 [-4.51; -0.16]
Standard error for difference			1.11
p-value			0.0356
Hedges' g [95% CI]			-0.20 [-0.43; 0.02]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	171	118	
LS Means [95% CI]	-5.92 [-7.72; -4.12]	-3.44 [-5.47; -1.42]	
Standard error	0.92	1.03	
Difference of LS Means [95% CI]			-2.48 [-4.86; -0.09]
Standard error for difference			1.21
p-value			0.0417
Hedges' g [95% CI]			-0.21 [-0.45; 0.02]
Average [b]			
n	271	291	
LS Means [95% CI]	-5.08 [-6.48; -3.68]	-3.51 [-4.97; -2.05]	
Standard error	0.71	0.74	
Difference of LS Means [95% CI]			-1.57 [-3.11; -0.03]
Standard error for difference			0.78
p-value			0.0456
Hedges' g [95% CI]			-0.13 [-0.29; 0.04]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Symptom Scales/Systemic Therapy Side Effects			
Week 4 Day 1			
Estimated change from baseline [a]			
n	251	254	
LS Means [95% CI]	5.94 [4.13; 7.76]	4.13 [2.28; 5.97]	
Standard error	0.93	0.94	
Difference of LS Means [95% CI]			1.82 [-0.22; 3.86]
Standard error for difference			1.04
p-value			0.0806
Hedges' g [95% CI]			0.12 [-0.05; 0.30]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	234	238	
LS Means [95% CI]	9.87 [7.92; 11.83]	6.33 [4.35; 8.30]	
Standard error	1.00	1.01	
Difference of LS Means [95% CI]			3.55 [1.26; 5.83]
Standard error for difference			1.16
p-value			0.0024
Hedges' g [95% CI]			0.23 [0.05; 0.41]
Week 10 Day 1			
Estimated change from baseline [a]			
n	234	220	
LS Means [95% CI]	8.34 [6.38; 10.30]	6.53 [4.52; 8.55]	
Standard error	1.00	1.03	
Difference of LS Means [95% CI]			1.80 [-0.52; 4.12]
Standard error for difference			1.18
p-value			0.1271
Hedges' g [95% CI]			0.12 [-0.07; 0.30]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	216	206	
LS Means [95% CI]	8.75 [6.74; 10.76]	6.16 [4.10; 8.22]	
Standard error	1.02	1.05	
Difference of LS Means [95% CI]			2.59 [0.18; 4.99]
Standard error for difference			1.22
p-value			0.0350
Hedges' g [95% CI]			0.17 [-0.02; 0.36]
Week 16 Day 1			
Estimated change from baseline [a]			
n	214	184	
LS Means [95% CI]	7.93 [5.90; 9.95]	5.99 [3.88; 8.10]	
Standard error	1.03	1.07	
Difference of LS Means [95% CI]			1.94 [-0.52; 4.40]
Standard error for difference			1.25
p-value			0.1225
Hedges' g [95% CI]			0.13 [-0.07; 0.33]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	206	184	
LS Means [95% CI]	7.38 [5.37; 9.39]	5.91 [3.82; 8.01]	
Standard error	1.02	1.07	
Difference of LS Means [95% CI]			1.47 [-0.98; 3.91]
Standard error for difference			1.24
p-value			0.2388
Hedges' g [95% CI]			0.10 [-0.10; 0.30]
Week 22 Day 1			
Estimated change from baseline [a]			
n	203	166	
LS Means [95% CI]	6.97 [4.87; 9.08]	6.64 [4.40; 8.88]	
Standard error	1.07	1.14	
Difference of LS Means [95% CI]			0.33 [-2.31; 2.98]
Standard error for difference			1.35
p-value			0.8046
Hedges' g [95% CI]			0.02 [-0.18; 0.23]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	194	143	
LS Means [95% CI]	6.15 [4.10; 8.20]	4.66 [2.46; 6.87]	
Standard error	1.04	1.12	
Difference of LS Means [95% CI]			1.49 [-1.08; 4.05]
Standard error for difference			1.31
p-value			0.2562
Hedges' g [95% CI]			0.11 [-0.11; 0.32]
Week 28 Day 1			
Estimated change from baseline [a]			
n	183	135	
LS Means [95% CI]	5.57 [3.47; 7.67]	5.12 [2.86; 7.39]	
Standard error	1.07	1.15	
Difference of LS Means [95% CI]			0.45 [-2.21; 3.10]
Standard error for difference			1.35
p-value			0.7422
Hedges' g [95% CI]			0.03 [-0.19; 0.25]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.

b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.

CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	171	118	
LS Means [95% CI]	5.14 [3.07; 7.22]	4.81 [2.53; 7.09]	
Standard error	1.05	1.16	
Difference of LS Means [95% CI]			0.33 [-2.32; 2.99]
Standard error for difference			1.35
p-value			0.8049
Hedges' g [95% CI]			0.02 [-0.21; 0.26]
Average [b]			
n	271	291	
LS Means [95% CI]	7.20 [5.49; 8.92]	5.63 [3.85; 7.40]	
Standard error	0.87	0.90	
Difference of LS Means [95% CI]			1.58 [-0.32; 3.47]
Standard error for difference			0.97
p-value			0.1035
Hedges' g [95% CI]			0.11 [-0.06; 0.27]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Symptom Scales/Endocrine Therapy Symptoms			
Week 4 Day 1			
Estimated change from baseline [a]			
n	251	254	
LS Means [95% CI]	-2.17 [-3.73; -0.60]	-0.94 [-2.52; 0.65]	
Standard error	0.80	0.81	
Difference of LS Means [95% CI]			-1.23 [-3.03; 0.56]
Standard error for difference			0.91
p-value			0.1782
Hedges' g [95% CI]			-0.10 [-0.27; 0.08]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	234	238	
LS Means [95% CI]	-2.36 [-4.02; -0.71]	-1.26 [-2.93; 0.41]	
Standard error	0.84	0.85	
Difference of LS Means [95% CI]			-1.10 [-3.05; 0.85]
Standard error for difference			0.99
p-value			0.2669
Hedges' g [95% CI]			-0.08 [-0.27; 0.10]
Week 10 Day 1			
Estimated change from baseline [a]			
n	234	220	
LS Means [95% CI]	-2.68 [-4.30; -1.07]	-0.88 [-2.54; 0.78]	
Standard error	0.82	0.84	
Difference of LS Means [95% CI]			-1.81 [-3.71; 0.10]
Standard error for difference			0.97
p-value			0.0629
Hedges' g [95% CI]			-0.14 [-0.33; 0.04]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	216	206	
LS Means [95% CI]	-2.01 [-3.68; -0.34]	-0.83 [-2.54; 0.88]	
Standard error	0.85	0.87	
Difference of LS Means [95% CI]			-1.18 [-3.18; 0.83]
Standard error for difference			1.02
p-value			0.2493
Hedges' g [95% CI]			-0.09 [-0.28; 0.10]
Week 16 Day 1			
Estimated change from baseline [a]			
n	214	184	
LS Means [95% CI]	-2.64 [-4.30; -0.98]	-0.33 [-2.07; 1.41]	
Standard error	0.85	0.89	
Difference of LS Means [95% CI]			-2.31 [-4.34; -0.28]
Standard error for difference			1.03
p-value			0.0257
Hedges' g [95% CI]			-0.19 [-0.39; 0.01]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	206	184	
LS Means [95% CI]	-3.05 [-4.80; -1.31]	-0.61 [-2.43; 1.21]	
Standard error	0.89	0.93	
Difference of LS Means [95% CI]			-2.44 [-4.60; -0.28]
Standard error for difference			1.10
p-value			0.0266
Hedges' g [95% CI]			-0.19 [-0.39; 0.01]
Week 22 Day 1			
Estimated change from baseline [a]			
n	203	166	
LS Means [95% CI]	-3.07 [-4.71; -1.42]	-0.10 [-1.85; 1.64]	
Standard error	0.84	0.89	
Difference of LS Means [95% CI]			-2.96 [-4.98; -0.95]
Standard error for difference			1.03
p-value			0.0041
Hedges' g [95% CI]			-0.25 [-0.46; -0.05]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	194	143	
LS Means [95% CI]	-3.47 [-5.18; -1.77]	0.30 [-1.54; 2.15]	
Standard error	0.87	0.94	
Difference of LS Means [95% CI]			-3.78 [-5.93; -1.62]
Standard error for difference			1.10
p-value			0.0006
Hedges' g [95% CI]			-0.32 [-0.54; -0.10]
Week 28 Day 1			
Estimated change from baseline [a]			
n	183	135	
LS Means [95% CI]	-3.69 [-5.43; -1.95]	0.27 [-1.63; 2.17]	
Standard error	0.89	0.97	
Difference of LS Means [95% CI]			-3.96 [-6.19; -1.73]
Standard error for difference			1.14
p-value			0.0005
Hedges' g [95% CI]			-0.34 [-0.56; -0.11]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	171	118	
LS Means [95% CI]	-2.40 [-4.20; -0.61]	0.53 [-1.46; 2.52]	
Standard error	0.91	1.01	
Difference of LS Means [95% CI]			-2.93 [-5.28; -0.58]
Standard error for difference			1.19
p-value			0.0146
Hedges' g [95% CI]			-0.25 [-0.49; -0.02]
Average [b]			
n	271	291	
LS Means [95% CI]	-2.75 [-4.16; -1.34]	-0.39 [-1.85; 1.08]	
Standard error	0.72	0.74	
Difference of LS Means [95% CI]			-2.37 [-3.93; -0.81]
Standard error for difference			0.79
p-value			0.0029
Hedges' g [95% CI]			-0.19 [-0.36; -0.03]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Symptom Scales/Skin Mucosis Symptoms			
Week 4 Day 1			
Estimated change from baseline [a]			
n	251	254	
LS Means [95% CI]	1.63 [-0.19; 3.44]	3.78 [1.93; 5.62]	
Standard error	0.92	0.94	
Difference of LS Means [95% CI]			-2.15 [-4.16; -0.13]
Standard error for difference			1.03
p-value			0.0371
Hedges' g [95% CI]			-0.14 [-0.32; 0.03]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	234	238	
LS Means [95% CI]	1.27 [-0.85; 3.38]	9.80 [7.67; 11.93]	
Standard error	1.08	1.09	
Difference of LS Means [95% CI]			-8.53 [-11.07; -6.00]
Standard error for difference			1.29
p-value			<.0001
Hedges' g [95% CI]			-0.51 [-0.70; -0.33]
Week 10 Day 1			
Estimated change from baseline [a]			
n	234	220	
LS Means [95% CI]	1.85 [-0.37; 4.08]	12.92 [10.65; 15.19]	
Standard error	1.13	1.16	
Difference of LS Means [95% CI]			-11.07 [-13.81; -8.32]
Standard error for difference			1.40
p-value			<.0001
Hedges' g [95% CI]			-0.64 [-0.83; -0.45]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	215	206	
LS Means [95% CI]	1.97 [-0.18; 4.13]	12.83 [10.63; 15.03]	
Standard error	1.10	1.12	
Difference of LS Means [95% CI]			-10.86 [-13.49; -8.23]
Standard error for difference			1.34
p-value			<.0001
Hedges' g [95% CI]			-0.67 [-0.87; -0.48]
Week 16 Day 1			
Estimated change from baseline [a]			
n	214	184	
LS Means [95% CI]	2.05 [0.00; 4.10]	12.18 [10.05; 14.32]	
Standard error	1.04	1.09	
Difference of LS Means [95% CI]			-10.13 [-12.62; -7.63]
Standard error for difference			1.27
p-value			<.0001
Hedges' g [95% CI]			-0.67 [-0.87; -0.47]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	206	184	
LS Means [95% CI]	2.63 [0.53; 4.74]	11.53 [9.34; 13.72]	
Standard error	1.07	1.11	
Difference of LS Means [95% CI]			-8.90 [-11.48; -6.32]
Standard error for difference			1.31
p-value			<.0001
Hedges' g [95% CI]			-0.58 [-0.78; -0.38]
Week 22 Day 1			
Estimated change from baseline [a]			
n	203	166	
LS Means [95% CI]	1.94 [-0.13; 4.01]	12.65 [10.45; 14.84]	
Standard error	1.05	1.12	
Difference of LS Means [95% CI]			-10.71 [-13.27; -8.15]
Standard error for difference			1.30
p-value			<.0001
Hedges' g [95% CI]			-0.72 [-0.94; -0.51]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	194	143	
LS Means [95% CI]	1.91 [-0.25; 4.08]	13.09 [10.72; 15.45]	
Standard error	1.10	1.20	
Difference of LS Means [95% CI]			-11.17 [-13.96; -8.38]
Standard error for difference			1.42
p-value			<.0001
Hedges' g [95% CI]			-0.74 [-0.97; -0.52]
Week 28 Day 1			
Estimated change from baseline [a]			
n	183	135	
LS Means [95% CI]	2.58 [0.40; 4.76]	13.36 [10.98; 15.74]	
Standard error	1.11	1.21	
Difference of LS Means [95% CI]			-10.78 [-13.59; -7.97]
Standard error for difference			1.43
p-value			<.0001
Hedges' g [95% CI]			-0.74 [-0.96; -0.51]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10SEP2024 7:16; Program name: T.2.12.15_EORTC_BR45_MMRM_FAS.sas; Output name: T.2.12.15_EORTC_BR45_MMRM_FAS.rtf; DI-EG project ID: D9670C00001;

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	171	118	
LS Means [95% CI]	2.44 [0.23; 4.64]	13.07 [10.62; 15.52]	
Standard error	1.12	1.25	
Difference of LS Means [95% CI]			-10.63 [-13.53; -7.74]
Standard error for difference			1.47
p-value			<.0001
Hedges' g [95% CI]			-0.74 [-0.99; -0.50]
Average [b]			
n	271	291	
LS Means [95% CI]	2.03 [0.25; 3.81]	11.52 [9.68; 13.36]	
Standard error	0.91	0.94	
Difference of LS Means [95% CI]			-9.49 [-11.49; -7.50]
Standard error for difference			1.02
p-value			<.0001
Hedges' g [95% CI]			-0.61 [-0.78; -0.44]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Symptom Scales/Endocrine Sexual Symptoms			
Week 4 Day 1			
Estimated change from baseline [a]			
n	251	253	
LS Means [95% CI]	3.05 [0.64; 5.46]	1.52 [-0.93; 3.98]	
Standard error	1.23	1.25	
Difference of LS Means [95% CI]			1.53 [-1.27; 4.32]
Standard error for difference			1.42
p-value			0.2842
Hedges' g [95% CI]			0.08 [-0.10; 0.25]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 7 Day 1			
Estimated change from baseline [a]			
n	234	237	
LS Means [95% CI]	3.99 [1.58; 6.40]	1.52 [-0.93; 3.98]	
Standard error	1.23	1.25	
Difference of LS Means [95% CI]			2.47 [-0.34; 5.27]
Standard error for difference			1.43
p-value			0.0848
Hedges' g [95% CI]			0.13 [-0.05; 0.31]
Week 10 Day 1			
Estimated change from baseline [a]			
n	234	219	
LS Means [95% CI]	4.35 [1.78; 6.92]	2.51 [-0.13; 5.15]	
Standard error	1.31	1.35	
Difference of LS Means [95% CI]			1.85 [-1.26; 4.95]
Standard error for difference			1.58
p-value			0.2434
Hedges' g [95% CI]			0.09 [-0.09; 0.28]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 13 Day 1			
Estimated change from baseline [a]			
n	216	205	
LS Means [95% CI]	4.16 [1.63; 6.69]	1.97 [-0.63; 4.57]	
Standard error	1.29	1.32	
Difference of LS Means [95% CI]			2.19 [-0.85; 5.23]
Standard error for difference			1.55
p-value			0.1571
Hedges' g [95% CI]			0.12 [-0.08; 0.31]
Week 16 Day 1			
Estimated change from baseline [a]			
n	214	183	
LS Means [95% CI]	4.56 [2.00; 7.13]	1.29 [-1.39; 3.97]	
Standard error	1.31	1.37	
Difference of LS Means [95% CI]			3.27 [0.13; 6.42]
Standard error for difference			1.60
p-value			0.0414
Hedges' g [95% CI]			0.17 [-0.02; 0.37]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.

b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.

CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 19 Day 1			
Estimated change from baseline [a]			
n	206	183	
LS Means [95% CI]	4.37 [1.84; 6.90]	-0.52 [-3.20; 2.15]	
Standard error	1.29	1.36	
Difference of LS Means [95% CI]			4.90 [1.79; 8.01]
Standard error for difference			1.58
p-value			0.0021
Hedges' g [95% CI]			0.26 [0.06; 0.46]
Week 22 Day 1			
Estimated change from baseline [a]			
n	203	165	
LS Means [95% CI]	4.79 [2.11; 7.48]	1.06 [-1.81; 3.93]	
Standard error	1.37	1.46	
Difference of LS Means [95% CI]			3.74 [0.33; 7.14]
Standard error for difference			1.73
p-value			0.0316
Hedges' g [95% CI]			0.19 [-0.01; 0.40]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 25 Day 1			
Estimated change from baseline [a]			
n	194	142	
LS Means [95% CI]	4.23 [1.61; 6.86]	-0.02 [-2.86; 2.82]	
Standard error	1.34	1.44	
Difference of LS Means [95% CI]			4.25 [0.92; 7.58]
Standard error for difference			1.69
p-value			0.0125
Hedges' g [95% CI]			0.24 [0.02; 0.45]
Week 28 Day 1			
Estimated change from baseline [a]			
n	183	134	
LS Means [95% CI]	3.49 [0.80; 6.17]	1.48 [-1.44; 4.39]	
Standard error	1.37	1.49	
Difference of LS Means [95% CI]			2.01 [-1.43; 5.46]
Standard error for difference			1.75
p-value			0.2519
Hedges' g [95% CI]			0.11 [-0.11; 0.33]

N: number of patients in analysis set; n: number of observations

a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Table 2.12.15 EORTC-QLQ-BR45 - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Breast-06	T-DXd N=436	Chemotherapy N=430	T-DXd vs. Chemotherapy
Week 31 Day 1			
Estimated change from baseline [a]			
n	171	117	
LS Means [95% CI]	3.95 [1.11; 6.78]	2.68 [-0.45; 5.80]	
Standard error	1.44	1.59	
Difference of LS Means [95% CI]			1.27 [-2.46; 5.00]
Standard error for difference			1.90
p-value			0.5034
Hedges' g [95% CI]			0.07 [-0.17; 0.30]
Average [b]			
n	271	290	
LS Means [95% CI]	4.10 [1.92; 6.27]	1.35 [-0.91; 3.61]	
Standard error	1.11	1.15	
Difference of LS Means [95% CI]			2.75 [0.32; 5.18]
Standard error for difference			1.24
p-value			0.0268
Hedges' g [95% CI]			0.14 [-0.02; 0.31]

N: number of patients in analysis set; n: number of observations
a. LS Means of changes from baseline reflect an overall average over the analyzed period and were estimated by application of a MMRM model including treatment, visit, treatment-by-visit interaction and the stratification factors as fixed effects, baseline score and baseline-by-visit interaction. The within-subject error was modelled as described in the GE-PSAP. Estimates were derived along two-sided 95% CI and a two-sided p-value for the estimated treatment difference.Hedges' g were derived based on the LS Means.
b. The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale. Time has been converted in months using 1 month = 30.4375 days.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements; Q1: 1st quartile; Q3: 3rd quartile

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Abbildung 2.12.10 EORTC-QLQ-BR45 – Plot of least-square means of repeated measures analysis of change from baseline – FAS

Daiichi Sankyo Europe GmbH
Data Intelligence – Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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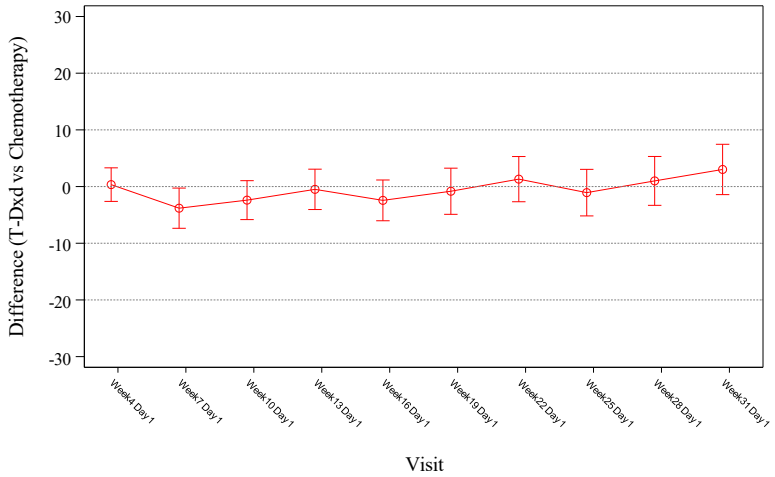
Statistical analyses for AMNOG (HTA Germany)

Figure 2.12.10 EORTC-QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Functional Scales/Body Image



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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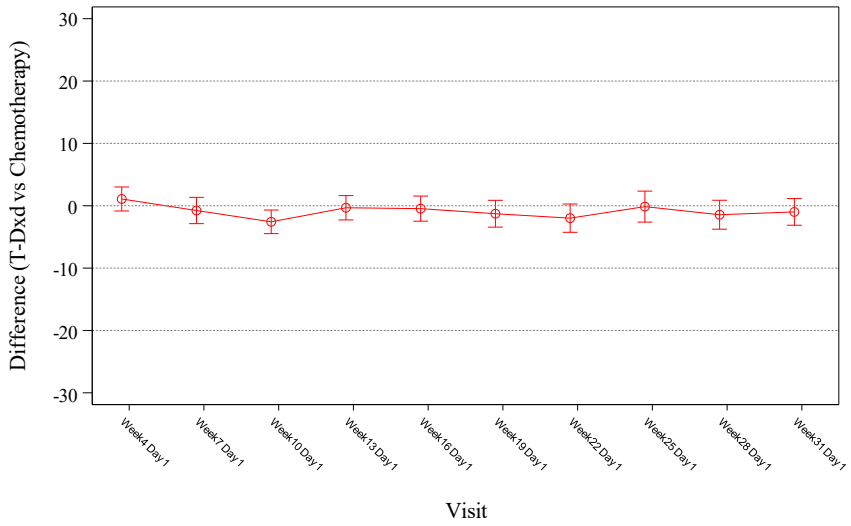
Figure 2.12.10 EORTC-QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Functional Scales/Sexual Functioning



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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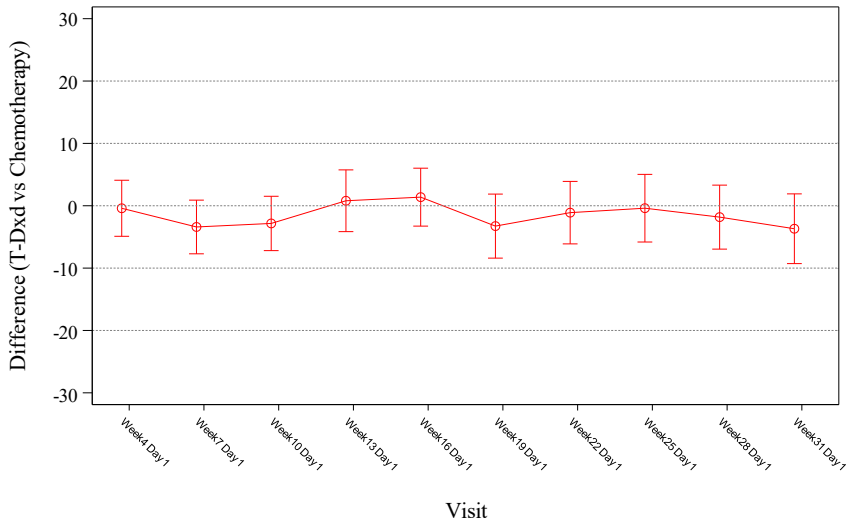
Figure 2.12.10 EORTC-QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Functional Scales/Breast Satisfaction



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
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CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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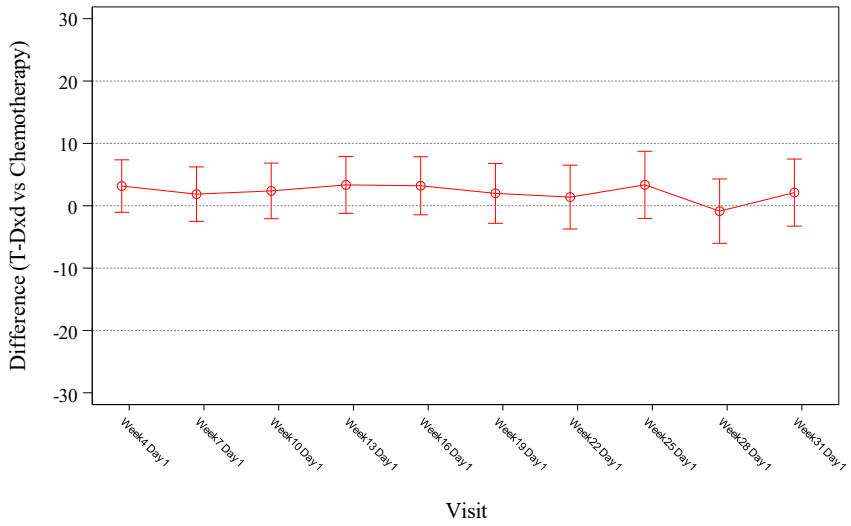
Figure 2.12.10 EORTC-QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Functional Scales/Future Perspective



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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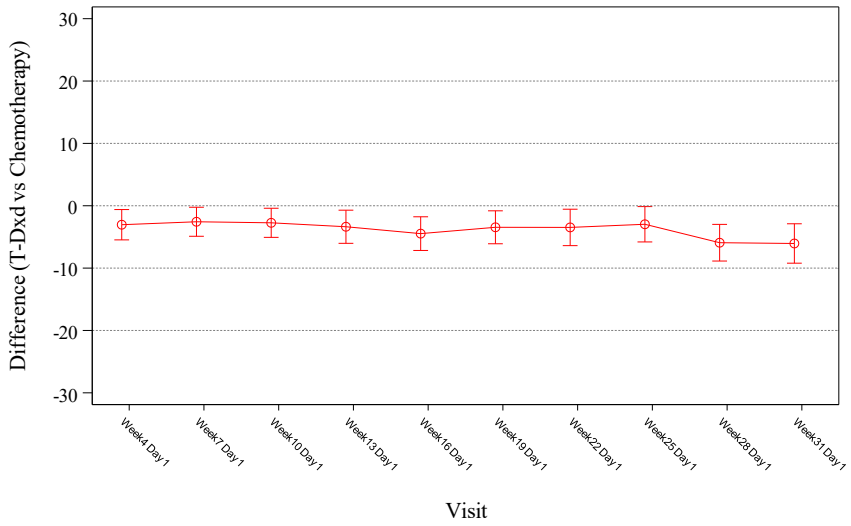
Figure 2.12.10 EORTC-QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Symptom Scales/Arm Symptoms



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
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CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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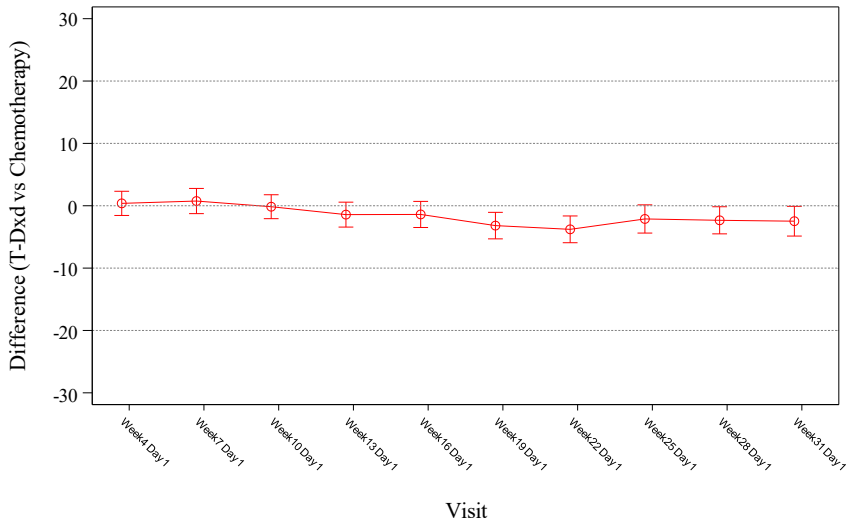
Figure 2.12.10 EORTC-QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Symptom Scales/Breast Symptoms



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
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CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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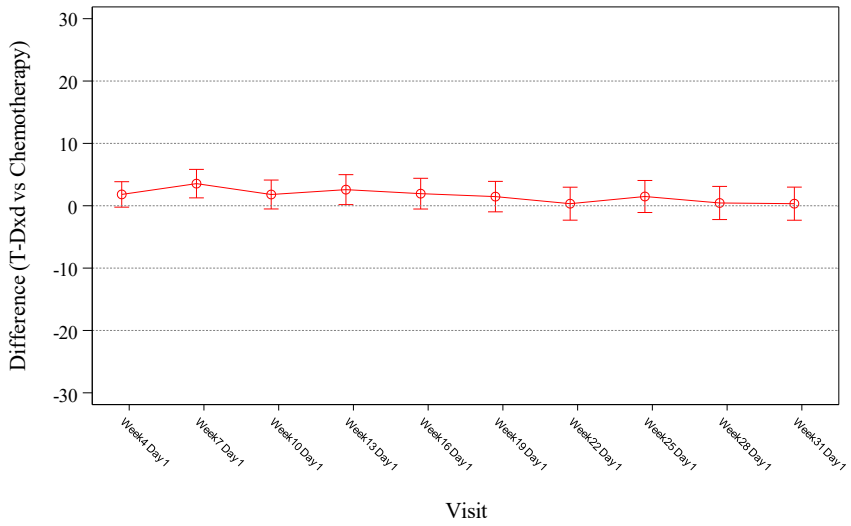
Figure 2.12.10 EORTC-QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Symptom Scales/Systemic Therapy Side Effects



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
The analyzed period is computed as the time from baseline until Investigator records PD or 7 months after randomization (whichever occurs first) with <= 75% missing data per scale.
Time has been converted in months using 1 month = 30.4375 days.
CI: Confidence Interval; LS: least square; MMRM: mixed model for repeated measurement.

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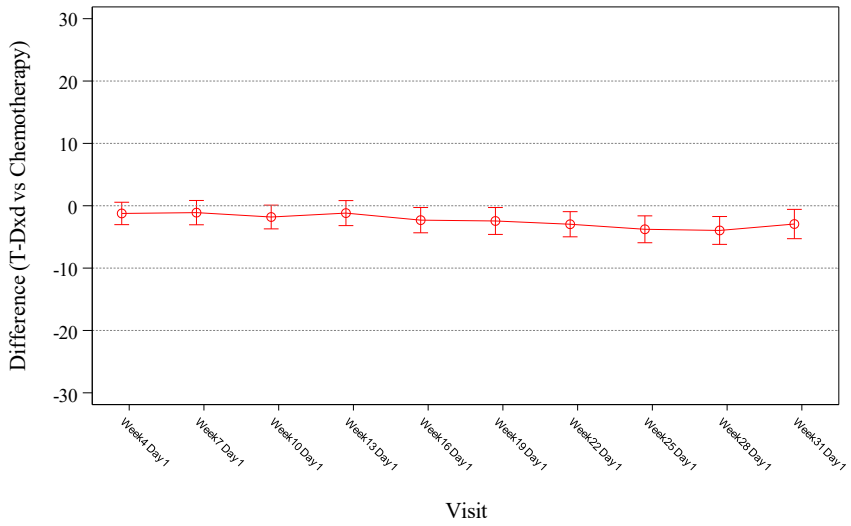
Figure 2.12.10 EORTC-QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Symptom Scales/Endocrine Therapy Symptoms



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
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Figure 2.12.10 EORTC-QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Symptom Scales/Skin Mucosis Symptoms

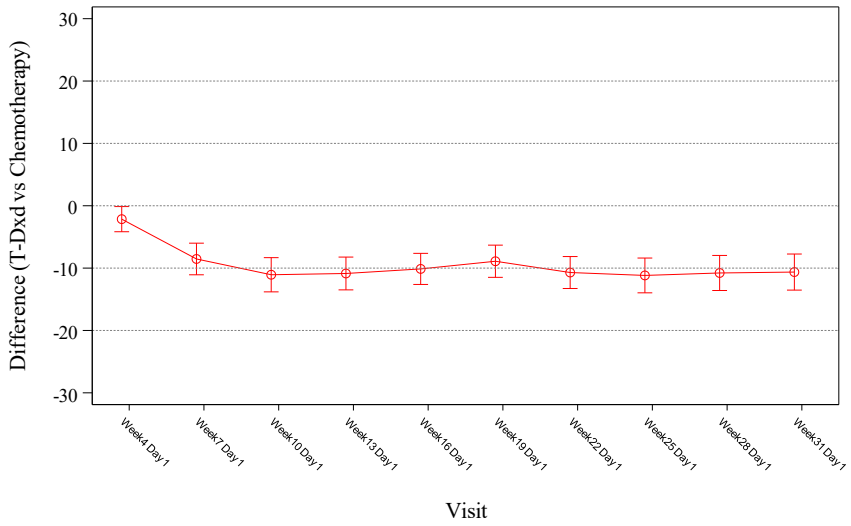

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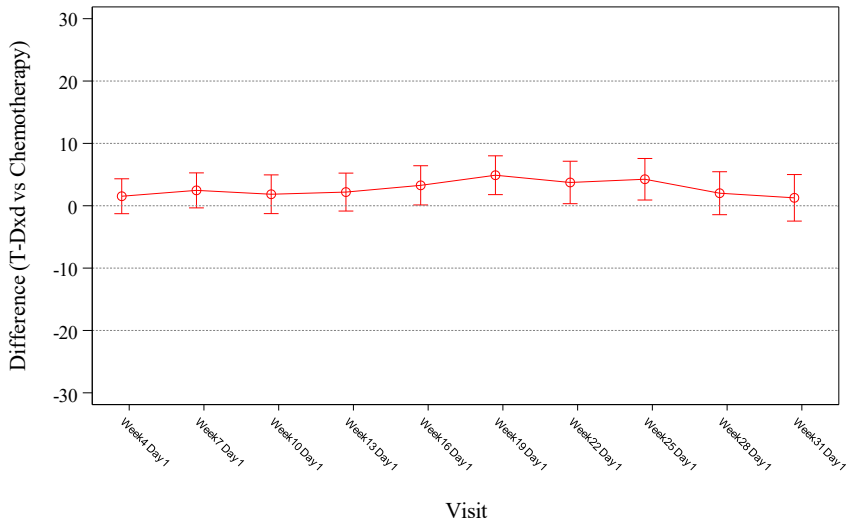
Figure 2.12.10 EORTC-QLQ-BR45 - Plot of least-square means of repeated measures analysis of change from baseline - Full Analysis Set
Symptom Scales/Endocrine Sexual Symptoms



Difference in LS Means based on mean changes from baseline estimated LS means (error bars: 95% CI) from MMRM model. Error bars are not displayed if number of subjects with an observation at the visit is less than 10. Lines are not displayed if number of subjects with an observation at the nominal time point is less than 5. Visit allocation as described in study SAP.
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Anhang 4-G 3.4 PGI-S

Tabelle 2.13.1 PGI-S – Zeit bis zur bestätigten Verschlechterung – FAS

Table 2.13.1 PGI-S - Time to confirmed deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	125 (28.7)	13.8 [9.6; 20.8]	149 (34.7)	8.3 [4.9; 10.4]	0.7574 [0.5948; 0.9624] 0.0235	0.0235
Subjects with censoring event	311 (71.3)		281 (65.3)			
Baseline score not allowing for deterioration	3 (0.7)		3 (0.7)			
Deterioration after 2 or more missed assessments	3 (0.7)		3 (0.7)			
No baseline data	157 (36.0)		87 (20.2)			
No deterioration	128 (29.4)		129 (30.0)			
No evaluable visit	20 (4.6)		59 (13.7)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

Tabelle 2.13.2 PGI-S – Zeit bis zur bestätigten Verschlechterung – Subgruppenanalyse – FAS

Table 2.13.2 PGI-S - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Age at randomization						0.2469
<65 years of age	93 / 302 (30.8)	11.8 [8.9; 25.6]	100 / 297 (33.7)	9.0 [5.5; 10.4]	0.8291 [0.6232; 1.1026] 0.1979	
≥65 years of age	32 / 134 (23.9)	18.7 [5.0; NE]	49 / 133 (36.8)	5.5 [2.7; 13.1]	0.5975 [0.3757; 0.9356] 0.0240	
Race						0.3739
Asian	62 / 154 (40.3)	18.7 [8.9; 29.8]	67 / 151 (44.4)	8.3 [4.8; 12.5]	0.7439 [0.5216; 1.0582] 0.0993	
White	56 / 231 (24.2)	10.3 [5.6; 15.8]	72 / 230 (31.3)	8.5 [3.5; 13.1]	0.8587 [0.6030; 1.2166] 0.3871	
Other	7 / 51 (13.7)	20.8 [2.1; NE]	10 / 49 (20.4)	2.1 [1.3; NE]	0.3752 [0.1264; 1.0207] 0.0513	
Region						0.9595
Asia	61 / 149 (40.9)	18.7 [8.9; 29.8]	66 / 147 (44.9)	8.3 [4.8; 12.5]	0.7593 [0.5315; 1.0820] 0.1271	
Europe	51 / 227 (22.5)	11.1 [5.6; NE]	65 / 213 (30.5)	6.0 [2.8; 13.1]	0.7728 [0.5330; 1.1144] 0.1652	
Rest of the World	13 / 60 (21.7)	15.8 [3.0; NE]	18 / 70 (25.7)	9.1 [2.8; NE]	0.7515 [0.3497; 1.5572] 0.4436	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 05SEP2024 15:55; Program name: T.2.13.2_PGIS_TTCDet_FAS_SUB.sas; Output name: T.2.13.2_PGIS_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.13.2 PGI-S - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
HER2 IHC expression						0.5365
IHC 1+	72 / 239 (30.1)	11.4 [6.2; 25.6]	85 / 234 (36.3)	7.7 [4.8; 10.4]	0.8220 [0.5967; 1.1289] 0.2243	
IHC 2+/ISH-	28 / 117 (23.9)	NE [6.9; NE]	38 / 118 (32.2)	8.5 [2.8; 13.1]	0.5904 [0.3574; 0.9634] 0.0348	
IHC >0 <1+	24 / 76 (31.6)	15.8 [4.2; NE]	24 / 76 (31.6)	11.0 [2.2; 21.4]	0.8317 [0.4664; 1.4794] 0.5294	
Prior CDK4/6 inhibitor use						0.5585
Yes	108 / 394 (27.4)	13.8 [8.3; 25.6]	131 / 389 (33.7)	9.0 [5.5; 11.0]	0.7782 [0.6011; 1.0052] 0.0538	
No	17 / 42 (40.5)	12.5 [5.0; 29.8]	18 / 41 (43.9)	4.9 [1.4; NE]	0.6049 [0.3017; 1.2011] 0.1447	
Prior Taxane Use In The Non-Metastatic Setting						0.7120
Yes	50 / 179 (27.9)	11.8 [6.9; NE]	65 / 177 (36.7)	6.3 [4.2; 9.0]	0.7200 [0.4929; 1.0452] 0.0838	
No	75 / 257 (29.2)	15.1 [9.7; 25.6]	84 / 253 (33.2)	9.7 [4.3; 13.1]	0.7868 [0.5738; 1.0772] 0.1334	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.13.2 PGI-S - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.2645
1	19 / 65 (29.2)	6.9 [2.1; NE]	27 / 82 (32.9)	4.9 [2.8; 15.7]	0.8572 [0.4665; 1.5426] 0.6047	
2	81 / 295 (27.5)	15.8 [9.6; 26.9]	101 / 288 (35.1)	7.7 [4.2; 10.4]	0.6651 [0.4926; 0.8953] 0.0070	
>=3	24 / 75 (32.0)	15.1 [3.0; NE]	20 / 58 (34.5)	16.6 [6.3; NE]	1.1253 [0.6216; 2.0606] 0.6898	
ER/PR status I						0.3440
ER+, PR+	67 / 253 (26.5)	19.3 [10.3; 26.9]	79 / 237 (33.3)	7.7 [4.2; 12.5]	0.6838 [0.4902; 0.9505] 0.0233	
ER+, PR-	56 / 167 (33.5)	11.1 [5.6; 18.7]	63 / 181 (34.8)	9.0 [4.8; 13.1]	0.8798 [0.6099; 1.2652] 0.4874	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 05SEP2024 15:55; Program name: T.2.13.2_PGIS_TTCDet_FAS_SUB.sas; Output name: T.2.13.2_PGIS_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.13.2 PGI-S - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3400
ER <=10%	4 / 21 (19.0)	NE [1.4; NE]	6 / 14 (42.9)	2.7 [0.7; NE]	0.4252 [0.1077; 1.5041] 0.1757	
ER >10%	104 / 364 (28.6)	12.5 [8.9; 19.3]	118 / 355 (33.2)	9.0 [5.5; 11.0]	0.7829 [0.5996; 1.0213] 0.0702	
Positive	17 / 51 (33.3)	26.9 [2.1; NE]	25 / 61 (41.0)	6.3 [2.8; NE]	0.7848 [0.4097; 1.4602] 0.4444	
Endocrine Resistance						0.3473
Primary	41 / 128 (32.0)	9.8 [4.2; 26.9]	48 / 140 (34.3)	7.7 [4.3; 10.4]	0.9068 [0.5915; 1.3818] 0.6497	
Secondary	84 / 308 (27.3)	15.8 [9.7; 25.6]	100 / 288 (34.7)	8.3 [4.2; 13.1]	0.7047 [0.5248; 0.9437] 0.0184	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.13.2 PGI-S - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0573
Capecitabine	75 / 266 (28.2)	15.1 [7.6; 26.9]	86 / 257 (33.5)	9.1 [6.3; 13.1]	0.8356 [0.6090; 1.1425] 0.2511	
Nab-Paclitaxel	36 / 103 (35.0)	11.1 [6.0; NE]	39 / 105 (37.1)	5.6 [2.8; NE]	0.8243 [0.5205; 1.3024] 0.4110	
Paclitaxel	14 / 67 (20.9)	NE [3.5; NE]	24 / 68 (35.3)	2.1 [1.4; 4.2]	0.3968 [0.1978; 0.7661] 0.0054	
Prior anthracycline use						0.9969
Yes	54 / 199 (27.1)	11.8 [7.7; NE]	73 / 208 (35.1)	6.3 [4.2; 9.6]	0.7592 [0.5297; 1.0813] 0.1277	
No	71 / 237 (30.0)	15.1 [8.3; 26.9]	76 / 222 (34.2)	9.7 [4.2; 13.8]	0.7533 [0.5415; 1.0458] 0.0883	
Liver metastases						0.0191
Yes	91 / 296 (30.7)	9.0 [5.0; 15.8]	96 / 283 (33.9)	9.0 [4.8; 12.4]	0.9408 [0.7043; 1.2558] 0.6771	
No	34 / 140 (24.3)	19.3 [12.5; NE]	53 / 147 (36.1)	6.0 [4.1; 13.1]	0.5026 [0.3211; 0.7753] 0.0018	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.13.2 PGI-S - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.3253
0	77 / 252 (30.6)	11.8 [6.9; 20.8]	90 / 257 (35.0)	8.5 [4.9; 12.5]	0.8416 [0.6183; 1.1420] 0.2644	
>=1	47 / 179 (26.3)	16.5 [9.7; 29.8]	56 / 164 (34.1)	5.6 [4.2; 10.4]	0.6458 [0.4332; 0.9572] 0.0290	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Tabelle 2.13.3 PGI-S – Zeit bis zur bestätigten Verschlechterung – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.13.3 PGI-S - Time to confirmed deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0191
Yes	91 / 296 (30.7)	9.0 [5.0; 15.8]	96 / 283 (33.9)	9.0 [4.8; 12.4]	0.9408 [0.7043; 1.2558] 0.6771	
No	34 / 140 (24.3)	19.3 [12.5; NE]	53 / 147 (36.1)	6.0 [4.1; 13.1]	0.5026 [0.3211; 0.7753] 0.0018	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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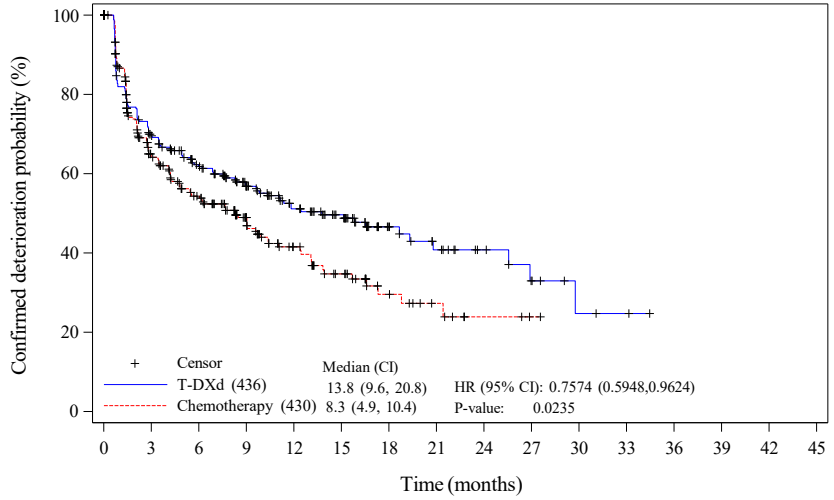
Abbildung 2.13.1 PGI-S – Zeit bis zur bestätigten Verschlechterung – Kaplan-Meier-Plot – FAS

Figure 2.13.1 PGI-S - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:

T-DXd(436)	436	170	134	103	74	57	28	19	12	7	3	2	0
Chemotherapy (430)	430	152	113	73	45	30	14	8	3	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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Abbildung 2.13.2 PGI-S – Zeit bis zur bestätigten Verschlechterung – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

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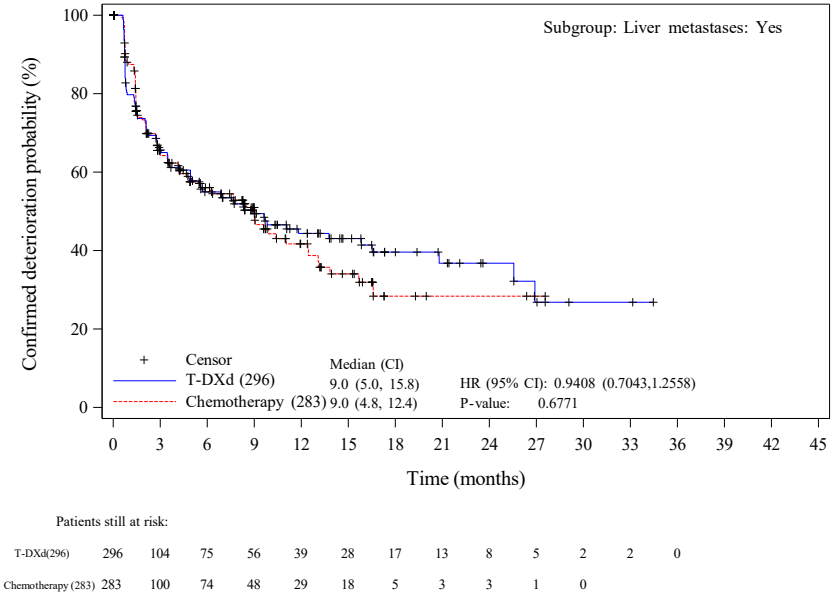
Figure 2.13.2 PGI-S - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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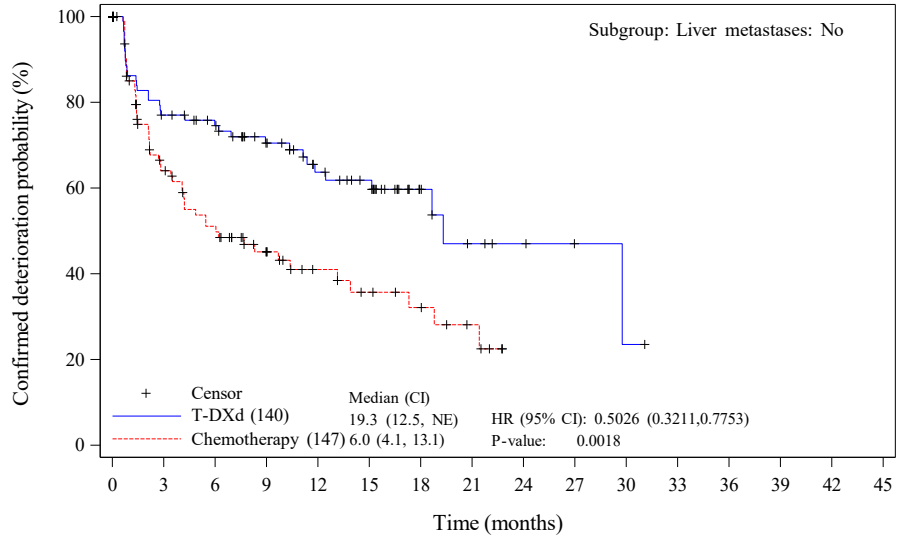
Figure 2.13.2 PGI-S - Time to confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 30JUL2024 5:11; Program name: F.2.13.2_PGIS_TTCDet_FAS_SUB.sas; Output name: F.2.13.2_PGIS_TTCDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.13.4 PGI-S – Zeit bis zur bestätigten Verschlechterung – Sensitivitätsanalyse – FAS

Table 2.13.4 PGI-S - Time to confirmed deterioration - Sensitivity analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	108 (24.8)	19.3 [12.5; NE]	125 (29.1)	9.9 [7.7; 17.3]	0.8077 [0.6225; 1.0461] 0.1064	0.1061
Subjects with censoring event	328 (75.2)		305 (70.9)			
Baseline score not allowing for deterioration	3 (0.7)		3 (0.7)			
Deterioration after 2 or more missed assessments	1 (0.2)		3 (0.7)			
No baseline data	157 (36.0)		87 (20.2)			
No deterioration	147 (33.7)		153 (35.6)			
No evaluable visit	20 (4.6)		59 (13.7)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

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Tabelle 2.13.9 PGI-S – Zeit bis zur erstmaligen Verschlechterung – FAS

Table 2.13.9 PGI-S - Time to first deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	171 (39.2)	4.2 [2.7; 5.6]	189 (44.0)	2.7 [2.1; 3.4]	0.8850 [0.7163; 1.0922] 0.2558	0.2435
Subjects with censoring event	265 (60.8)		241 (56.0)			
Baseline score not allowing for deterioration	3 (0.7)		3 (0.7)			
No baseline data	157 (36.0)		87 (20.2)			
No deterioration	85 (19.5)		92 (21.4)			
No evaluable visit	20 (4.6)		59 (13.7)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

Tabelle 2.13.10 PGI-S – Zeit bis zur erstmaligen Verschlechterung – Subgruppenanalyse – FAS

Table 2.13.10 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Age at randomization						0.3434
<65 years of age	126 / 302 (41.7)	4.2 [2.2; 6.2]	126 / 297 (42.4)	2.8 [2.1; 4.2]	0.9599 [0.7489; 1.2304] 0.7449	
≥65 years of age	45 / 134 (33.6)	4.2 [1.5; 8.3]	63 / 133 (47.4)	2.1 [1.5; 3.4]	0.7610 [0.5148; 1.1160] 0.1545	
Race						0.0398
Asian	85 / 154 (55.2)	5.0 [2.7; 7.6]	83 / 151 (55.0)	3.4 [2.1; 5.7]	0.9283 [0.6845; 1.2595] 0.6281	
White	78 / 231 (33.8)	2.8 [1.4; 4.9]	93 / 230 (40.4)	2.7 [1.8; 3.5]	1.0045 [0.7411; 1.3580] 0.9970	
Other	8 / 51 (15.7)	NE [1.4; NE]	13 / 49 (26.5)	1.5 [0.8; 2.1]	0.3156 [0.1215; 0.7686] 0.0089	
Region						0.8579
Asia	84 / 149 (56.4)	4.9 [2.2; 7.6]	82 / 147 (55.8)	3.4 [2.2; 5.7]	0.9350 [0.6881; 1.2709] 0.6634	
Europe	70 / 227 (30.8)	4.2 [1.5; 5.7]	83 / 213 (39.0)	2.1 [1.5; 2.8]	0.8293 [0.6004; 1.1414] 0.2421	
Rest of the World	17 / 60 (28.3)	3.4 [0.8; NE]	24 / 70 (34.3)	2.9 [1.4; 9.1]	1.0977 [0.5736; 2.0650] 0.7817	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 05SEP2024 15:48; Program name: T.2.13.10_PGIS_TTFDet_FAS_SUB.sas; Output name: T.2.13.10_PGIS_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.13.10 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
HER2 IHC expression						0.2353
IHC 1+	95 / 239 (39.7)	3.5 [1.5; 6.2]	107 / 234 (45.7)	2.9 [2.1; 4.2]	0.9510 [0.7190; 1.2558] 0.6961	
IHC 2+/ISH-	41 / 117 (35.0)	5.0 [2.9; 11.1]	51 / 118 (43.2)	2.1 [1.5; 3.6]	0.6529 [0.4285; 0.9886] 0.0421	
IHC >0 <1+	34 / 76 (44.7)	2.7 [1.4; 6.2]	29 / 76 (38.2)	2.2 [1.4; 11.0]	1.1780 [0.7141; 1.9589] 0.5062	
Prior CDK4/6 inhibitor use						0.2161
Yes	150 / 394 (38.1)	4.2 [2.7; 5.6]	164 / 389 (42.2)	2.7 [2.1; 4.1]	0.9303 [0.7443; 1.1617] 0.5130	
No	21 / 42 (50.0)	5.0 [1.4; 12.5]	25 / 41 (61.0)	1.5 [1.3; 3.6]	0.6393 [0.3516; 1.1506] 0.1294	
Prior Taxane Use In The Non-Metastatic Setting						0.2079
Yes	71 / 179 (39.7)	4.2 [2.7; 7.6]	86 / 177 (48.6)	2.7 [1.5; 3.5]	0.7398 [0.5365; 1.0163] 0.0615	
No	100 / 257 (38.9)	4.2 [2.0; 5.6]	103 / 253 (40.7)	2.8 [2.1; 6.0]	1.0095 [0.7657; 1.3303] 0.9619	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 05SEP2024 15:48; Program name: T.2.13.10_PGIS_TTFDet_FAS_SUB.sas; Output name: T.2.13.10_PGIS_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.13.10 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0197
1	25 / 65 (38.5)	2.7 [0.8; 5.0]	38 / 82 (46.3)	2.1 [1.4; 2.9]	0.7518 [0.4464; 1.2441] 0.2601	
2	111 / 295 (37.6)	4.9 [2.8; 7.6]	127 / 288 (44.1)	2.7 [1.8; 3.5]	0.7754 [0.5984; 1.0036] 0.0522	
>=3	34 / 75 (45.3)	2.8 [1.4; 10.4]	23 / 58 (39.7)	9.0 [2.8; NE]	1.7405 [1.0284; 2.9995] 0.0394	
ER/PR status I						0.4596
ER+, PR+	95 / 253 (37.5)	5.1 [2.8; 8.3]	99 / 237 (41.8)	2.8 [2.1; 4.2]	0.8571 [0.6455; 1.1381] 0.2783	
ER+, PR-	74 / 167 (44.3)	2.8 [2.0; 5.0]	83 / 181 (45.9)	2.7 [2.1; 4.2]	0.9868 [0.7191; 1.3516] 0.9248	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 05SEP2024 15:48; Program name: T.2.13.10_PGIS_TTFDet_FAS_SUB.sas; Output name: T.2.13.10_PGIS_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.13.10 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.0435
ER <=10%	5 / 21 (23.8)	NE [0.7; NE]	8 / 14 (57.1)	1.3 [0.7; 4.2]	0.2871 [0.0751; 0.9347] 0.0337	
ER >10%	142 / 364 (39.0)	4.2 [2.1; 5.6]	150 / 355 (42.3)	2.8 [2.1; 4.2]	0.9461 [0.7511; 1.1912] 0.6247	
Positive	24 / 51 (47.1)	4.2 [0.9; 15.9]	31 / 61 (50.8)	1.8 [1.4; 4.8]	0.8645 [0.4966; 1.4832] 0.5919	
Endocrine Resistance						0.5728
Primary	52 / 128 (40.6)	3.5 [1.5; 6.9]	66 / 140 (47.1)	2.2 [1.7; 3.4]	0.8289 [0.5728; 1.1931] 0.3126	
Secondary	119 / 308 (38.6)	4.8 [2.2; 7.0]	122 / 288 (42.4)	2.8 [2.1; 4.8]	0.9319 [0.7228; 1.2012] 0.5748	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.13.10 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0676
Capecitabine	101 / 266 (38.0)	4.2 [2.1; 6.2]	110 / 257 (42.8)	3.0 [2.1; 4.9]	0.9844 [0.7498; 1.2911] 0.8831	
Nab-Paclitaxel	50 / 103 (48.5)	3.5 [2.1; 8.3]	51 / 105 (48.6)	2.7 [1.7; 5.5]	0.9348 [0.6305; 1.3850] 0.7393	
Paclitaxel	20 / 67 (29.9)	5.6 [1.4; NE]	28 / 68 (41.2)	1.5 [0.8; 2.2]	0.4790 [0.2604; 0.8635] 0.0134	
Prior anthracycline use						0.2421
Yes	75 / 199 (37.7)	4.2 [2.7; 7.6]	98 / 208 (47.1)	2.7 [2.1; 2.9]	0.7685 [0.5656; 1.0398] 0.0870	
No	96 / 237 (40.5)	4.2 [2.1; 5.6]	91 / 222 (41.0)	3.5 [2.1; 6.2]	1.0162 [0.7623; 1.3556] 0.9238	
Liver metastases						0.2298
Yes	116 / 296 (39.2)	2.8 [1.6; 5.1]	123 / 283 (43.5)	2.7 [1.7; 3.6]	0.9894 [0.7668; 1.2758] 0.9234	
No	55 / 140 (39.3)	5.6 [2.8; 11.1]	66 / 147 (44.9)	2.8 [2.1; 4.9]	0.7195 [0.4985; 1.0343] 0.0733	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 05SEP2024 15:48; Program name: T.2.13.10_PGIS_TTFDet_FAS_SUB.sas; Output name: T.2.13.10_PGIS_TTFDet_FAS_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.13.10 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.9497
0	104 / 252 (41.3)	3.4 [2.1; 5.0]	122 / 257 (47.5)	2.7 [2.1; 3.6]	0.8921 [0.6848; 1.1594] 0.3856	
>=1	66 / 179 (36.9)	5.6 [2.2; 10.4]	64 / 164 (39.0)	2.7 [1.7; 5.5]	0.8932 [0.6313; 1.2648] 0.5144	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Tabelle 2.13.11 PGI-S – Zeit bis zur erstmaligen Verschlechterung – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.13.11 PGI-S - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Race						0.0398
Asian	85 / 154 (55.2)	5.0 [2.7; 7.6]	83 / 151 (55.0)	3.4 [2.1; 5.7]	0.9283 [0.6845; 1.2595] 0.6281	
White	78 / 231 (33.8)	2.8 [1.4; 4.9]	93 / 230 (40.4)	2.7 [1.8; 3.5]	1.0045 [0.7411; 1.3580] 0.9970	
Other	8 / 51 (15.7)	NE [1.4; NE]	13 / 49 (26.5)	1.5 [0.8; 2.1]	0.3156 [0.1215; 0.7686] 0.0089	
Number of prior lines of endocrine therapy in the metastatic setting						0.0197
1	25 / 65 (38.5)	2.7 [0.8; 5.0]	38 / 82 (46.3)	2.1 [1.4; 2.9]	0.7518 [0.4464; 1.2441] 0.2601	
2	111 / 295 (37.6)	4.9 [2.8; 7.6]	127 / 288 (44.1)	2.7 [1.8; 3.5]	0.7754 [0.5984; 1.0036] 0.0522	
>=3	34 / 75 (45.3)	2.8 [1.4; 10.4]	23 / 58 (39.7)	9.0 [2.8; NE]	1.7405 [1.0284; 2.9995] 0.0394	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 05SEP2024 15:52; Program name: T.2.13.11_PGIS_TTFDet_FAS_SUB_SIG.sas; Output name: T.2.13.11_PGIS_TTFDet_FAS_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.13.11 PGI-S - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.0435
ER <=10%	5 / 21 (23.8)	NE [0.7; NE]	8 / 14 (57.1)	1.3 [0.7; 4.2]	0.2871 [0.0751; 0.9347] 0.0337	
ER >10%	142 / 364 (39.0)	4.2 [2.1; 5.6]	150 / 355 (42.3)	2.8 [2.1; 4.2]	0.9461 [0.7511; 1.1912] 0.6247	
Positive	24 / 51 (47.1)	4.2 [0.9; 15.9]	31 / 61 (50.8)	1.8 [1.4; 4.8]	0.8645 [0.4966; 1.4832] 0.5919	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Abbildung 2.13.5 PGI-S – Zeit bis zur erstmaligen Verschlechterung – Kaplan-Meier-Plot – FAS

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Data Intelligence – Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 2024-03-18)

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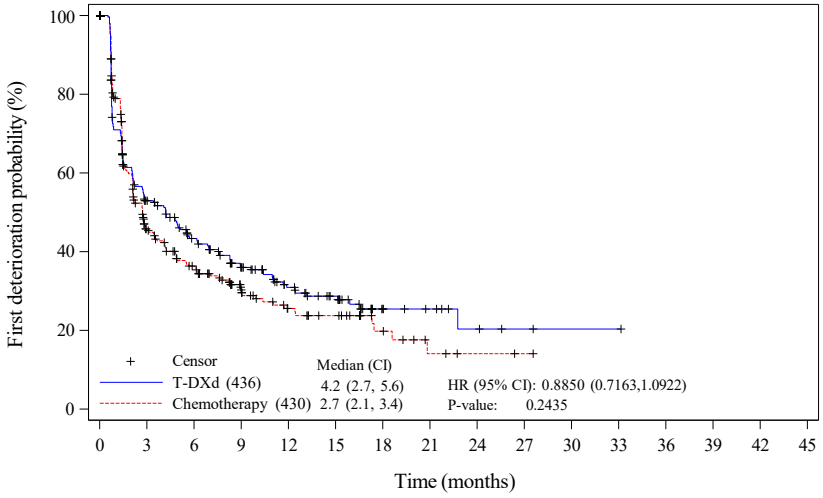
Statistical analyses for AMNOG (HTA Germany)

Figure 2.13.5 PGI-S - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:

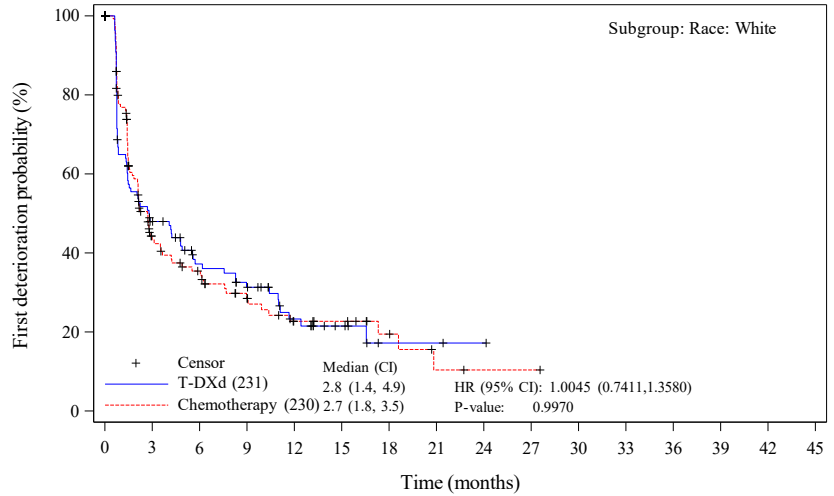
T-DXd(436)	436	128	93	67	44	32	12	8	4	2	1	1	0
Chemotherapy (430)	430	106	75	45	28	22	10	4	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10DEC2024 10:37; Program name: F.2.13.5_PGIS_TTFDet_FAS.sas; Output name: F.2.13.5_PGIS_TTFDet_FAS.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.13.6 PGI-S – Zeit bis zur erstmaligen Verschlechterung – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

Figure 2.13.6 PGI-S - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Patients still at risk:

T-DXd(231)	231	49	32	25	13	7	2	2	1	0
Chemotherapy (230)	230	45	33	22	13	11	6	2	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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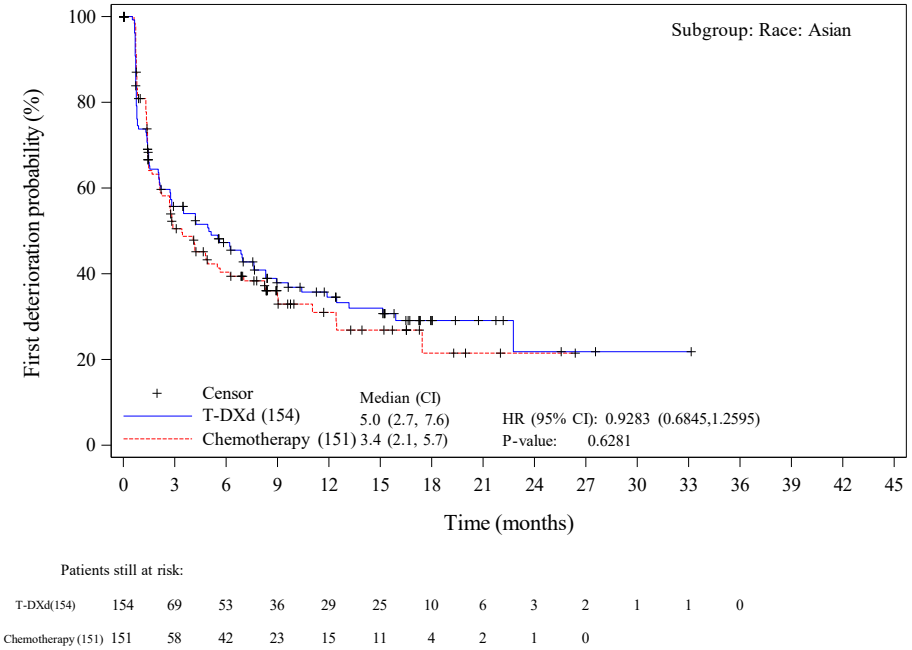
Figure 2.13.6 PGI-S - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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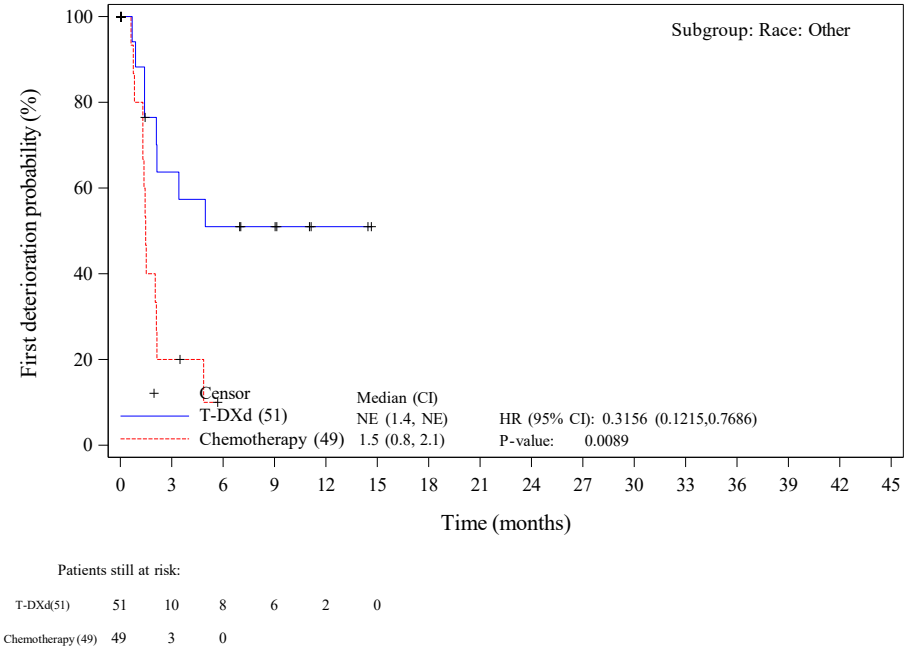
Figure 2.13.6 PGI-S - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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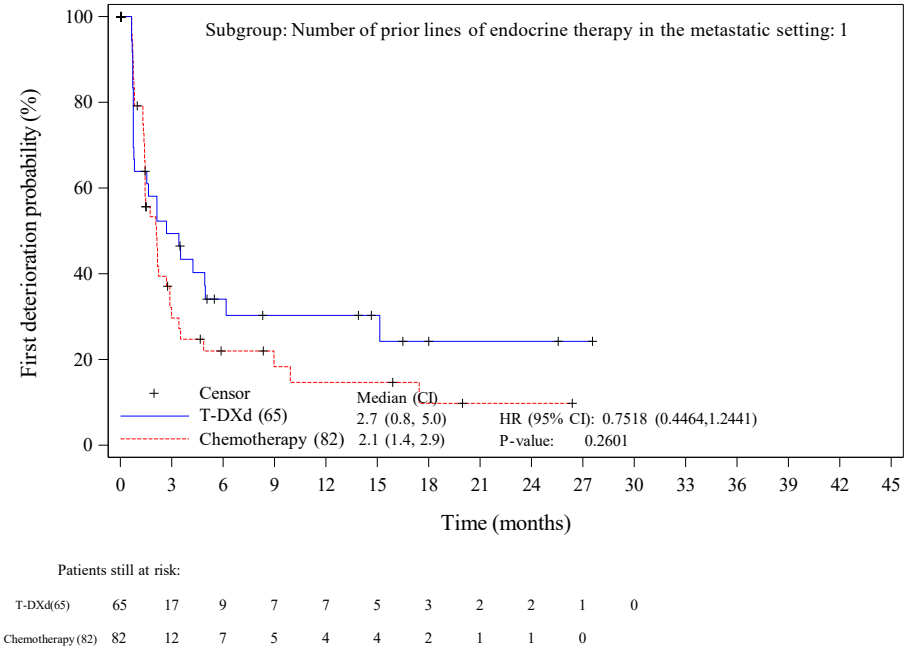
Figure 2.13.6 PGI-S - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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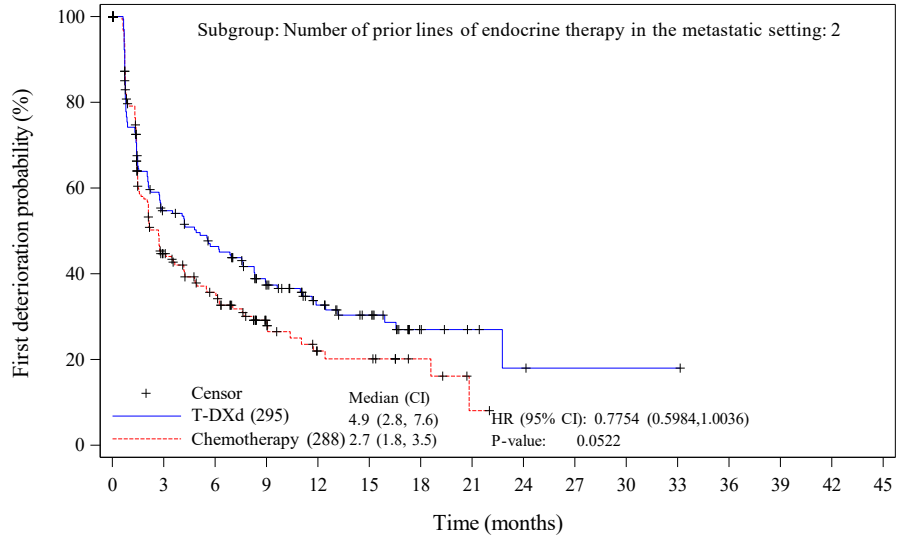
Figure 2.13.6 PGI-S - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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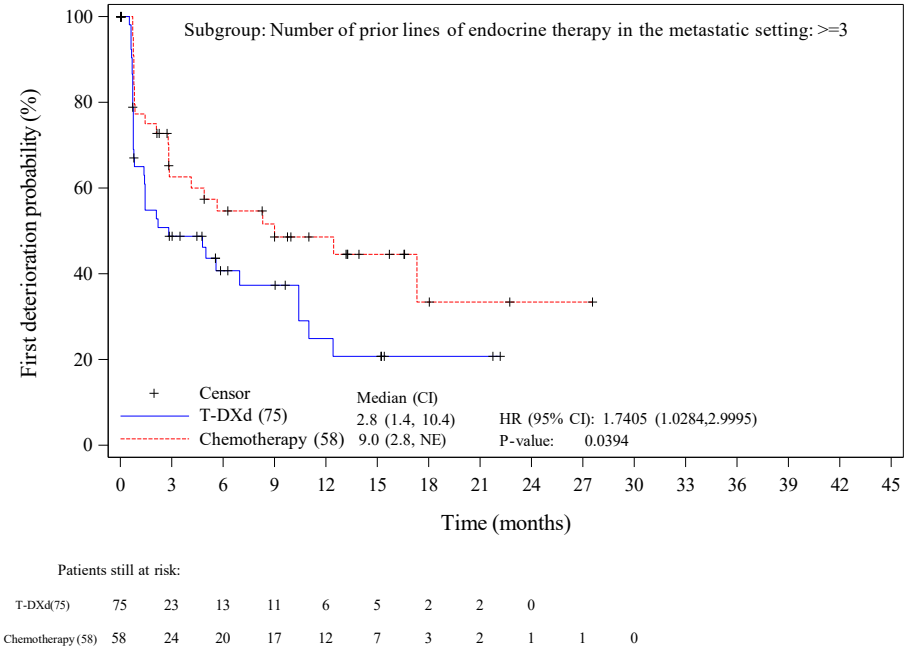
Figure 2.13.6 PGI-S - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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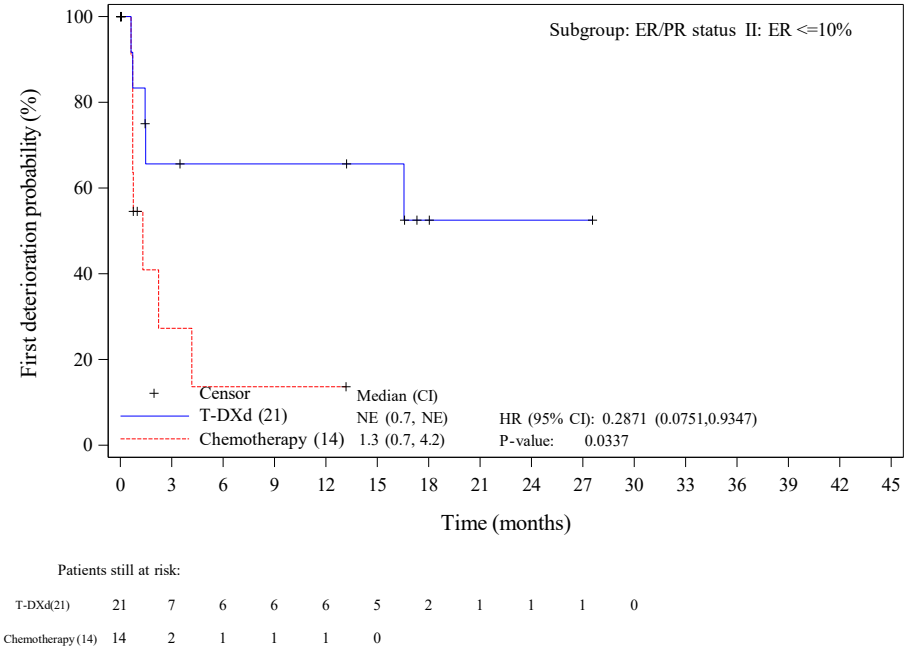
Figure 2.13.6 PGI-S - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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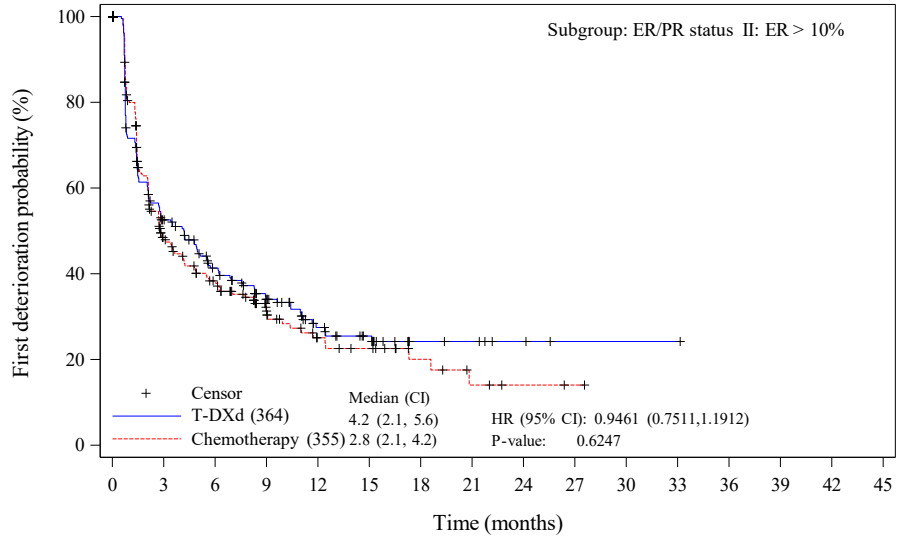
Figure 2.13.6 PGI-S - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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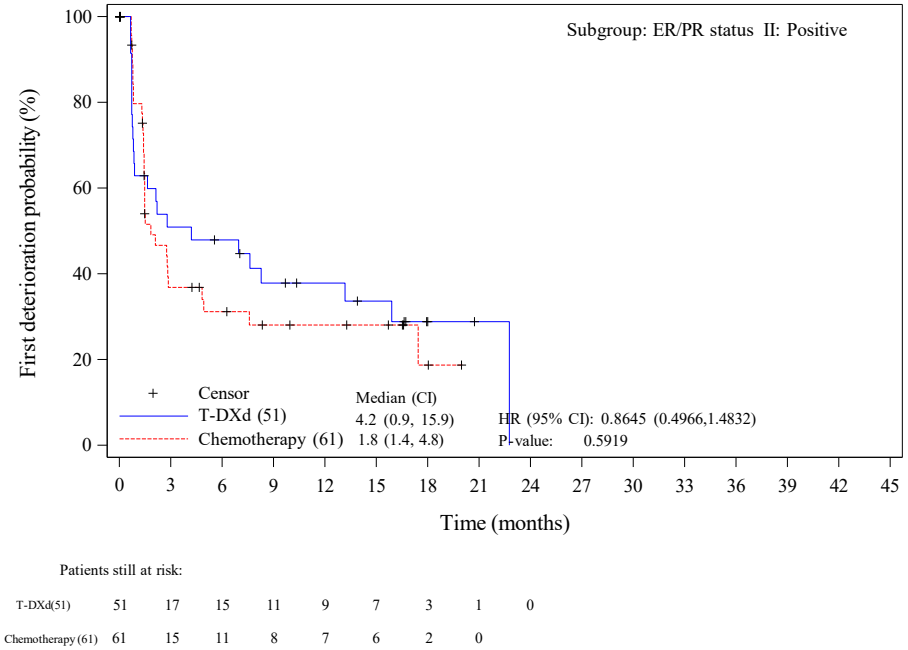
Figure 2.13.6 PGI-S - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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Anhang 4-G 3.5 PGI-C

Tabelle 2.14.1 PGI-C – Zeit bis zur bestätigten Verschlechterung – FAS

Table 2.14.1 PGI-C - Time to confirmed deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	51 (11.7)	NE [NE; NE]	54 (12.6)	NE [NE; NE]	0.6493 [0.4411; 0.9544] 0.0278	0.0268
Subjects with censoring event	385 (88.3)		376 (87.4)			
Deterioration after 2 or more missed assessments	3 (0.7)		1 (0.2)			
No deterioration	352 (80.7)		309 (71.9)			
No evaluable visit	30 (6.9)		66 (15.3)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Tabelle 2.14.2 PGI-C – Zeit bis zur bestätigten Verschlechterung – Subgruppenanalyse – FAS

Table 2.14.2 PGI-C - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Age at randomization						0.4895
<65 years of age	40 / 302 (13.2)	NE [31.0; NE]	38 / 297 (12.8)	NE [NE; NE]	0.6903 [0.4411; 1.0820] 0.1021	
≥65 years of age	11 / 134 (8.2)	NE [NE; NE]	16 / 133 (12.0)	NE [20.8; NE]	0.5091 [0.2275; 1.0962] 0.0830	
Race						0.4081
Asian	9 / 154 (5.8)	NE [NE; NE]	13 / 151 (8.6)	NE [NE; NE]	0.5229 [0.2150; 1.2164] 0.1297	
White	39 / 231 (16.9)	31.0 [24.8; NE]	35 / 230 (15.2)	NE [20.8; NE]	0.7465 [0.4706; 1.1874] 0.2126	
Region						0.1517
Asia	8 / 149 (5.4)	NE [NE; NE]	13 / 147 (8.8)	NE [NE; NE]	0.4647 [0.1833; 1.1066] 0.0820	
Europe	39 / 227 (17.2)	31.0 [24.8; NE]	30 / 213 (14.1)	NE [20.8; NE]	0.7961 [0.4935; 1.2959] 0.3528	
Rest of the World	4 / 60 (6.7)	NE [NE; NE]	11 / 70 (15.7)	NE [18.1; NE]	0.2746 [0.0756; 0.8101] 0.0189	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.14.2 PGI-C - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
HER2 IHC expression						0.7733
IHC 1+	22 / 239 (9.2)	NE [NE; NE]	29 / 234 (12.4)	NE [NE; NE]	0.5644 [0.3202; 0.9810] 0.0411	
IHC 2+/ISH-	20 / 117 (17.1)	NE [31.0; NE]	16 / 118 (13.6)	NE [15.1; NE]	0.7307 [0.3738; 1.4463] 0.3604	
IHC >0 <1+	8 / 76 (10.5)	NE [19.3; NE]	9 / 76 (11.8)	NE [18.1; NE]	0.6485 [0.2433; 1.6972] 0.3694	
Prior CDK4/6 inhibitor use						0.1138
Yes	50 / 394 (12.7)	NE [31.0; NE]	49 / 389 (12.6)	NE [NE; NE]	0.6895 [0.4634; 1.0263] 0.0646	
No	1 / 42 (2.4)	NE [NE; NE]	5 / 41 (12.2)	NE [NE; NE]	0.1602 [0.0084; 0.9946] 0.0557	
Prior Taxane Use In The Non-Metastatic Setting						0.7838
Yes	21 / 179 (11.7)	NE [31.0; NE]	23 / 177 (13.0)	NE [NE; NE]	0.5984 [0.3272; 1.0884] 0.0887	
No	30 / 257 (11.7)	NE [NE; NE]	31 / 253 (12.3)	NE [NE; NE]	0.6890 [0.4150; 1.1421] 0.1448	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.14.2 PGI-C - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0374
1	6 / 65 (9.2)	NE [NE; NE]	11 / 82 (13.4)	NE [18.1; NE]	0.4712 [0.1614; 1.2463] 0.1316	
2	28 / 295 (9.5)	NE [NE; NE]	37 / 288 (12.8)	NE [NE; NE]	0.5226 [0.3167; 0.8528] 0.0087	
>=3	17 / 75 (22.7)	31.0 [16.6; NE]	6 / 58 (10.3)	NE [21.3; NE]	1.6886 [0.6933; 4.7138] 0.2683	
ER/PR status I						0.8489
ER+, PR+	29 / 253 (11.5)	NE [31.0; NE]	29 / 237 (12.2)	NE [NE; NE]	0.7006 [0.4170; 1.1770] 0.1743	
ER+, PR-	21 / 167 (12.6)	NE [NE; NE]	20 / 181 (11.0)	NE [21.3; NE]	0.7154 [0.3843; 1.3353] 0.2858	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.14.2 PGI-C - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2414
ER >10%	42 / 364 (11.5)	NE [31.0; NE]	38 / 355 (10.7)	NE [NE; NE]	0.7433 [0.4778; 1.1600] 0.1867	
Positive	7 / 51 (13.7)	NE [NE; NE]	14 / 61 (23.0)	NE [21.3; NE]	0.4298 [0.1626; 1.0350] 0.0609	
Endocrine Resistance						0.3482
Primary	13 / 128 (10.2)	NE [NE; NE]	20 / 140 (14.3)	NE [NE; NE]	0.4902 [0.2372; 0.9789] 0.0422	
Secondary	38 / 308 (12.3)	NE [31.0; NE]	34 / 288 (11.8)	NE [NE; NE]	0.7425 [0.4665; 1.1863] 0.2077	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.14.2 PGI-C - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.5650
Capecitabine	29 / 266 (10.9)	NE [NE; NE]	33 / 257 (12.8)	NE [NE; NE]	0.5807 [0.3502; 0.9578] 0.0312	
Nab-Paclitaxel	8 / 103 (7.8)	NE [NE; NE]	13 / 105 (12.4)	NE [NE; NE]	0.5638 [0.2227; 1.3410] 0.1976	
Paclitaxel	14 / 67 (20.9)	31.0 [19.3; NE]	8 / 68 (11.8)	NE [NE; NE]	0.8428 [0.3438; 2.1765] 0.7119	
Prior anthracycline use						0.8718
Yes	25 / 199 (12.6)	NE [31.0; NE]	26 / 208 (12.5)	NE [NE; NE]	0.6636 [0.3799; 1.1569] 0.1440	
No	26 / 237 (11.0)	NE [NE; NE]	28 / 222 (12.6)	NE [21.3; NE]	0.6364 [0.3707; 1.0888] 0.0955	
Liver metastases						0.7301
Yes	38 / 296 (12.8)	NE [31.0; NE]	40 / 283 (14.1)	NE [21.3; NE]	0.6038 [0.3844; 0.9464] 0.0261	
No	13 / 140 (9.3)	NE [NE; NE]	14 / 147 (9.5)	NE [NE; NE]	0.7274 [0.3373; 1.5577] 0.4073	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.14.2 PGI-C - Time to confirmed deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.7907
0	29 / 252 (11.5)	NE [31.0; NE]	32 / 257 (12.5)	NE [NE; NE]	0.5891 [0.3519; 0.9806] 0.0396	
>=1	21 / 179 (11.7)	NE [NE; NE]	22 / 164 (13.4)	NE [21.3; NE]	0.6814 [0.3717; 1.2457] 0.2076	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Tabelle 2.14.3 PGI-C – Zeit bis zur bestätigten Verschlechterung – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.14.3 PGI-C - Time to confirmed deterioration - - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0374
1	6 / 65 (9.2)	NE [NE; NE]	11 / 82 (13.4)	NE [18.1; NE]	0.4712 [0.1614; 1.2463] 0.1316	
2	28 / 295 (9.5)	NE [NE; NE]	37 / 288 (12.8)	NE [NE; NE]	0.5226 [0.3167; 0.8528] 0.0087	
>=3	17 / 75 (22.7)	31.0 [16.6; NE]	6 / 58 (10.3)	NE [21.3; NE]	1.6886 [0.6933; 4.7138] 0.2683	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Abbildung 2.14.1 PGI-C – Zeit bis zur bestätigten Verschlechterung – Kaplan-Meier-Plot – FAS

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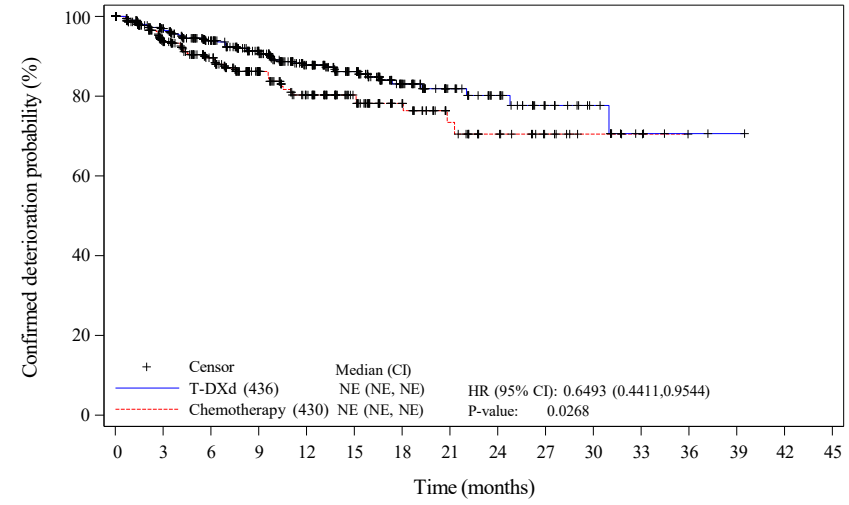
Figure 2.14.1 PGI-C - Time to confirmed deterioration - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:

T-DXd(436)	436	365	306	257	187	140	82	52	37	20	12	4	2	1	0
Chemotherapy (430)	430	280	222	147	108	76	46	25	16	8	3	2	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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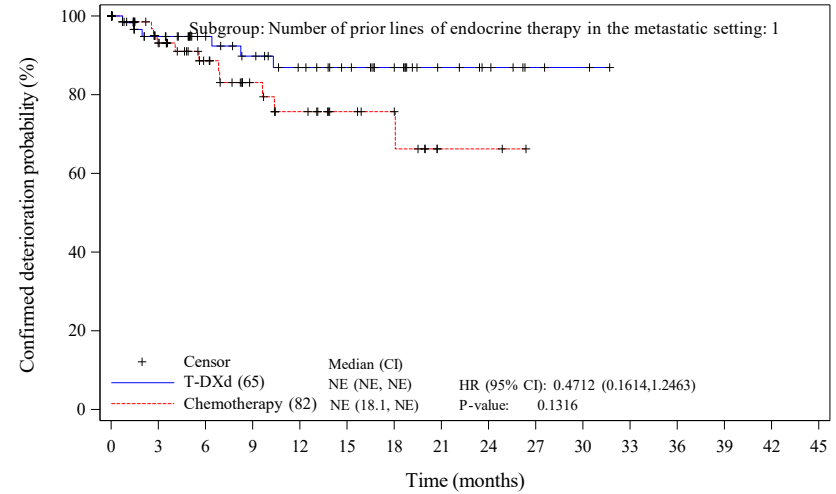
Abbildung 2.14.2 PGI-C – Zeit bis zur bestätigten Verschlechterung – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

Figure 2.14.2 PGI-C - Time to Confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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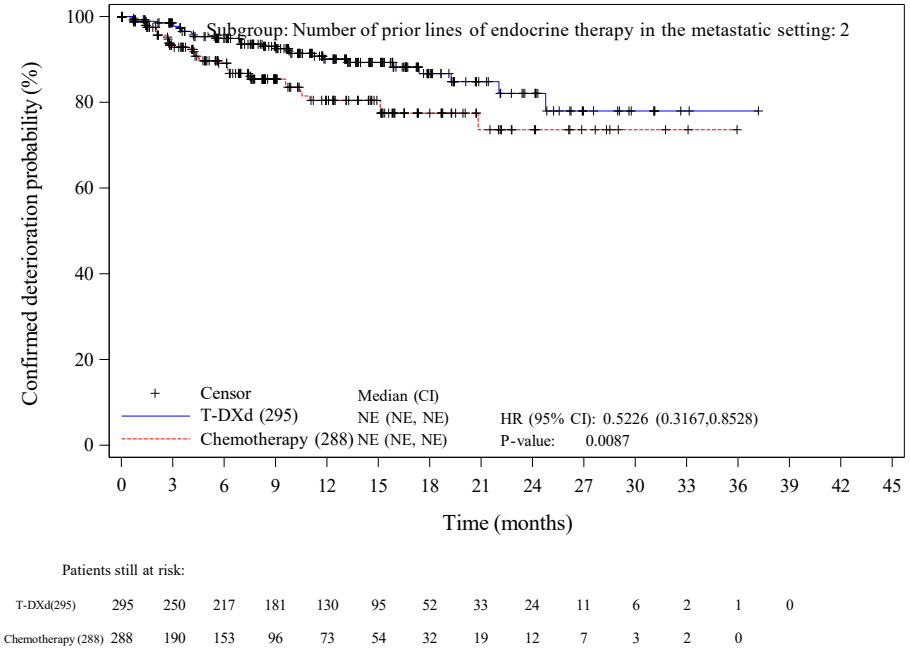
Figure 2.14.2 PGI-C - Time to Confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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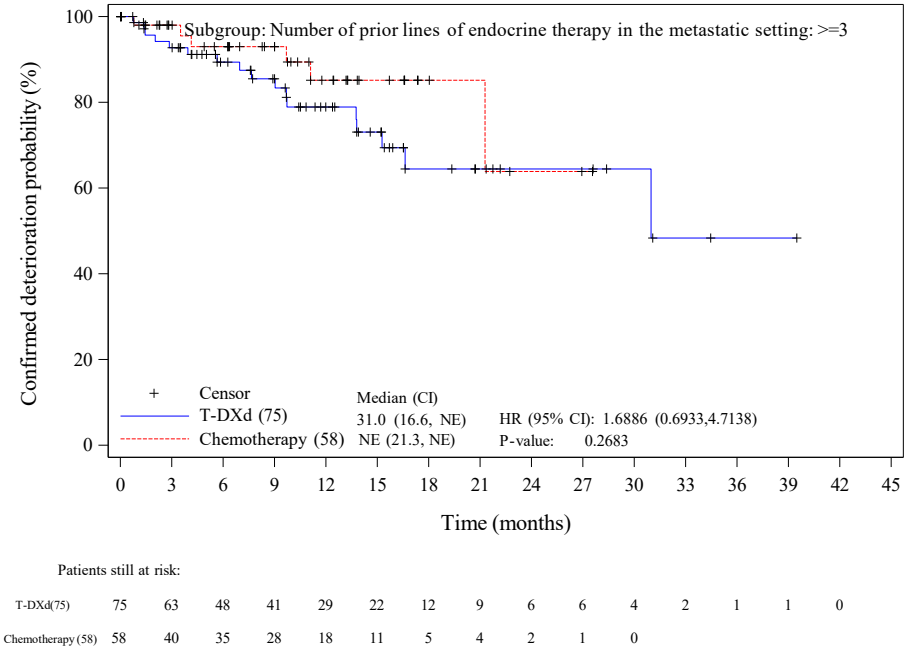
Figure 2.14.2 PGI-C - Time to Confirmed deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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Tabelle 2.14.4 PGI-C – Zeit bis zur bestätigten Verschlechterung – Sensitivitätsanalyse – FAS

Table 2.14.4 PGI-C - Time to confirmed deterioration - Sensitivity analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	31 (7.1)	NE [NE; NE]	26 (6.0)	NE [NE; NE]	0.8365 [0.4958; 1.4224] 0.5044	0.5049
Subjects with censoring event	405 (92.9)		404 (94.0)			
Deterioration after 2 or more missed assessments	1 (0.2)		0			
No deterioration	374 (85.8)		338 (78.6)			
No evaluable visit	30 (6.9)		66 (15.3)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

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Tabelle 2.14.9 PGI-C – Zeit bis zur erstmaligen Verschlechterung – FAS

Table 2.14.9 PGI-C - Time to first deterioration - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Subjects with event	83 (19.0)	NE [31.0; NE]	85 (19.8)	NE [NE; NE]	0.6758 [0.4982; 0.9164] 0.0116	0.0111
Subjects with censoring event	353 (81.0)		345 (80.2)			
No deterioration	323 (74.1)		279 (64.9)			
No evaluable visit	30 (6.9)		66 (15.3)			

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

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Tabelle 2.14.10 PGI-C – Zeit bis zur erstmaligen Verschlechterung – Subgruppenanalyse – FAS

Table 2.14.10 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Age at randomization						0.5549
<65 years of age	61 / 302 (20.2)	NE [31.0; NE]	58 / 297 (19.5)	NE [21.3; NE]	0.7033 [0.4896; 1.0114] 0.0551	
≥65 years of age	22 / 134 (16.4)	NE [23.5; NE]	27 / 133 (20.3)	NE [NE; NE]	0.5882 [0.3297; 1.0373] 0.0651	
Race						0.1203
Asian	17 / 154 (11.0)	NE [NE; NE]	19 / 151 (12.6)	NE [NE; NE]	0.6515 [0.3343; 1.2595] 0.1978	
White	61 / 231 (26.4)	24.8 [19.3; NE]	55 / 230 (23.9)	NE [15.1; NE]	0.7495 [0.5189; 1.0846] 0.1231	
Other	5 / 51 (9.8)	NE [NE; NE]	11 / 49 (22.4)	12.4 [6.9; NE]	0.2544 [0.0784; 0.7167] 0.0080	
Region						0.9640
Asia	16 / 149 (10.7)	NE [NE; NE]	19 / 147 (12.9)	NE [NE; NE]	0.6144 [0.3111; 1.1980] 0.1491	
Europe	57 / 227 (25.1)	24.8 [22.0; NE]	52 / 213 (24.4)	NE [12.4; NE]	0.6705 [0.4583; 0.9825] 0.0382	
Rest of the World	10 / 60 (16.7)	NE [18.7; NE]	14 / 70 (20.0)	NE [10.4; NE]	0.5580 [0.2394; 1.2537] 0.1556	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.14.10 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
HER2 IHC expression						0.4161
IHC 1+	37 / 239 (15.5)	NE [NE; NE]	46 / 234 (19.7)	NE [NE; NE]	0.5934 [0.3822; 0.9149] 0.0173	
IHC 2+/ISH-	31 / 117 (26.5)	31.0 [22.0; NE]	22 / 118 (18.6)	21.3 [15.1; NE]	0.8864 [0.5107; 1.5619] 0.6676	
IHC >0 <1+	14 / 76 (18.4)	NE [18.7; NE]	17 / 76 (22.4)	NE [18.1; NE]	0.5504 [0.2665; 1.1186] 0.0946	
Prior CDK4/6 inhibitor use						0.8018
Yes	78 / 394 (19.8)	NE [24.8; NE]	80 / 389 (20.6)	NE [21.3; NE]	0.6606 [0.4822; 0.9045] 0.0091	
No	5 / 42 (11.9)	NE [NE; NE]	5 / 41 (12.2)	NE [NE; NE]	0.7921 [0.2195; 2.8578] 0.7128	
Prior Taxane Use In The Non-Metastatic Setting						0.4581
Yes	34 / 179 (19.0)	31.0 [31.0; NE]	39 / 177 (22.0)	NE [15.9; NE]	0.5899 [0.3693; 0.9376] 0.0242	
No	49 / 257 (19.1)	NE [24.8; NE]	46 / 253 (18.2)	NE [21.3; NE]	0.7528 [0.5024; 1.1300] 0.1667	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.14.10 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0373
1	10 / 65 (15.4)	NE [NE; NE]	16 / 82 (19.5)	NE [10.4; NE]	0.5483 [0.2391; 1.1976] 0.1319	
2	51 / 295 (17.3)	NE [NE; NE]	60 / 288 (20.8)	NE [NE; NE]	0.5831 [0.3994; 0.8480] 0.0044	
>=3	22 / 75 (29.3)	18.7 [15.3; NE]	9 / 58 (15.5)	NE [21.3; NE]	1.4957 [0.7053; 3.4441] 0.3100	
ER/PR status I						0.9615
ER+, PR+	48 / 253 (19.0)	31.0 [24.8; NE]	45 / 237 (19.0)	NE [NE; NE]	0.7466 [0.4963; 1.1251] 0.1592	
ER+, PR-	33 / 167 (19.8)	NE [NE; NE]	31 / 181 (17.1)	NE [21.3; NE]	0.7642 [0.4655; 1.2575] 0.2836	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.14.10 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2372
ER >10%	70 / 364 (19.2)	NE [31.0; NE]	65 / 355 (18.3)	NE [NE; NE]	0.7367 [0.5243; 1.0365] 0.0767	
Positive	9 / 51 (17.6)	NE [18.6; NE]	17 / 61 (27.9)	NE [9.3; NE]	0.4447 [0.1889; 0.9781] 0.0441	
Endocrine Resistance						0.9686
Primary	24 / 128 (18.8)	NE [19.3; NE]	28 / 140 (20.0)	NE [18.1; NE]	0.6773 [0.3889; 1.1705] 0.1606	
Secondary	59 / 308 (19.2)	NE [31.0; NE]	57 / 288 (19.8)	NE [NE; NE]	0.6790 [0.4706; 0.9805] 0.0368	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.14.10 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.6790
Capecitabine	52 / 266 (19.5)	NE [24.8; NE]	49 / 257 (19.1)	NE [21.3; NE]	0.7113 [0.4806; 1.0543] 0.0864	
Nab-Paclitaxel	15 / 103 (14.6)	NE [NE; NE]	19 / 105 (18.1)	NE [NE; NE]	0.7000 [0.3490; 1.3784] 0.3014	
Paclitaxel	16 / 67 (23.9)	31.0 [15.9; NE]	17 / 68 (25.0)	NE [6.9; NE]	0.4073 [0.1944; 0.8390] 0.0122	
Prior anthracycline use						0.8018
Yes	41 / 199 (20.6)	NE [31.0; NE]	42 / 208 (20.2)	NE [NE; NE]	0.6929 [0.4481; 1.0708] 0.0959	
No	42 / 237 (17.7)	NE [24.8; NE]	43 / 222 (19.4)	NE [21.3; NE]	0.6634 [0.4320; 1.0178] 0.0578	
Liver metastases						0.1883
Yes	59 / 296 (19.9)	NE [31.0; NE]	65 / 283 (23.0)	NE [15.9; NE]	0.5799 [0.4053; 0.8280] 0.0024	
No	24 / 140 (17.1)	NE [24.8; NE]	20 / 147 (13.6)	NE [NE; NE]	0.9427 [0.5206; 1.7261] 0.8456	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.14.10 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.5119
0	43 / 252 (17.1)	NE [31.0; NE]	48 / 257 (18.7)	NE [NE; NE]	0.5929 [0.3896; 0.8988] 0.0128	
>=1	39 / 179 (21.8)	NE [22.0; NE]	37 / 164 (22.6)	NE [15.9; NE]	0.7387 [0.4696; 1.1641] 0.1882	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Tabelle 2.14.11 PGI-C – Zeit bis zur erstmaligen Verschlechterung – Subgruppenanalyse – Interaktions-p-Wert <0,05 – FAS

Table 2.14.11 PGI-C - Time to first deterioration - Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

DESTINY Breast-06	T-DXd N=436		Chemotherapy N=430		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0373
1	10 / 65 (15.4)	NE [NE; NE]	16 / 82 (19.5)	NE [10.4; NE]	0.5483 [0.2391; 1.1976] 0.1319	
2	51 / 295 (17.3)	NE [NE; NE]	60 / 288 (20.8)	NE [NE; NE]	0.5831 [0.3994; 0.8480] 0.0044	
>=3	22 / 75 (29.3)	18.7 [15.3; NE]	9 / 58 (15.5)	NE [21.3; NE]	1.4957 [0.7053; 3.4441] 0.3100	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Abbildung 2.14.5 PGI-C – Zeit bis zur erstmaligen Verschlechterung – Kaplan-Meier-Plot – FAS

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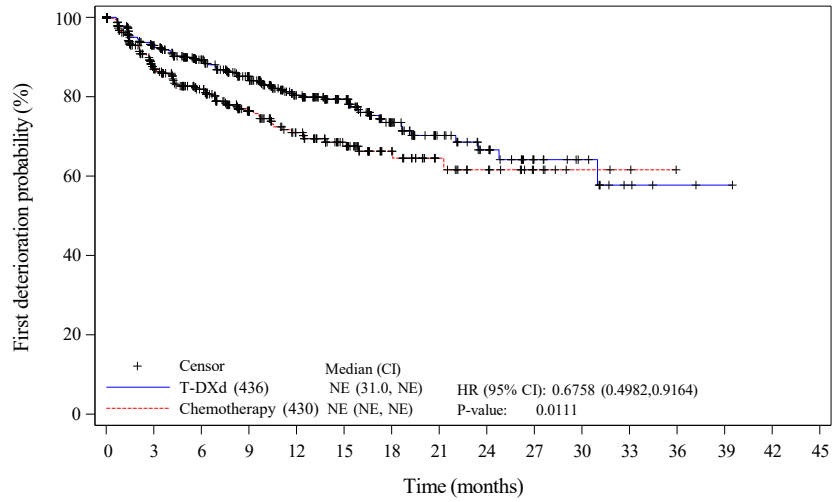
Figure 2.14.5 PGI-C - Time to first deterioration - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:

T-DXd(436)	436	350	291	241	173	133	75	45	31	16	11	4	2	1	0
Chemotherapy (430)	430	260	203	128	94	67	40	22	15	7	3	2	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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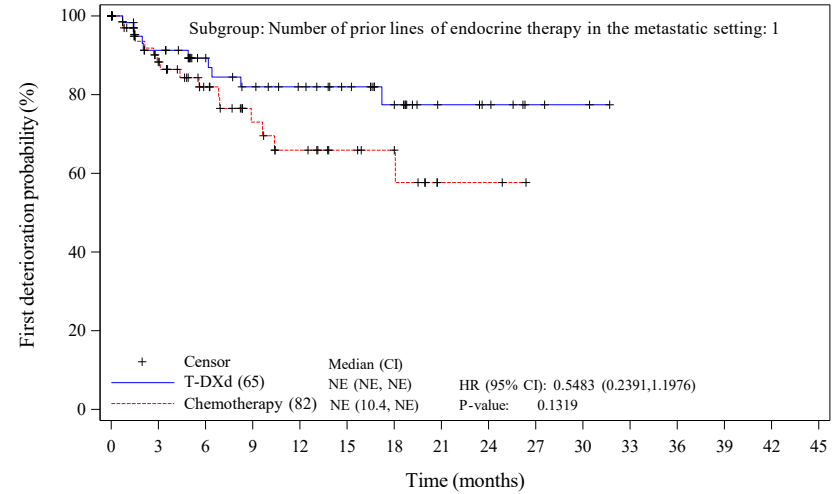
Abbildung 2.14.6 PGI-C – Zeit bis zur erstmaligen Verschlechterung – Kaplan-Meier-Plot – Analyse nach Subgruppe – FAS

Figure 2.14.6 PGI-C - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Patients still at risk:

T-DXd(65)	65	49	38	32	28	23	17	9	7	3	2	0
Chemotherapy (82)	82	48	32	21	16	11	9	2	2	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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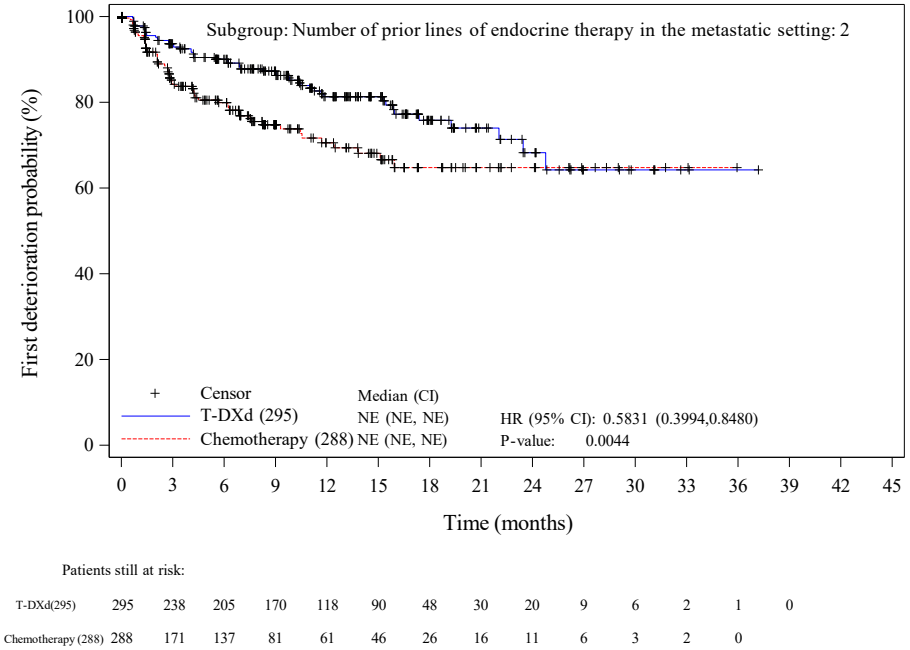
Figure 2.14.6 PGI-C - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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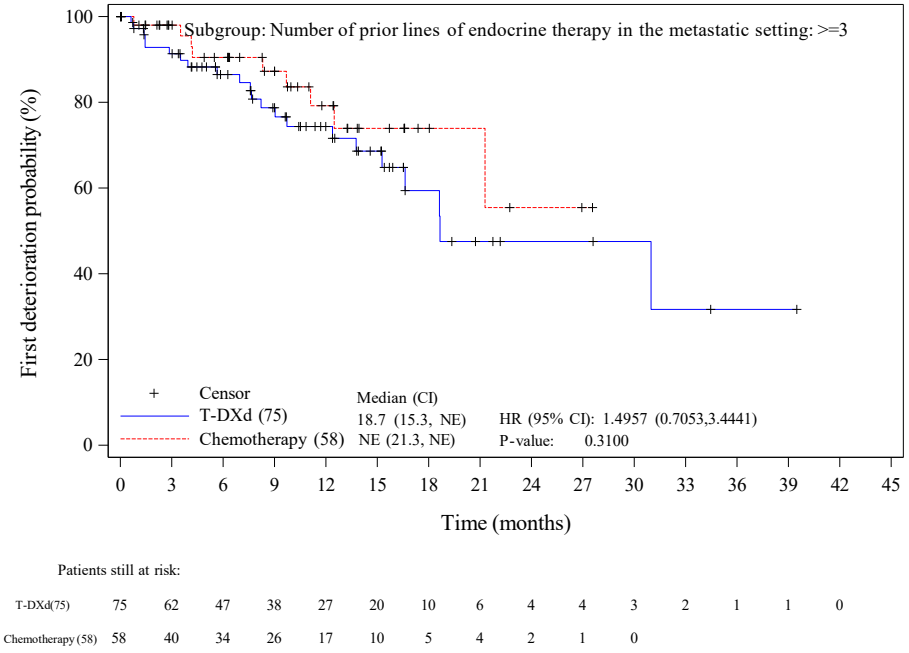
Figure 2.14.6 PGI-C - Time to first deterioration - Kaplan-Meier plot - Analysis by subgroup - Full Analysis Set



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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Anhang 4-G 3.6 Rücklauf

Tabelle 10.16.1 PRO – Patienten mit Baseline- und mind. einem Post-Baseline-Wert – FAS

Table 10.16.1 Questionnaire completion - Patients with baseline and at least one post-baseline measurement - Descriptive summary - Full Analysis Set

	T-DXd N=436	Chemotherapy N=430
Questionnaire - Scale	n (%)	n (%)
EORTC QLQ-C30 - Global Health Status	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Functional Scales/Physical Functioning	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Functional Scales/Role Functioning	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Functional Scales/Emotional Functioning	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Functional Scales/Cognitive Functioning	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Functional Scales/Social Functioning	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Symptom Scales/Fatigue	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Symptom Scales/Nausea and Vomiting	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Symptom Scales/Pain	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Common Symptoms/Dyspnoea	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Common Symptoms/Insomnia	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Common Symptoms/Appetite Loss	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Common Symptoms/Constipation	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Common Symptoms/Diarrhea	287 (65.8)	300 (69.8)
EORTC QLQ-C30 - Common Symptoms/Financial Difficulties	287 (65.8)	300 (69.8)
EORTC QLQ-BR45 - Functional Scales/Body Image	272 (62.4)	292 (67.9)
EORTC QLQ-BR45 - Functional Scales/Sexual Functioning	272 (62.4)	292 (67.9)
EORTC QLQ-BR45 - Functional Scales/Breast Satisfaction	272 (62.4)	290 (67.4)

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

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Table 10.16.1 Questionnaire completion - Patients with baseline and at least one post-baseline measurement - Descriptive summary - Full Analysis Set

	T-DXd N=436	Chemotherapy N=430
Questionnaire - Scale	n (%)	n (%)
EORTC QLQ-BR45 - Functional Scales/Sexual Enjoyment	48 (11.0)	57 (13.3)
EORTC QLQ-BR45 - Functional Scales/Future Perspective	272 (62.4)	292 (67.9)
EORTC QLQ-BR45 - Symptom Scales/Arm Symptoms	272 (62.4)	292 (67.9)
EORTC QLQ-BR45 - Symptom Scales/Breast Symptoms	272 (62.4)	292 (67.9)
EORTC QLQ-BR45 - Symptom Scales/Systemic Therapy Side Effects	272 (62.4)	292 (67.9)
EORTC QLQ-BR45 - Symptom Scales/Endocrine Therapy Symptoms	272 (62.4)	292 (67.9)
EORTC QLQ-BR45 - Symptom Scales/Skin Mucosis Symptoms	272 (62.4)	292 (67.9)
EORTC QLQ-BR45 - Symptom Scales/Endocrine Sexual Symptoms	272 (62.4)	291 (67.7)
EORTC QLQ-BR45 - Symptom Scales/Upset by Hair Loss	73 (16.7)	76 (17.7)
EQ-5D-5L - VAS	259 (59.4)	286 (66.5)
PGI-C	407 (93.3)	366 (85.1)
PGI-S	259 (59.4)	284 (66.0)

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

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Tabelle 14.2.9.1.2 PRO Rücklaufquoten – ITT-Population

Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Baseline	Expected forms[a] (n)	436	430
		Received forms[b] (n)	290	320
		Evaluable forms[c] (n)	290	320
		Compliance rate[d] (%)	66.5	74.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 4 Day 1	Expected forms[a] (n)	434	414
		Received forms[b] (n)	382	325
		Evaluable forms[c] (n)	382	325
		Compliance rate[d] (%)	88.0	78.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 7 Day 1	Expected forms[a] (n)	432	409
		Received forms[b] (n)	358	315
		Evaluable forms[c] (n)	358	315
		Compliance rate[d] (%)	82.9	77.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 10 Day 1	Expected forms[a] (n)	431	401
		Received forms[b] (n)	351	286
		Evaluable forms[c] (n)	351	286
		Compliance rate[d] (%)	81.4	71.3
		Evaluability rate[e] (%)	100.0	100.0

[a] A questionnaire that is expected to be completed at a scheduled assessment time.
[b] A questionnaire that is expected to be completed, has been received and has a completion date and at least one individual item completed.
[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
[f] The total number of patients expected to have completed at least a baseline questionnaire.
[g] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire (as defined above).
[h] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire divided by the total number of patients expected to have completed at least a baseline questionnaire multiplied by 100.
Baseline is defined as the last assessment on or prior to randomization, or before the first dose if assessment only available after randomization.
EORTC = European Organization for the Research and Treatment of Cancer. PGI-TT = Patient Global Impression of Treatment Tolerability. QLQ = Quality of Life Questionnaire. T-DXd = trastuzumab deruxtecan.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 13 Day 1	Expected forms[a] (n)	431	393
		Received forms[b] (n)	332	280
		Evaluable forms[c] (n)	332	280
		Compliance rate[d] (%)	77.0	71.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 16 Day 1	Expected forms[a] (n)	426	384
		Received forms[b] (n)	318	246
		Evaluable forms[c] (n)	318	246
		Compliance rate[d] (%)	74.6	64.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 19 Day 1	Expected forms[a] (n)	419	379
		Received forms[b] (n)	310	243
		Evaluable forms[c] (n)	310	243
		Compliance rate[d] (%)	74.0	64.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 22 Day 1	Expected forms[a] (n)	410	367
		Received forms[b] (n)	302	232
		Evaluable forms[c] (n)	302	232
		Compliance rate[d] (%)	73.7	63.2
		Evaluability rate[e] (%)	100.0	100.0

[a] A questionnaire that is expected to be completed at a scheduled assessment time.
[b] A questionnaire that is expected to be completed, has been received and has a completion date and at least one individual item completed.
[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
[f] The total number of patients expected to have completed at least a baseline questionnaire.
[g] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire (as defined above).
[h] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire divided by the total number of patients expected to have completed at least a baseline questionnaire multiplied by 100.
Baseline is defined as the last assessment on or prior to randomization, or before the first dose if assessment only available after randomization.
EORTC = European Organization for the Research and Treatment of Cancer. PGI-TT = Patient Global Impression of Treatment Tolerability. QLQ = Quality of Life Questionnaire. T-DXd = trastuzumab deruxtecan.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 25 Day 1	Expected forms[a] (n)	400	361
		Received forms[b] (n)	297	214
		Evaluable forms[c] (n)	297	214
		Compliance rate[d] (%)	74.3	59.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 28 Day 1	Expected forms[a] (n)	394	352
		Received forms[b] (n)	277	199
		Evaluable forms[c] (n)	277	199
		Compliance rate[d] (%)	70.3	56.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 31 Day 1	Expected forms[a] (n)	387	342
		Received forms[b] (n)	271	182
		Evaluable forms[c] (n)	271	182
		Compliance rate[d] (%)	70.0	53.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 34 Day 1	Expected forms[a] (n)	380	334
		Received forms[b] (n)	257	183
		Evaluable forms[c] (n)	257	183
		Compliance rate[d] (%)	67.6	54.8
		Evaluability rate[e] (%)	100.0	100.0

[a] A questionnaire that is expected to be completed at a scheduled assessment time.
[b] A questionnaire that is expected to be completed, has been received and has a completion date and at least one individual item completed.
[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
[f] The total number of patients expected to have completed at least a baseline questionnaire.
[g] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire (as defined above).
[h] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire divided by the total number of patients expected to have completed at least a baseline questionnaire multiplied by 100.
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EORTC = European Organization for the Research and Treatment of Cancer. PGI-TT = Patient Global Impression of Treatment Tolerability. QLQ = Quality of Life Questionnaire. T-DXd = trastuzumab deruxtecan.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 37 Day 1	Expected forms[a] (n)	369	315
		Received forms[b] (n)	249	163
		Evaluable forms[c] (n)	249	163
		Compliance rate[d] (%)	67.5	51.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 40 Day 1	Expected forms[a] (n)	366	305
		Received forms[b] (n)	235	142
		Evaluable forms[c] (n)	235	142
		Compliance rate[d] (%)	64.2	46.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 43 Day 1	Expected forms[a] (n)	364	293
		Received forms[b] (n)	225	131
		Evaluable forms[c] (n)	225	131
		Compliance rate[d] (%)	61.8	44.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 46 Day 1	Expected forms[a] (n)	354	271
		Received forms[b] (n)	204	118
		Evaluable forms[c] (n)	204	118
		Compliance rate[d] (%)	57.6	43.5
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 49 Day 1	Expected forms[a] (n)	349	255
		Received forms[b] (n)	196	102
		Evaluable forms[c] (n)	196	102
		Compliance rate[d] (%)	56.2	40.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 52 Day 1	Expected forms[a] (n)	335	242
		Received forms[b] (n)	177	95
		Evaluable forms[c] (n)	177	95
		Compliance rate[d] (%)	52.8	39.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 55 Day 1	Expected forms[a] (n)	322	227
		Received forms[b] (n)	161	90
		Evaluable forms[c] (n)	161	90
		Compliance rate[d] (%)	50.0	39.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 58 Day 1	Expected forms[a] (n)	306	214
		Received forms[b] (n)	150	86
		Evaluable forms[c] (n)	150	86
		Compliance rate[d] (%)	49.0	40.2
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 61 Day 1	Expected forms[a] (n)	290	204
		Received forms[b] (n)	151	79
		Evaluable forms[c] (n)	151	79
		Compliance rate[d] (%)	52.1	38.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 64 Day 1	Expected forms[a] (n)	280	184
		Received forms[b] (n)	136	68
		Evaluable forms[c] (n)	136	68
		Compliance rate[d] (%)	48.6	37.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 67 Day 1	Expected forms[a] (n)	257	171
		Received forms[b] (n)	126	61
		Evaluable forms[c] (n)	126	61
		Compliance rate[d] (%)	49.0	35.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 70 Day 1	Expected forms[a] (n)	234	155
		Received forms[b] (n)	113	56
		Evaluable forms[c] (n)	113	56
		Compliance rate[d] (%)	48.3	36.1
		Evaluability rate[e] (%)	100.0	100.0

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
[f] The total number of patients expected to have completed at least a baseline questionnaire.
[g] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire (as defined above).
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 73 Day 1	Expected forms[a] (n)	220	140
		Received forms[b] (n)	109	46
		Evaluable forms[c] (n)	109	46
		Compliance rate[d] (%)	49.5	32.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 76 Day 1	Expected forms[a] (n)	190	123
		Received forms[b] (n)	87	42
		Evaluable forms[c] (n)	87	42
		Compliance rate[d] (%)	45.8	34.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 79 Day 1	Expected forms[a] (n)	178	105
		Received forms[b] (n)	84	33
		Evaluable forms[c] (n)	84	33
		Compliance rate[d] (%)	47.2	31.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 82 Day 1	Expected forms[a] (n)	164	96
		Received forms[b] (n)	75	32
		Evaluable forms[c] (n)	75	32
		Compliance rate[d] (%)	45.7	33.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 85 Day 1	Expected forms[a] (n)	148	89
		Received forms[b] (n)	71	31
		Evaluable forms[c] (n)	71	31
		Compliance rate[d] (%)	48.0	34.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 88 Day 1	Expected forms[a] (n)	132	79
		Received forms[b] (n)	60	27
		Evaluable forms[c] (n)	60	27
		Compliance rate[d] (%)	45.5	34.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 91 Day 1	Expected forms[a] (n)	122	69
		Received forms[b] (n)	56	24
		Evaluable forms[c] (n)	56	24
		Compliance rate[d] (%)	45.9	34.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 94 Day 1	Expected forms[a] (n)	113	66
		Received forms[b] (n)	46	19
		Evaluable forms[c] (n)	46	19
		Compliance rate[d] (%)	40.7	28.8
		Evaluability rate[e] (%)	100.0	100.0

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[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 97 Day 1	Expected forms[a] (n)	104	61
		Received forms[b] (n)	42	17
		Evaluable forms[c] (n)	42	17
		Compliance rate[d] (%)	40.4	27.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 100 Day 1	Expected forms[a] (n)	99	56
		Received forms[b] (n)	40	15
		Evaluable forms[c] (n)	40	15
		Compliance rate[d] (%)	40.4	26.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 103 Day 1	Expected forms[a] (n)	85	48
		Received forms[b] (n)	38	12
		Evaluable forms[c] (n)	38	12
		Compliance rate[d] (%)	44.7	25.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 106 Day 1	Expected forms[a] (n)	73	46
		Received forms[b] (n)	32	13
		Evaluable forms[c] (n)	32	13
		Compliance rate[d] (%)	43.8	28.3
		Evaluability rate[e] (%)	100.0	100.0

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[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 109 Day 1	Expected forms[a] (n)	63	40
		Received forms[b] (n)	28	9
		Evaluable forms[c] (n)	28	9
		Compliance rate[d] (%)	44.4	22.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 112 Day 1	Expected forms[a] (n)	53	36
		Received forms[b] (n)	26	9
		Evaluable forms[c] (n)	26	9
		Compliance rate[d] (%)	49.1	25.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 115 Day 1	Expected forms[a] (n)	47	32
		Received forms[b] (n)	21	9
		Evaluable forms[c] (n)	21	9
		Compliance rate[d] (%)	44.7	28.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 118 Day 1	Expected forms[a] (n)	43	26
		Received forms[b] (n)	20	7
		Evaluable forms[c] (n)	20	7
		Compliance rate[d] (%)	46.5	26.9
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 121 Day 1	Expected forms[a] (n)	36	20
		Received forms[b] (n)	16	6
		Evaluable forms[c] (n)	16	6
		Compliance rate[d] (%)	44.4	30.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 124 Day 1	Expected forms[a] (n)	32	18
		Received forms[b] (n)	15	5
		Evaluable forms[c] (n)	15	5
		Compliance rate[d] (%)	46.9	27.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 127 Day 1	Expected forms[a] (n)	28	14
		Received forms[b] (n)	12	4
		Evaluable forms[c] (n)	12	4
		Compliance rate[d] (%)	42.9	28.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 130 Day 1	Expected forms[a] (n)	25	11
		Received forms[b] (n)	9	3
		Evaluable forms[c] (n)	9	3
		Compliance rate[d] (%)	36.0	27.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 133 Day 1	Expected forms[a] (n)	21	11
		Received forms[b] (n)	10	3
		Evaluable forms[c] (n)	10	3
		Compliance rate[d] (%)	47.6	27.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 136 Day 1	Expected forms[a] (n)	20	9
		Received forms[b] (n)	10	3
		Evaluable forms[c] (n)	10	3
		Compliance rate[d] (%)	50.0	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 139 Day 1	Expected forms[a] (n)	14	9
		Received forms[b] (n)	6	3
		Evaluable forms[c] (n)	6	3
		Compliance rate[d] (%)	42.9	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 142 Day 1	Expected forms[a] (n)	13	6
		Received forms[b] (n)	6	2
		Evaluable forms[c] (n)	6	2
		Compliance rate[d] (%)	46.2	33.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 145 Day 1	Expected forms[a] (n)	13	5
		Received forms[b] (n)	4	2
		Evaluable forms[c] (n)	4	2
		Compliance rate[d] (%)	30.8	40.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 148 Day 1	Expected forms[a] (n)	10	3
		Received forms[b] (n)	3	1
		Evaluable forms[c] (n)	3	1
		Compliance rate[d] (%)	30.0	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 151 Day 1	Expected forms[a] (n)	9	2
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	22.2	50.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 154 Day 1	Expected forms[a] (n)	5	2
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	40.0	50.0
		Evaluability rate[e] (%)	100.0	100.0

[a] A questionnaire that is expected to be completed at a scheduled assessment time.
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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 157 Day 1	Expected forms[a] (n)	5	2
		Received forms[b] (n)	1	1
		Evaluable forms[c] (n)	1	1
		Compliance rate[d] (%)	20.0	50.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 160 Day 1	Expected forms[a] (n)	4	1
		Received forms[b] (n)	2	0
		Evaluable forms[c] (n)	2	0
		Compliance rate[d] (%)	50.0	0.0
		Evaluability rate[e] (%)	100.0	
	Week 163 Day 1	Expected forms[a] (n)	3	1
		Received forms[b] (n)	2	0
		Evaluable forms[c] (n)	2	0
		Compliance rate[d] (%)	66.7	0.0
		Evaluability rate[e] (%)	100.0	
	Week 166 Day 1	Expected forms[a] (n)	2	1
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	50.0	0.0
		Evaluability rate[e] (%)	100.0	

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-C30	Week 169 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Week 172 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Overall patient compliance	Expected forms[f] (n)	436	430
		Evaluable forms[g] (n)	287	300
		Compliance rate[h] (%)	65.8	69.8

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Baseline	Expected forms[a] (n)	436	430
		Received forms[b] (n)	277	315
		Evaluable forms[c] (n)	277	315
		Compliance rate[d] (%)	63.5	73.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 4 Day 1	Expected forms[a] (n)	434	414
		Received forms[b] (n)	377	322
		Evaluable forms[c] (n)	377	322
		Compliance rate[d] (%)	86.9	77.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 7 Day 1	Expected forms[a] (n)	432	409
		Received forms[b] (n)	353	311
		Evaluable forms[c] (n)	353	311
		Compliance rate[d] (%)	81.7	76.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 10 Day 1	Expected forms[a] (n)	431	401
		Received forms[b] (n)	350	283
		Evaluable forms[c] (n)	350	283
		Compliance rate[d] (%)	81.2	70.6
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 13 Day 1	Expected forms[a] (n)	431	393
		Received forms[b] (n)	330	279
		Evaluable forms[c] (n)	330	279
		Compliance rate[d] (%)	76.6	71.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 16 Day 1	Expected forms[a] (n)	426	384
		Received forms[b] (n)	317	244
		Evaluable forms[c] (n)	317	244
		Compliance rate[d] (%)	74.4	63.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 19 Day 1	Expected forms[a] (n)	419	379
		Received forms[b] (n)	306	243
		Evaluable forms[c] (n)	306	243
		Compliance rate[d] (%)	73.0	64.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 22 Day 1	Expected forms[a] (n)	410	367
		Received forms[b] (n)	301	229
		Evaluable forms[c] (n)	301	229
		Compliance rate[d] (%)	73.4	62.4
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 25 Day 1	Expected forms[a] (n)	400	361
		Received forms[b] (n)	295	213
		Evaluable forms[c] (n)	295	213
		Compliance rate[d] (%)	73.8	59.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 28 Day 1	Expected forms[a] (n)	394	352
		Received forms[b] (n)	276	199
		Evaluable forms[c] (n)	276	199
		Compliance rate[d] (%)	70.1	56.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 31 Day 1	Expected forms[a] (n)	387	342
		Received forms[b] (n)	271	182
		Evaluable forms[c] (n)	271	182
		Compliance rate[d] (%)	70.0	53.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 34 Day 1	Expected forms[a] (n)	380	334
		Received forms[b] (n)	256	181
		Evaluable forms[c] (n)	256	181
		Compliance rate[d] (%)	67.4	54.2
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 37 Day 1	Expected forms[a] (n)	369	315
		Received forms[b] (n)	248	162
		Evaluable forms[c] (n)	248	162
		Compliance rate[d] (%)	67.2	51.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 40 Day 1	Expected forms[a] (n)	366	305
		Received forms[b] (n)	235	142
		Evaluable forms[c] (n)	235	142
		Compliance rate[d] (%)	64.2	46.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 43 Day 1	Expected forms[a] (n)	364	293
		Received forms[b] (n)	223	130
		Evaluable forms[c] (n)	223	130
		Compliance rate[d] (%)	61.3	44.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 46 Day 1	Expected forms[a] (n)	354	271
		Received forms[b] (n)	204	117
		Evaluable forms[c] (n)	204	117
		Compliance rate[d] (%)	57.6	43.2
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 49 Day 1	Expected forms[a] (n)	349	255
		Received forms[b] (n)	196	102
		Evaluable forms[c] (n)	196	102
		Compliance rate[d] (%)	56.2	40.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 52 Day 1	Expected forms[a] (n)	335	242
		Received forms[b] (n)	177	95
		Evaluable forms[c] (n)	177	95
		Compliance rate[d] (%)	52.8	39.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 55 Day 1	Expected forms[a] (n)	322	227
		Received forms[b] (n)	161	90
		Evaluable forms[c] (n)	161	90
		Compliance rate[d] (%)	50.0	39.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 58 Day 1	Expected forms[a] (n)	306	214
		Received forms[b] (n)	149	85
		Evaluable forms[c] (n)	149	85
		Compliance rate[d] (%)	48.7	39.7
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 61 Day 1	Expected forms[a] (n)	290	204
		Received forms[b] (n)	151	79
		Evaluable forms[c] (n)	151	79
		Compliance rate[d] (%)	52.1	38.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 64 Day 1	Expected forms[a] (n)	280	184
		Received forms[b] (n)	135	67
		Evaluable forms[c] (n)	135	67
		Compliance rate[d] (%)	48.2	36.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 67 Day 1	Expected forms[a] (n)	257	171
		Received forms[b] (n)	126	61
		Evaluable forms[c] (n)	126	61
		Compliance rate[d] (%)	49.0	35.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 70 Day 1	Expected forms[a] (n)	234	155
		Received forms[b] (n)	113	56
		Evaluable forms[c] (n)	113	56
		Compliance rate[d] (%)	48.3	36.1
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 73 Day 1	Expected forms[a] (n)	220	140
		Received forms[b] (n)	109	46
		Evaluable forms[c] (n)	109	46
		Compliance rate[d] (%)	49.5	32.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 76 Day 1	Expected forms[a] (n)	190	123
		Received forms[b] (n)	87	42
		Evaluable forms[c] (n)	87	42
		Compliance rate[d] (%)	45.8	34.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 79 Day 1	Expected forms[a] (n)	178	105
		Received forms[b] (n)	84	33
		Evaluable forms[c] (n)	84	33
		Compliance rate[d] (%)	47.2	31.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 82 Day 1	Expected forms[a] (n)	164	96
		Received forms[b] (n)	75	32
		Evaluable forms[c] (n)	75	32
		Compliance rate[d] (%)	45.7	33.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 85 Day 1	Expected forms[a] (n)	148	89
		Received forms[b] (n)	71	31
		Evaluable forms[c] (n)	71	31
		Compliance rate[d] (%)	48.0	34.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 88 Day 1	Expected forms[a] (n)	132	79
		Received forms[b] (n)	60	27
		Evaluable forms[c] (n)	60	27
		Compliance rate[d] (%)	45.5	34.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 91 Day 1	Expected forms[a] (n)	122	69
		Received forms[b] (n)	56	24
		Evaluable forms[c] (n)	56	24
		Compliance rate[d] (%)	45.9	34.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 94 Day 1	Expected forms[a] (n)	113	66
		Received forms[b] (n)	46	19
		Evaluable forms[c] (n)	46	19
		Compliance rate[d] (%)	40.7	28.8
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 97 Day 1	Expected forms[a] (n)	104	61
		Received forms[b] (n)	42	17
		Evaluable forms[c] (n)	42	17
		Compliance rate[d] (%)	40.4	27.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 100 Day 1	Expected forms[a] (n)	99	56
		Received forms[b] (n)	40	15
		Evaluable forms[c] (n)	40	15
		Compliance rate[d] (%)	40.4	26.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 103 Day 1	Expected forms[a] (n)	85	48
		Received forms[b] (n)	38	12
		Evaluable forms[c] (n)	38	12
		Compliance rate[d] (%)	44.7	25.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 106 Day 1	Expected forms[a] (n)	73	46
		Received forms[b] (n)	32	13
		Evaluable forms[c] (n)	32	13
		Compliance rate[d] (%)	43.8	28.3
		Evaluability rate[e] (%)	100.0	100.0

[a] A questionnaire that is expected to be completed at a scheduled assessment time.
[b] A questionnaire that is expected to be completed, has been received and has a completion date and at least one individual item completed.
[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 109 Day 1	Expected forms[a] (n)	63	40
		Received forms[b] (n)	28	9
		Evaluable forms[c] (n)	28	9
		Compliance rate[d] (%)	44.4	22.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 112 Day 1	Expected forms[a] (n)	53	36
		Received forms[b] (n)	26	9
		Evaluable forms[c] (n)	26	9
		Compliance rate[d] (%)	49.1	25.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 115 Day 1	Expected forms[a] (n)	47	32
		Received forms[b] (n)	21	9
		Evaluable forms[c] (n)	21	9
		Compliance rate[d] (%)	44.7	28.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 118 Day 1	Expected forms[a] (n)	43	26
		Received forms[b] (n)	20	7
		Evaluable forms[c] (n)	20	7
		Compliance rate[d] (%)	46.5	26.9
		Evaluability rate[e] (%)	100.0	100.0

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 121 Day 1	Expected forms[a] (n)	36	20
		Received forms[b] (n)	16	6
		Evaluable forms[c] (n)	16	6
		Compliance rate[d] (%)	44.4	30.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 124 Day 1	Expected forms[a] (n)	32	18
		Received forms[b] (n)	15	5
		Evaluable forms[c] (n)	15	5
		Compliance rate[d] (%)	46.9	27.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 127 Day 1	Expected forms[a] (n)	28	14
		Received forms[b] (n)	12	4
		Evaluable forms[c] (n)	12	4
		Compliance rate[d] (%)	42.9	28.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 130 Day 1	Expected forms[a] (n)	25	11
		Received forms[b] (n)	9	3
		Evaluable forms[c] (n)	9	3
		Compliance rate[d] (%)	36.0	27.3
		Evaluability rate[e] (%)	100.0	100.0

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 133 Day 1	Expected forms[a] (n)	21	11
		Received forms[b] (n)	10	3
		Evaluable forms[c] (n)	10	3
		Compliance rate[d] (%)	47.6	27.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 136 Day 1	Expected forms[a] (n)	20	9
		Received forms[b] (n)	10	3
		Evaluable forms[c] (n)	10	3
		Compliance rate[d] (%)	50.0	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 139 Day 1	Expected forms[a] (n)	14	9
		Received forms[b] (n)	6	3
		Evaluable forms[c] (n)	6	3
		Compliance rate[d] (%)	42.9	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 142 Day 1	Expected forms[a] (n)	13	6
		Received forms[b] (n)	6	2
		Evaluable forms[c] (n)	6	2
		Compliance rate[d] (%)	46.2	33.3
		Evaluability rate[e] (%)	100.0	100.0

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 145 Day 1	Expected forms[a] (n)	13	5
		Received forms[b] (n)	4	2
		Evaluable forms[c] (n)	4	2
		Compliance rate[d] (%)	30.8	40.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 148 Day 1	Expected forms[a] (n)	10	3
		Received forms[b] (n)	3	1
		Evaluable forms[c] (n)	3	1
		Compliance rate[d] (%)	30.0	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 151 Day 1	Expected forms[a] (n)	9	2
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	22.2	50.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 154 Day 1	Expected forms[a] (n)	5	2
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	40.0	50.0
		Evaluability rate[e] (%)	100.0	100.0

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 157 Day 1	Expected forms[a] (n)	5	2
		Received forms[b] (n)	1	1
		Evaluable forms[c] (n)	1	1
		Compliance rate[d] (%)	20.0	50.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 160 Day 1	Expected forms[a] (n)	4	1
		Received forms[b] (n)	2	0
		Evaluable forms[c] (n)	2	0
		Compliance rate[d] (%)	50.0	0.0
		Evaluability rate[e] (%)	100.0	
	Week 163 Day 1	Expected forms[a] (n)	3	1
		Received forms[b] (n)	2	0
		Evaluable forms[c] (n)	2	0
		Compliance rate[d] (%)	66.7	0.0
		Evaluability rate[e] (%)	100.0	
	Week 166 Day 1	Expected forms[a] (n)	2	1
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	50.0	0.0
		Evaluability rate[e] (%)	100.0	

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EORTC QLQ-BR45	Week 169 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Week 172 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Overall patient compliance	Expected forms[f] (n)	436	430
		Evaluable forms[g] (n)	272	292
		Compliance rate[h] (%)	62.4	67.9

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Baseline	Expected forms[a] (n)	436	430
		Received forms[b] (n)	268	310
		Evaluable forms[c] (n)	268	310
		Compliance rate[d] (%)	61.5	72.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 4 Day 1	Expected forms[a] (n)	434	414
		Received forms[b] (n)	375	320
		Evaluable forms[c] (n)	375	320
		Compliance rate[d] (%)	86.4	77.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 7 Day 1	Expected forms[a] (n)	432	409
		Received forms[b] (n)	350	309
		Evaluable forms[c] (n)	350	309
		Compliance rate[d] (%)	81.0	75.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 10 Day 1	Expected forms[a] (n)	431	401
		Received forms[b] (n)	345	281
		Evaluable forms[c] (n)	345	281
		Compliance rate[d] (%)	80.0	70.1
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 13 Day 1	Expected forms[a] (n)	431	393
		Received forms[b] (n)	326	278
		Evaluable forms[c] (n)	326	278
		Compliance rate[d] (%)	75.6	70.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 16 Day 1	Expected forms[a] (n)	426	384
		Received forms[b] (n)	314	244
		Evaluable forms[c] (n)	314	244
		Compliance rate[d] (%)	73.7	63.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 19 Day 1	Expected forms[a] (n)	419	379
		Received forms[b] (n)	304	243
		Evaluable forms[c] (n)	304	243
		Compliance rate[d] (%)	72.6	64.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 22 Day 1	Expected forms[a] (n)	410	367
		Received forms[b] (n)	297	228
		Evaluable forms[c] (n)	297	228
		Compliance rate[d] (%)	72.4	62.1
		Evaluability rate[e] (%)	100.0	100.0

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[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 25 Day 1	Expected forms[a] (n)	400	361
		Received forms[b] (n)	295	213
		Evaluable forms[c] (n)	295	213
		Compliance rate[d] (%)	73.8	59.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 28 Day 1	Expected forms[a] (n)	394	352
		Received forms[b] (n)	275	198
		Evaluable forms[c] (n)	275	198
		Compliance rate[d] (%)	69.8	56.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 31 Day 1	Expected forms[a] (n)	387	342
		Received forms[b] (n)	269	181
		Evaluable forms[c] (n)	269	181
		Compliance rate[d] (%)	69.5	52.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 34 Day 1	Expected forms[a] (n)	380	334
		Received forms[b] (n)	254	181
		Evaluable forms[c] (n)	254	181
		Compliance rate[d] (%)	66.8	54.2
		Evaluability rate[e] (%)	100.0	100.0

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[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 37 Day 1	Expected forms[a] (n)	369	315
		Received forms[b] (n)	246	162
		Evaluable forms[c] (n)	246	162
		Compliance rate[d] (%)	66.7	51.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 40 Day 1	Expected forms[a] (n)	366	305
		Received forms[b] (n)	232	141
		Evaluable forms[c] (n)	232	141
		Compliance rate[d] (%)	63.4	46.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 43 Day 1	Expected forms[a] (n)	364	293
		Received forms[b] (n)	221	129
		Evaluable forms[c] (n)	221	129
		Compliance rate[d] (%)	60.7	44.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 46 Day 1	Expected forms[a] (n)	354	271
		Received forms[b] (n)	203	117
		Evaluable forms[c] (n)	203	117
		Compliance rate[d] (%)	57.3	43.2
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 49 Day 1	Expected forms[a] (n)	349	255
		Received forms[b] (n)	195	102
		Evaluable forms[c] (n)	195	102
		Compliance rate[d] (%)	55.9	40.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 52 Day 1	Expected forms[a] (n)	335	242
		Received forms[b] (n)	176	95
		Evaluable forms[c] (n)	176	95
		Compliance rate[d] (%)	52.5	39.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 55 Day 1	Expected forms[a] (n)	322	227
		Received forms[b] (n)	161	90
		Evaluable forms[c] (n)	161	90
		Compliance rate[d] (%)	50.0	39.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 58 Day 1	Expected forms[a] (n)	306	214
		Received forms[b] (n)	149	85
		Evaluable forms[c] (n)	149	85
		Compliance rate[d] (%)	48.7	39.7
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 61 Day 1	Expected forms[a] (n)	290	204
		Received forms[b] (n)	151	79
		Evaluable forms[c] (n)	151	79
		Compliance rate[d] (%)	52.1	38.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 64 Day 1	Expected forms[a] (n)	280	184
		Received forms[b] (n)	134	67
		Evaluable forms[c] (n)	134	67
		Compliance rate[d] (%)	47.9	36.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 67 Day 1	Expected forms[a] (n)	257	171
		Received forms[b] (n)	126	61
		Evaluable forms[c] (n)	126	61
		Compliance rate[d] (%)	49.0	35.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 70 Day 1	Expected forms[a] (n)	234	155
		Received forms[b] (n)	112	56
		Evaluable forms[c] (n)	112	56
		Compliance rate[d] (%)	47.9	36.1
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 73 Day 1	Expected forms[a] (n)	220	140
		Received forms[b] (n)	108	46
		Evaluable forms[c] (n)	108	46
		Compliance rate[d] (%)	49.1	32.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 76 Day 1	Expected forms[a] (n)	190	123
		Received forms[b] (n)	87	41
		Evaluable forms[c] (n)	87	41
		Compliance rate[d] (%)	45.8	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 79 Day 1	Expected forms[a] (n)	178	105
		Received forms[b] (n)	83	33
		Evaluable forms[c] (n)	83	33
		Compliance rate[d] (%)	46.6	31.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 82 Day 1	Expected forms[a] (n)	164	96
		Received forms[b] (n)	74	32
		Evaluable forms[c] (n)	74	32
		Compliance rate[d] (%)	45.1	33.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 85 Day 1	Expected forms[a] (n)	148	89
		Received forms[b] (n)	71	31
		Evaluable forms[c] (n)	71	31
		Compliance rate[d] (%)	48.0	34.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 88 Day 1	Expected forms[a] (n)	132	79
		Received forms[b] (n)	59	27
		Evaluable forms[c] (n)	59	27
		Compliance rate[d] (%)	44.7	34.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 91 Day 1	Expected forms[a] (n)	122	69
		Received forms[b] (n)	56	24
		Evaluable forms[c] (n)	56	24
		Compliance rate[d] (%)	45.9	34.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 94 Day 1	Expected forms[a] (n)	113	66
		Received forms[b] (n)	46	19
		Evaluable forms[c] (n)	46	19
		Compliance rate[d] (%)	40.7	28.8
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 97 Day 1	Expected forms[a] (n)	104	61
		Received forms[b] (n)	42	17
		Evaluable forms[c] (n)	42	17
		Compliance rate[d] (%)	40.4	27.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 100 Day 1	Expected forms[a] (n)	99	56
		Received forms[b] (n)	40	15
		Evaluable forms[c] (n)	40	15
		Compliance rate[d] (%)	40.4	26.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 103 Day 1	Expected forms[a] (n)	85	48
		Received forms[b] (n)	38	11
		Evaluable forms[c] (n)	38	11
		Compliance rate[d] (%)	44.7	22.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 106 Day 1	Expected forms[a] (n)	73	46
		Received forms[b] (n)	32	13
		Evaluable forms[c] (n)	32	13
		Compliance rate[d] (%)	43.8	28.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 109 Day 1	Expected forms[a] (n)	63	40
		Received forms[b] (n)	28	9
		Evaluable forms[c] (n)	28	9
		Compliance rate[d] (%)	44.4	22.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 112 Day 1	Expected forms[a] (n)	53	36
		Received forms[b] (n)	26	9
		Evaluable forms[c] (n)	26	9
		Compliance rate[d] (%)	49.1	25.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 115 Day 1	Expected forms[a] (n)	47	32
		Received forms[b] (n)	21	9
		Evaluable forms[c] (n)	21	9
		Compliance rate[d] (%)	44.7	28.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 118 Day 1	Expected forms[a] (n)	43	26
		Received forms[b] (n)	20	7
		Evaluable forms[c] (n)	20	7
		Compliance rate[d] (%)	46.5	26.9
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 121 Day 1	Expected forms[a] (n)	36	20
		Received forms[b] (n)	16	6
		Evaluable forms[c] (n)	16	6
		Compliance rate[d] (%)	44.4	30.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 124 Day 1	Expected forms[a] (n)	32	18
		Received forms[b] (n)	14	5
		Evaluable forms[c] (n)	14	5
		Compliance rate[d] (%)	43.8	27.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 127 Day 1	Expected forms[a] (n)	28	14
		Received forms[b] (n)	12	4
		Evaluable forms[c] (n)	12	4
		Compliance rate[d] (%)	42.9	28.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 130 Day 1	Expected forms[a] (n)	25	11
		Received forms[b] (n)	9	3
		Evaluable forms[c] (n)	9	3
		Compliance rate[d] (%)	36.0	27.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 133 Day 1	Expected forms[a] (n)	21	11
		Received forms[b] (n)	10	3
		Evaluable forms[c] (n)	10	3
		Compliance rate[d] (%)	47.6	27.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 136 Day 1	Expected forms[a] (n)	20	9
		Received forms[b] (n)	10	3
		Evaluable forms[c] (n)	10	3
		Compliance rate[d] (%)	50.0	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 139 Day 1	Expected forms[a] (n)	14	9
		Received forms[b] (n)	6	3
		Evaluable forms[c] (n)	6	3
		Compliance rate[d] (%)	42.9	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 142 Day 1	Expected forms[a] (n)	13	6
		Received forms[b] (n)	6	2
		Evaluable forms[c] (n)	6	2
		Compliance rate[d] (%)	46.2	33.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 145 Day 1	Expected forms[a] (n)	13	5
		Received forms[b] (n)	4	2
		Evaluable forms[c] (n)	4	2
		Compliance rate[d] (%)	30.8	40.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 148 Day 1	Expected forms[a] (n)	10	3
		Received forms[b] (n)	3	1
		Evaluable forms[c] (n)	3	1
		Compliance rate[d] (%)	30.0	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 151 Day 1	Expected forms[a] (n)	9	2
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	22.2	50.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 154 Day 1	Expected forms[a] (n)	5	2
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	40.0	50.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 157 Day 1	Expected forms[a] (n)	5	2
		Received forms[b] (n)	1	1
		Evaluable forms[c] (n)	1	1
		Compliance rate[d] (%)	20.0	50.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 160 Day 1	Expected forms[a] (n)	4	1
		Received forms[b] (n)	2	0
		Evaluable forms[c] (n)	2	0
		Compliance rate[d] (%)	50.0	0.0
		Evaluability rate[e] (%)	100.0	
	Week 163 Day 1	Expected forms[a] (n)	3	1
		Received forms[b] (n)	2	0
		Evaluable forms[c] (n)	2	0
		Compliance rate[d] (%)	66.7	0.0
		Evaluability rate[e] (%)	100.0	
	Week 166 Day 1	Expected forms[a] (n)	2	1
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	50.0	0.0
		Evaluability rate[e] (%)	100.0	

[a] A questionnaire that is expected to be completed at a scheduled assessment time.
[b] A questionnaire that is expected to be completed, has been received and has a completion date and at least one individual item completed.
[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
[f] The total number of patients expected to have completed at least a baseline questionnaire.
[g] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire (as defined above).
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
EQ-5D-5L	Week 169 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Week 172 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Overall patient compliance	Expected forms[f] (n)	436	430
		Evaluable forms[g] (n)	263	288
		Compliance rate[h] (%)	60.3	67.0

[a] A questionnaire that is expected to be completed at a scheduled assessment time.
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[f] The total number of patients expected to have completed at least a baseline questionnaire.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Baseline	Expected forms[a] (n)	436	430
		Received forms[b] (n)	249	301
		Evaluable forms[c] (n)	249	301
		Compliance rate[d] (%)	57.1	70.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 4 Day 1	Expected forms[a] (n)	433	413
		Received forms[b] (n)	358	309
		Evaluable forms[c] (n)	358	309
		Compliance rate[d] (%)	82.7	74.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 7 Day 1	Expected forms[a] (n)	427	396
		Received forms[b] (n)	334	298
		Evaluable forms[c] (n)	334	298
		Compliance rate[d] (%)	78.2	75.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 10 Day 1	Expected forms[a] (n)	411	346
		Received forms[b] (n)	320	258
		Evaluable forms[c] (n)	320	258
		Compliance rate[d] (%)	77.9	74.6
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 13 Day 1	Expected forms[a] (n)	401	323
		Received forms[b] (n)	303	246
		Evaluable forms[c] (n)	303	246
		Compliance rate[d] (%)	75.6	76.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 16 Day 1	Expected forms[a] (n)	384	296
		Received forms[b] (n)	283	213
		Evaluable forms[c] (n)	283	213
		Compliance rate[d] (%)	73.7	72.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 19 Day 1	Expected forms[a] (n)	377	285
		Received forms[b] (n)	280	209
		Evaluable forms[c] (n)	280	209
		Compliance rate[d] (%)	74.3	73.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 22 Day 1	Expected forms[a] (n)	362	262
		Received forms[b] (n)	273	189
		Evaluable forms[c] (n)	273	189
		Compliance rate[d] (%)	75.4	72.1
		Evaluability rate[e] (%)	100.0	100.0

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[f] The total number of patients expected to have completed at least a baseline questionnaire.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 25 Day 1	Expected forms[a] (n)	344	244
		Received forms[b] (n)	261	174
		Evaluable forms[c] (n)	261	174
		Compliance rate[d] (%)	75.9	71.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 28 Day 1	Expected forms[a] (n)	330	208
		Received forms[b] (n)	247	149
		Evaluable forms[c] (n)	247	149
		Compliance rate[d] (%)	74.8	71.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 31 Day 1	Expected forms[a] (n)	319	197
		Received forms[b] (n)	237	137
		Evaluable forms[c] (n)	237	137
		Compliance rate[d] (%)	74.3	69.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 34 Day 1	Expected forms[a] (n)	303	173
		Received forms[b] (n)	220	133
		Evaluable forms[c] (n)	220	133
		Compliance rate[d] (%)	72.6	76.9
		Evaluability rate[e] (%)	100.0	100.0

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
[f] The total number of patients expected to have completed at least a baseline questionnaire.
[g] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire (as defined above).
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 37 Day 1	Expected forms[a] (n)	288	153
		Received forms[b] (n)	214	113
		Evaluable forms[c] (n)	214	113
		Compliance rate[d] (%)	74.3	73.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 40 Day 1	Expected forms[a] (n)	273	138
		Received forms[b] (n)	200	101
		Evaluable forms[c] (n)	200	101
		Compliance rate[d] (%)	73.3	73.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 43 Day 1	Expected forms[a] (n)	260	124
		Received forms[b] (n)	185	93
		Evaluable forms[c] (n)	185	93
		Compliance rate[d] (%)	71.2	75.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 46 Day 1	Expected forms[a] (n)	235	110
		Received forms[b] (n)	169	79
		Evaluable forms[c] (n)	169	79
		Compliance rate[d] (%)	71.9	71.8
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 49 Day 1	Expected forms[a] (n)	221	105
		Received forms[b] (n)	162	77
		Evaluable forms[c] (n)	162	77
		Compliance rate[d] (%)	73.3	73.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 52 Day 1	Expected forms[a] (n)	210	95
		Received forms[b] (n)	143	65
		Evaluable forms[c] (n)	143	65
		Compliance rate[d] (%)	68.1	68.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 55 Day 1	Expected forms[a] (n)	199	91
		Received forms[b] (n)	138	63
		Evaluable forms[c] (n)	138	63
		Compliance rate[d] (%)	69.3	69.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 58 Day 1	Expected forms[a] (n)	194	89
		Received forms[b] (n)	130	62
		Evaluable forms[c] (n)	130	62
		Compliance rate[d] (%)	67.0	69.7
		Evaluability rate[e] (%)	100.0	100.0

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[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 61 Day 1	Expected forms[a] (n)	175	75
		Received forms[b] (n)	120	51
		Evaluable forms[c] (n)	120	51
		Compliance rate[d] (%)	68.6	68.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 64 Day 1	Expected forms[a] (n)	162	66
		Received forms[b] (n)	107	45
		Evaluable forms[c] (n)	107	45
		Compliance rate[d] (%)	66.0	68.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 67 Day 1	Expected forms[a] (n)	151	59
		Received forms[b] (n)	100	39
		Evaluable forms[c] (n)	100	39
		Compliance rate[d] (%)	66.2	66.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 70 Day 1	Expected forms[a] (n)	132	49
		Received forms[b] (n)	85	32
		Evaluable forms[c] (n)	85	32
		Compliance rate[d] (%)	64.4	65.3
		Evaluability rate[e] (%)	100.0	100.0

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[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
[f] The total number of patients expected to have completed at least a baseline questionnaire.
[g] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire (as defined above).
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 73 Day 1	Expected forms[a] (n)	119	42
		Received forms[b] (n)	78	27
		Evaluable forms[c] (n)	78	27
		Compliance rate[d] (%)	65.5	64.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 76 Day 1	Expected forms[a] (n)	107	39
		Received forms[b] (n)	65	27
		Evaluable forms[c] (n)	65	27
		Compliance rate[d] (%)	60.7	69.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 79 Day 1	Expected forms[a] (n)	89	36
		Received forms[b] (n)	60	23
		Evaluable forms[c] (n)	60	23
		Compliance rate[d] (%)	67.4	63.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 82 Day 1	Expected forms[a] (n)	82	34
		Received forms[b] (n)	56	24
		Evaluable forms[c] (n)	56	24
		Compliance rate[d] (%)	68.3	70.6
		Evaluability rate[e] (%)	100.0	100.0

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[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 85 Day 1	Expected forms[a] (n)	76	32
		Received forms[b] (n)	54	23
		Evaluable forms[c] (n)	54	23
		Compliance rate[d] (%)	71.1	71.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 88 Day 1	Expected forms[a] (n)	68	29
		Received forms[b] (n)	45	21
		Evaluable forms[c] (n)	45	21
		Compliance rate[d] (%)	66.2	72.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 91 Day 1	Expected forms[a] (n)	63	23
		Received forms[b] (n)	40	18
		Evaluable forms[c] (n)	40	18
		Compliance rate[d] (%)	63.5	78.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 94 Day 1	Expected forms[a] (n)	57	21
		Received forms[b] (n)	33	14
		Evaluable forms[c] (n)	33	14
		Compliance rate[d] (%)	57.9	66.7
		Evaluability rate[e] (%)	100.0	100.0

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[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 97 Day 1	Expected forms[a] (n)	48	18
		Received forms[b] (n)	30	13
		Evaluable forms[c] (n)	30	13
		Compliance rate[d] (%)	62.5	72.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 100 Day 1	Expected forms[a] (n)	45	14
		Received forms[b] (n)	27	11
		Evaluable forms[c] (n)	27	11
		Compliance rate[d] (%)	60.0	78.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 103 Day 1	Expected forms[a] (n)	41	13
		Received forms[b] (n)	27	7
		Evaluable forms[c] (n)	27	7
		Compliance rate[d] (%)	65.9	53.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 106 Day 1	Expected forms[a] (n)	36	11
		Received forms[b] (n)	22	9
		Evaluable forms[c] (n)	22	9
		Compliance rate[d] (%)	61.1	81.8
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 109 Day 1	Expected forms[a] (n)	30	7
		Received forms[b] (n)	21	4
		Evaluable forms[c] (n)	21	4
		Compliance rate[d] (%)	70.0	57.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 112 Day 1	Expected forms[a] (n)	25	6
		Received forms[b] (n)	18	4
		Evaluable forms[c] (n)	18	4
		Compliance rate[d] (%)	72.0	66.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 115 Day 1	Expected forms[a] (n)	22	6
		Received forms[b] (n)	14	4
		Evaluable forms[c] (n)	14	4
		Compliance rate[d] (%)	63.6	66.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 118 Day 1	Expected forms[a] (n)	21	4
		Received forms[b] (n)	13	4
		Evaluable forms[c] (n)	13	4
		Compliance rate[d] (%)	61.9	100.0
		Evaluability rate[e] (%)	100.0	100.0

[a] A questionnaire that is expected to be completed at a scheduled assessment time.
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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
[f] The total number of patients expected to have completed at least a baseline questionnaire.
[g] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire (as defined above).
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 121 Day 1	Expected forms[a] (n)	18	2
		Received forms[b] (n)	11	2
		Evaluable forms[c] (n)	11	2
		Compliance rate[d] (%)	61.1	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 124 Day 1	Expected forms[a] (n)	16	2
		Received forms[b] (n)	10	2
		Evaluable forms[c] (n)	10	2
		Compliance rate[d] (%)	62.5	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 127 Day 1	Expected forms[a] (n)	13	2
		Received forms[b] (n)	8	2
		Evaluable forms[c] (n)	8	2
		Compliance rate[d] (%)	61.5	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 130 Day 1	Expected forms[a] (n)	12	2
		Received forms[b] (n)	6	2
		Evaluable forms[c] (n)	6	2
		Compliance rate[d] (%)	50.0	100.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 133 Day 1	Expected forms[a] (n)	9	2
		Received forms[b] (n)	6	2
		Evaluable forms[c] (n)	6	2
		Compliance rate[d] (%)	66.7	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 136 Day 1	Expected forms[a] (n)	8	2
		Received forms[b] (n)	5	2
		Evaluable forms[c] (n)	5	2
		Compliance rate[d] (%)	62.5	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 139 Day 1	Expected forms[a] (n)	6	2
		Received forms[b] (n)	2	2
		Evaluable forms[c] (n)	2	2
		Compliance rate[d] (%)	33.3	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 142 Day 1	Expected forms[a] (n)	4	1
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	50.0	100.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 145 Day 1	Expected forms[a] (n)	4	1
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	50.0	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 148 Day 1	Expected forms[a] (n)	4	1
		Received forms[b] (n)	1	1
		Evaluable forms[c] (n)	1	1
		Compliance rate[d] (%)	25.0	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 151 Day 1	Expected forms[a] (n)	3	1
		Received forms[b] (n)	1	1
		Evaluable forms[c] (n)	1	1
		Compliance rate[d] (%)	33.3	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 154 Day 1	Expected forms[a] (n)	2	1
		Received forms[b] (n)	1	1
		Evaluable forms[c] (n)	1	1
		Compliance rate[d] (%)	50.0	100.0
		Evaluability rate[e] (%)	100.0	100.0

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
[f] The total number of patients expected to have completed at least a baseline questionnaire.
[g] The total number of patients with an evaluable baseline and at least one evaluable follow-up questionnaire (as defined above).
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 157 Day 1	Expected forms[a] (n)	2	1
		Received forms[b] (n)	1	1
		Evaluable forms[c] (n)	1	1
		Compliance rate[d] (%)	50.0	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 160 Day 1	Expected forms[a] (n)	2	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	50.0	
		Evaluability rate[e] (%)	100.0	
	Week 163 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Week 166 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	

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[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PRO-CTCAE	Week 169 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Week 172 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Overall patient compliance	Expected forms[f] (n)	436	430
		Evaluable forms[g] (n)	244	278
		Compliance rate[h] (%)	56.0	64.7

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Baseline	Expected forms[a] (n)	436	430
		Received forms[b] (n)	264	307
		Evaluable forms[c] (n)	264	307
		Compliance rate[d] (%)	60.6	71.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 4 Day 1	Expected forms[a] (n)	434	414
		Received forms[b] (n)	377	318
		Evaluable forms[c] (n)	377	318
		Compliance rate[d] (%)	86.9	76.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 7 Day 1	Expected forms[a] (n)	432	409
		Received forms[b] (n)	350	307
		Evaluable forms[c] (n)	350	307
		Compliance rate[d] (%)	81.0	75.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 10 Day 1	Expected forms[a] (n)	431	401
		Received forms[b] (n)	343	281
		Evaluable forms[c] (n)	343	281
		Compliance rate[d] (%)	79.6	70.1
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 13 Day 1	Expected forms[a] (n)	431	393
		Received forms[b] (n)	324	277
		Evaluable forms[c] (n)	324	277
		Compliance rate[d] (%)	75.2	70.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 16 Day 1	Expected forms[a] (n)	426	384
		Received forms[b] (n)	308	243
		Evaluable forms[c] (n)	308	243
		Compliance rate[d] (%)	72.3	63.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 19 Day 1	Expected forms[a] (n)	419	379
		Received forms[b] (n)	301	241
		Evaluable forms[c] (n)	301	241
		Compliance rate[d] (%)	71.8	63.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 22 Day 1	Expected forms[a] (n)	410	367
		Received forms[b] (n)	297	226
		Evaluable forms[c] (n)	297	226
		Compliance rate[d] (%)	72.4	61.6
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 25 Day 1	Expected forms[a] (n)	400	361
		Received forms[b] (n)	292	213
		Evaluable forms[c] (n)	292	213
		Compliance rate[d] (%)	73.0	59.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 28 Day 1	Expected forms[a] (n)	394	352
		Received forms[b] (n)	276	198
		Evaluable forms[c] (n)	276	198
		Compliance rate[d] (%)	70.1	56.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 31 Day 1	Expected forms[a] (n)	387	342
		Received forms[b] (n)	267	180
		Evaluable forms[c] (n)	267	180
		Compliance rate[d] (%)	69.0	52.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 34 Day 1	Expected forms[a] (n)	380	334
		Received forms[b] (n)	251	181
		Evaluable forms[c] (n)	251	181
		Compliance rate[d] (%)	66.1	54.2
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 37 Day 1	Expected forms[a] (n)	369	315
		Received forms[b] (n)	245	161
		Evaluable forms[c] (n)	245	161
		Compliance rate[d] (%)	66.4	51.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 40 Day 1	Expected forms[a] (n)	366	305
		Received forms[b] (n)	230	141
		Evaluable forms[c] (n)	230	141
		Compliance rate[d] (%)	62.8	46.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 43 Day 1	Expected forms[a] (n)	364	293
		Received forms[b] (n)	219	129
		Evaluable forms[c] (n)	219	129
		Compliance rate[d] (%)	60.2	44.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 46 Day 1	Expected forms[a] (n)	354	271
		Received forms[b] (n)	201	116
		Evaluable forms[c] (n)	201	116
		Compliance rate[d] (%)	56.8	42.8
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 49 Day 1	Expected forms[a] (n)	349	255
		Received forms[b] (n)	194	102
		Evaluable forms[c] (n)	194	102
		Compliance rate[d] (%)	55.6	40.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 52 Day 1	Expected forms[a] (n)	335	242
		Received forms[b] (n)	174	94
		Evaluable forms[c] (n)	174	94
		Compliance rate[d] (%)	51.9	38.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 55 Day 1	Expected forms[a] (n)	322	227
		Received forms[b] (n)	161	89
		Evaluable forms[c] (n)	161	89
		Compliance rate[d] (%)	50.0	39.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 58 Day 1	Expected forms[a] (n)	306	214
		Received forms[b] (n)	149	85
		Evaluable forms[c] (n)	149	85
		Compliance rate[d] (%)	48.7	39.7
		Evaluability rate[e] (%)	100.0	100.0

[a] A questionnaire that is expected to be completed at a scheduled assessment time.
[b] A questionnaire that is expected to be completed, has been received and has a completion date and at least one individual item completed.
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[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 61 Day 1	Expected forms[a] (n)	290	204
		Received forms[b] (n)	151	79
		Evaluable forms[c] (n)	151	79
		Compliance rate[d] (%)	52.1	38.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 64 Day 1	Expected forms[a] (n)	280	184
		Received forms[b] (n)	133	67
		Evaluable forms[c] (n)	133	67
		Compliance rate[d] (%)	47.5	36.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 67 Day 1	Expected forms[a] (n)	257	171
		Received forms[b] (n)	126	61
		Evaluable forms[c] (n)	126	61
		Compliance rate[d] (%)	49.0	35.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 70 Day 1	Expected forms[a] (n)	234	155
		Received forms[b] (n)	112	55
		Evaluable forms[c] (n)	112	55
		Compliance rate[d] (%)	47.9	35.5
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 73 Day 1	Expected forms[a] (n)	220	140
		Received forms[b] (n)	107	46
		Evaluable forms[c] (n)	107	46
		Compliance rate[d] (%)	48.6	32.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 76 Day 1	Expected forms[a] (n)	190	123
		Received forms[b] (n)	87	41
		Evaluable forms[c] (n)	87	41
		Compliance rate[d] (%)	45.8	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 79 Day 1	Expected forms[a] (n)	178	105
		Received forms[b] (n)	82	33
		Evaluable forms[c] (n)	82	33
		Compliance rate[d] (%)	46.1	31.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 82 Day 1	Expected forms[a] (n)	164	96
		Received forms[b] (n)	74	32
		Evaluable forms[c] (n)	74	32
		Compliance rate[d] (%)	45.1	33.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 85 Day 1	Expected forms[a] (n)	148	89
		Received forms[b] (n)	72	31
		Evaluable forms[c] (n)	72	31
		Compliance rate[d] (%)	48.6	34.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 88 Day 1	Expected forms[a] (n)	132	79
		Received forms[b] (n)	59	27
		Evaluable forms[c] (n)	59	27
		Compliance rate[d] (%)	44.7	34.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 91 Day 1	Expected forms[a] (n)	122	69
		Received forms[b] (n)	56	24
		Evaluable forms[c] (n)	56	24
		Compliance rate[d] (%)	45.9	34.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 94 Day 1	Expected forms[a] (n)	113	66
		Received forms[b] (n)	46	19
		Evaluable forms[c] (n)	46	19
		Compliance rate[d] (%)	40.7	28.8
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 97 Day 1	Expected forms[a] (n)	104	61
		Received forms[b] (n)	42	17
		Evaluable forms[c] (n)	42	17
		Compliance rate[d] (%)	40.4	27.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 100 Day 1	Expected forms[a] (n)	99	56
		Received forms[b] (n)	40	15
		Evaluable forms[c] (n)	40	15
		Compliance rate[d] (%)	40.4	26.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 103 Day 1	Expected forms[a] (n)	85	48
		Received forms[b] (n)	38	11
		Evaluable forms[c] (n)	38	11
		Compliance rate[d] (%)	44.7	22.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 106 Day 1	Expected forms[a] (n)	73	46
		Received forms[b] (n)	32	13
		Evaluable forms[c] (n)	32	13
		Compliance rate[d] (%)	43.8	28.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 109 Day 1	Expected forms[a] (n)	63	40
		Received forms[b] (n)	28	9
		Evaluable forms[c] (n)	28	9
		Compliance rate[d] (%)	44.4	22.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 112 Day 1	Expected forms[a] (n)	53	36
		Received forms[b] (n)	26	9
		Evaluable forms[c] (n)	26	9
		Compliance rate[d] (%)	49.1	25.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 115 Day 1	Expected forms[a] (n)	47	32
		Received forms[b] (n)	21	9
		Evaluable forms[c] (n)	21	9
		Compliance rate[d] (%)	44.7	28.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 118 Day 1	Expected forms[a] (n)	43	26
		Received forms[b] (n)	20	7
		Evaluable forms[c] (n)	20	7
		Compliance rate[d] (%)	46.5	26.9
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 121 Day 1	Expected forms[a] (n)	36	20
		Received forms[b] (n)	16	6
		Evaluable forms[c] (n)	16	6
		Compliance rate[d] (%)	44.4	30.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 124 Day 1	Expected forms[a] (n)	32	18
		Received forms[b] (n)	14	5
		Evaluable forms[c] (n)	14	5
		Compliance rate[d] (%)	43.8	27.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 127 Day 1	Expected forms[a] (n)	28	14
		Received forms[b] (n)	12	4
		Evaluable forms[c] (n)	12	4
		Compliance rate[d] (%)	42.9	28.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 130 Day 1	Expected forms[a] (n)	25	11
		Received forms[b] (n)	9	3
		Evaluable forms[c] (n)	9	3
		Compliance rate[d] (%)	36.0	27.3
		Evaluability rate[e] (%)	100.0	100.0

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 133 Day 1	Expected forms[a] (n)	21	11
		Received forms[b] (n)	10	3
		Evaluable forms[c] (n)	10	3
		Compliance rate[d] (%)	47.6	27.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 136 Day 1	Expected forms[a] (n)	20	9
		Received forms[b] (n)	10	3
		Evaluable forms[c] (n)	10	3
		Compliance rate[d] (%)	50.0	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 139 Day 1	Expected forms[a] (n)	14	9
		Received forms[b] (n)	6	3
		Evaluable forms[c] (n)	6	3
		Compliance rate[d] (%)	42.9	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 142 Day 1	Expected forms[a] (n)	13	6
		Received forms[b] (n)	6	2
		Evaluable forms[c] (n)	6	2
		Compliance rate[d] (%)	46.2	33.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 145 Day 1	Expected forms[a] (n)	13	5
		Received forms[b] (n)	4	2
		Evaluable forms[c] (n)	4	2
		Compliance rate[d] (%)	30.8	40.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 148 Day 1	Expected forms[a] (n)	10	3
		Received forms[b] (n)	3	1
		Evaluable forms[c] (n)	3	1
		Compliance rate[d] (%)	30.0	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 151 Day 1	Expected forms[a] (n)	9	2
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	22.2	50.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 154 Day 1	Expected forms[a] (n)	5	2
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	40.0	50.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 157 Day 1	Expected forms[a] (n)	5	2
		Received forms[b] (n)	1	1
		Evaluable forms[c] (n)	1	1
		Compliance rate[d] (%)	20.0	50.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 160 Day 1	Expected forms[a] (n)	4	1
		Received forms[b] (n)	2	0
		Evaluable forms[c] (n)	2	0
		Compliance rate[d] (%)	50.0	0.0
		Evaluability rate[e] (%)	100.0	
	Week 163 Day 1	Expected forms[a] (n)	3	1
		Received forms[b] (n)	2	0
		Evaluable forms[c] (n)	2	0
		Compliance rate[d] (%)	66.7	0.0
		Evaluability rate[e] (%)	100.0	
	Week 166 Day 1	Expected forms[a] (n)	2	1
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	50.0	0.0
		Evaluability rate[e] (%)	100.0	

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF SEVERITY	Week 169 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Week 172 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Overall patient compliance	Expected forms[f] (n)	436	430
		Evaluable forms[g] (n)	259	284
		Compliance rate[h] (%)	59.4	66.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 4 Day 1	Expected forms[a] (n)	432	412
		Received forms[b] (n)	349	296
		Evaluable forms[c] (n)	349	296
		Compliance rate[d] (%)	80.8	71.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 7 Day 1	Expected forms[a] (n)	432	409
		Received forms[b] (n)	344	305
		Evaluable forms[c] (n)	344	305
		Compliance rate[d] (%)	79.6	74.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 10 Day 1	Expected forms[a] (n)	431	401
		Received forms[b] (n)	342	279
		Evaluable forms[c] (n)	342	279
		Compliance rate[d] (%)	79.4	69.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 13 Day 1	Expected forms[a] (n)	431	393
		Received forms[b] (n)	324	277
		Evaluable forms[c] (n)	324	277
		Compliance rate[d] (%)	75.2	70.5
		Evaluability rate[e] (%)	100.0	100.0

[a] A questionnaire that is expected to be completed at a scheduled assessment time.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 16 Day 1	Expected forms[a] (n)	426	384
		Received forms[b] (n)	308	243
		Evaluable forms[c] (n)	308	243
		Compliance rate[d] (%)	72.3	63.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 19 Day 1	Expected forms[a] (n)	419	379
		Received forms[b] (n)	300	241
		Evaluable forms[c] (n)	300	241
		Compliance rate[d] (%)	71.6	63.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 22 Day 1	Expected forms[a] (n)	410	367
		Received forms[b] (n)	296	226
		Evaluable forms[c] (n)	296	226
		Compliance rate[d] (%)	72.2	61.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 25 Day 1	Expected forms[a] (n)	400	361
		Received forms[b] (n)	292	212
		Evaluable forms[c] (n)	292	212
		Compliance rate[d] (%)	73.0	58.7
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 28 Day 1	Expected forms[a] (n)	394	352
		Received forms[b] (n)	276	198
		Evaluable forms[c] (n)	276	198
		Compliance rate[d] (%)	70.1	56.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 31 Day 1	Expected forms[a] (n)	387	342
		Received forms[b] (n)	267	180
		Evaluable forms[c] (n)	267	180
		Compliance rate[d] (%)	69.0	52.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 34 Day 1	Expected forms[a] (n)	380	334
		Received forms[b] (n)	251	180
		Evaluable forms[c] (n)	251	180
		Compliance rate[d] (%)	66.1	53.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 37 Day 1	Expected forms[a] (n)	369	315
		Received forms[b] (n)	244	161
		Evaluable forms[c] (n)	244	161
		Compliance rate[d] (%)	66.1	51.1
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 40 Day 1	Expected forms[a] (n)	366	305
		Received forms[b] (n)	229	140
		Evaluable forms[c] (n)	229	140
		Compliance rate[d] (%)	62.6	45.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 43 Day 1	Expected forms[a] (n)	364	293
		Received forms[b] (n)	219	128
		Evaluable forms[c] (n)	219	128
		Compliance rate[d] (%)	60.2	43.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 46 Day 1	Expected forms[a] (n)	354	271
		Received forms[b] (n)	201	116
		Evaluable forms[c] (n)	201	116
		Compliance rate[d] (%)	56.8	42.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 49 Day 1	Expected forms[a] (n)	349	255
		Received forms[b] (n)	194	102
		Evaluable forms[c] (n)	194	102
		Compliance rate[d] (%)	55.6	40.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 52 Day 1	Expected forms[a] (n)	335	242
		Received forms[b] (n)	174	94
		Evaluable forms[c] (n)	174	94
		Compliance rate[d] (%)	51.9	38.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 55 Day 1	Expected forms[a] (n)	322	227
		Received forms[b] (n)	161	89
		Evaluable forms[c] (n)	161	89
		Compliance rate[d] (%)	50.0	39.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 58 Day 1	Expected forms[a] (n)	306	214
		Received forms[b] (n)	149	85
		Evaluable forms[c] (n)	149	85
		Compliance rate[d] (%)	48.7	39.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 61 Day 1	Expected forms[a] (n)	290	204
		Received forms[b] (n)	151	79
		Evaluable forms[c] (n)	151	79
		Compliance rate[d] (%)	52.1	38.7
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 64 Day 1	Expected forms[a] (n)	280	184
		Received forms[b] (n)	132	67
		Evaluable forms[c] (n)	132	67
		Compliance rate[d] (%)	47.1	36.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 67 Day 1	Expected forms[a] (n)	257	171
		Received forms[b] (n)	126	61
		Evaluable forms[c] (n)	126	61
		Compliance rate[d] (%)	49.0	35.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 70 Day 1	Expected forms[a] (n)	234	155
		Received forms[b] (n)	112	55
		Evaluable forms[c] (n)	112	55
		Compliance rate[d] (%)	47.9	35.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 73 Day 1	Expected forms[a] (n)	220	140
		Received forms[b] (n)	107	46
		Evaluable forms[c] (n)	107	46
		Compliance rate[d] (%)	48.6	32.9
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 76 Day 1	Expected forms[a] (n)	190	123
		Received forms[b] (n)	87	40
		Evaluable forms[c] (n)	87	40
		Compliance rate[d] (%)	45.8	32.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 79 Day 1	Expected forms[a] (n)	178	105
		Received forms[b] (n)	82	33
		Evaluable forms[c] (n)	82	33
		Compliance rate[d] (%)	46.1	31.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 82 Day 1	Expected forms[a] (n)	164	96
		Received forms[b] (n)	74	32
		Evaluable forms[c] (n)	74	32
		Compliance rate[d] (%)	45.1	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 85 Day 1	Expected forms[a] (n)	148	89
		Received forms[b] (n)	72	31
		Evaluable forms[c] (n)	72	31
		Compliance rate[d] (%)	48.6	34.8
		Evaluability rate[e] (%)	100.0	100.0

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[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 88 Day 1	Expected forms[a] (n)	132	79
		Received forms[b] (n)	59	27
		Evaluable forms[c] (n)	59	27
		Compliance rate[d] (%)	44.7	34.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 91 Day 1	Expected forms[a] (n)	122	69
		Received forms[b] (n)	56	24
		Evaluable forms[c] (n)	56	24
		Compliance rate[d] (%)	45.9	34.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 94 Day 1	Expected forms[a] (n)	113	66
		Received forms[b] (n)	46	19
		Evaluable forms[c] (n)	46	19
		Compliance rate[d] (%)	40.7	28.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 97 Day 1	Expected forms[a] (n)	104	61
		Received forms[b] (n)	42	17
		Evaluable forms[c] (n)	42	17
		Compliance rate[d] (%)	40.4	27.9
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 100 Day 1	Expected forms[a] (n)	99	56
		Received forms[b] (n)	40	15
		Evaluable forms[c] (n)	40	15
		Compliance rate[d] (%)	40.4	26.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 103 Day 1	Expected forms[a] (n)	85	48
		Received forms[b] (n)	38	11
		Evaluable forms[c] (n)	38	11
		Compliance rate[d] (%)	44.7	22.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 106 Day 1	Expected forms[a] (n)	73	46
		Received forms[b] (n)	32	13
		Evaluable forms[c] (n)	32	13
		Compliance rate[d] (%)	43.8	28.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 109 Day 1	Expected forms[a] (n)	63	40
		Received forms[b] (n)	28	9
		Evaluable forms[c] (n)	28	9
		Compliance rate[d] (%)	44.4	22.5
		Evaluability rate[e] (%)	100.0	100.0

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Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 112 Day 1	Expected forms[a] (n)	53	36
		Received forms[b] (n)	26	9
		Evaluable forms[c] (n)	26	9
		Compliance rate[d] (%)	49.1	25.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 115 Day 1	Expected forms[a] (n)	47	32
		Received forms[b] (n)	21	9
		Evaluable forms[c] (n)	21	9
		Compliance rate[d] (%)	44.7	28.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 118 Day 1	Expected forms[a] (n)	43	26
		Received forms[b] (n)	20	7
		Evaluable forms[c] (n)	20	7
		Compliance rate[d] (%)	46.5	26.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 121 Day 1	Expected forms[a] (n)	36	20
		Received forms[b] (n)	16	6
		Evaluable forms[c] (n)	16	6
		Compliance rate[d] (%)	44.4	30.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 124 Day 1	Expected forms[a] (n)	32	18
		Received forms[b] (n)	14	5
		Evaluable forms[c] (n)	14	5
		Compliance rate[d] (%)	43.8	27.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 127 Day 1	Expected forms[a] (n)	28	14
		Received forms[b] (n)	12	4
		Evaluable forms[c] (n)	12	4
		Compliance rate[d] (%)	42.9	28.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 130 Day 1	Expected forms[a] (n)	25	11
		Received forms[b] (n)	9	3
		Evaluable forms[c] (n)	9	3
		Compliance rate[d] (%)	36.0	27.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 133 Day 1	Expected forms[a] (n)	21	11
		Received forms[b] (n)	10	3
		Evaluable forms[c] (n)	10	3
		Compliance rate[d] (%)	47.6	27.3
		Evaluability rate[e] (%)	100.0	100.0

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
[d] The number of evaluable forms divided by the number of expected forms multiplied by 100.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 136 Day 1	Expected forms[a] (n)	20	9
		Received forms[b] (n)	10	3
		Evaluable forms[c] (n)	10	3
		Compliance rate[d] (%)	50.0	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 139 Day 1	Expected forms[a] (n)	14	9
		Received forms[b] (n)	6	3
		Evaluable forms[c] (n)	6	3
		Compliance rate[d] (%)	42.9	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 142 Day 1	Expected forms[a] (n)	13	6
		Received forms[b] (n)	6	2
		Evaluable forms[c] (n)	6	2
		Compliance rate[d] (%)	46.2	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 145 Day 1	Expected forms[a] (n)	13	5
		Received forms[b] (n)	4	2
		Evaluable forms[c] (n)	4	2
		Compliance rate[d] (%)	30.8	40.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 148 Day 1	Expected forms[a] (n)	10	3
		Received forms[b] (n)	3	1
		Evaluable forms[c] (n)	3	1
		Compliance rate[d] (%)	30.0	33.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 151 Day 1	Expected forms[a] (n)	9	2
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	22.2	50.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 154 Day 1	Expected forms[a] (n)	5	2
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	40.0	50.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 157 Day 1	Expected forms[a] (n)	5	2
		Received forms[b] (n)	1	1
		Evaluable forms[c] (n)	1	1
		Compliance rate[d] (%)	20.0	50.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 160 Day 1	Expected forms[a] (n)	4	1
		Received forms[b] (n)	2	0
		Evaluable forms[c] (n)	2	0
		Compliance rate[d] (%)	50.0	0.0
		Evaluability rate[e] (%)	100.0	
	Week 163 Day 1	Expected forms[a] (n)	3	1
		Received forms[b] (n)	2	0
		Evaluable forms[c] (n)	2	0
		Compliance rate[d] (%)	66.7	0.0
		Evaluability rate[e] (%)	100.0	
	Week 166 Day 1	Expected forms[a] (n)	2	1
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	50.0	0.0
		Evaluability rate[e] (%)	100.0	
	Week 169 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	

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[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
[f] The total number of patients expected to have completed at least a baseline questionnaire.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF CHANGE	Week 172 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Baseline	Expected forms[a] (n)	436	430
		Received forms[b] (n)	257	303
		Evaluable forms[c] (n)	257	303
		Compliance rate[d] (%)	58.9	70.5
		Evaluability rate[e] (%)	100.0	100.0
	Week 4 Day 1	Expected forms[a] (n)	433	412
		Received forms[b] (n)	374	316
		Evaluable forms[c] (n)	374	316
		Compliance rate[d] (%)	86.4	76.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 7 Day 1	Expected forms[a] (n)	427	397
		Received forms[b] (n)	345	304
		Evaluable forms[c] (n)	345	304
		Compliance rate[d] (%)	80.8	76.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 10 Day 1	Expected forms[a] (n)	411	346
		Received forms[b] (n)	337	262
		Evaluable forms[c] (n)	337	262
		Compliance rate[d] (%)	82.0	75.7
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 13 Day 1	Expected forms[a] (n)	401	323
		Received forms[b] (n)	313	253
		Evaluable forms[c] (n)	313	253
		Compliance rate[d] (%)	78.1	78.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 16 Day 1	Expected forms[a] (n)	384	296
		Received forms[b] (n)	292	217
		Evaluable forms[c] (n)	292	217
		Compliance rate[d] (%)	76.0	73.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 19 Day 1	Expected forms[a] (n)	377	285
		Received forms[b] (n)	289	209
		Evaluable forms[c] (n)	289	209
		Compliance rate[d] (%)	76.7	73.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 22 Day 1	Expected forms[a] (n)	362	262
		Received forms[b] (n)	283	192
		Evaluable forms[c] (n)	283	192
		Compliance rate[d] (%)	78.2	73.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 25 Day 1	Expected forms[a] (n)	344	244
		Received forms[b] (n)	274	176
		Evaluable forms[c] (n)	274	176
		Compliance rate[d] (%)	79.7	72.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 28 Day 1	Expected forms[a] (n)	330	208
		Received forms[b] (n)	258	152
		Evaluable forms[c] (n)	258	152
		Compliance rate[d] (%)	78.2	73.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 31 Day 1	Expected forms[a] (n)	318	197
		Received forms[b] (n)	245	140
		Evaluable forms[c] (n)	245	140
		Compliance rate[d] (%)	77.0	71.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 34 Day 1	Expected forms[a] (n)	303	173
		Received forms[b] (n)	228	135
		Evaluable forms[c] (n)	228	135
		Compliance rate[d] (%)	75.2	78.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 37 Day 1	Expected forms[a] (n)	289	153
		Received forms[b] (n)	222	115
		Evaluable forms[c] (n)	222	115
		Compliance rate[d] (%)	76.8	75.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 40 Day 1	Expected forms[a] (n)	273	138
		Received forms[b] (n)	204	103
		Evaluable forms[c] (n)	204	103
		Compliance rate[d] (%)	74.7	74.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 43 Day 1	Expected forms[a] (n)	260	124
		Received forms[b] (n)	192	95
		Evaluable forms[c] (n)	192	95
		Compliance rate[d] (%)	73.8	76.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 46 Day 1	Expected forms[a] (n)	234	110
		Received forms[b] (n)	174	80
		Evaluable forms[c] (n)	174	80
		Compliance rate[d] (%)	74.4	72.7
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 49 Day 1	Expected forms[a] (n)	221	105
		Received forms[b] (n)	166	78
		Evaluable forms[c] (n)	166	78
		Compliance rate[d] (%)	75.1	74.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 52 Day 1	Expected forms[a] (n)	210	95
		Received forms[b] (n)	147	65
		Evaluable forms[c] (n)	147	65
		Compliance rate[d] (%)	70.0	68.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 55 Day 1	Expected forms[a] (n)	199	91
		Received forms[b] (n)	143	64
		Evaluable forms[c] (n)	143	64
		Compliance rate[d] (%)	71.9	70.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 58 Day 1	Expected forms[a] (n)	194	89
		Received forms[b] (n)	134	63
		Evaluable forms[c] (n)	134	63
		Compliance rate[d] (%)	69.1	70.8
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 61 Day 1	Expected forms[a] (n)	175	75
		Received forms[b] (n)	125	52
		Evaluable forms[c] (n)	125	52
		Compliance rate[d] (%)	71.4	69.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 64 Day 1	Expected forms[a] (n)	162	66
		Received forms[b] (n)	110	45
		Evaluable forms[c] (n)	110	45
		Compliance rate[d] (%)	67.9	68.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 67 Day 1	Expected forms[a] (n)	151	59
		Received forms[b] (n)	104	40
		Evaluable forms[c] (n)	104	40
		Compliance rate[d] (%)	68.9	67.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 70 Day 1	Expected forms[a] (n)	132	49
		Received forms[b] (n)	89	32
		Evaluable forms[c] (n)	89	32
		Compliance rate[d] (%)	67.4	65.3
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 73 Day 1	Expected forms[a] (n)	119	42
		Received forms[b] (n)	83	27
		Evaluable forms[c] (n)	83	27
		Compliance rate[d] (%)	69.7	64.3
		Evaluability rate[e] (%)	100.0	100.0
	Week 76 Day 1	Expected forms[a] (n)	107	39
		Received forms[b] (n)	69	26
		Evaluable forms[c] (n)	69	26
		Compliance rate[d] (%)	64.5	66.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 79 Day 1	Expected forms[a] (n)	89	36
		Received forms[b] (n)	64	23
		Evaluable forms[c] (n)	64	23
		Compliance rate[d] (%)	71.9	63.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 82 Day 1	Expected forms[a] (n)	82	34
		Received forms[b] (n)	59	24
		Evaluable forms[c] (n)	59	24
		Compliance rate[d] (%)	72.0	70.6
		Evaluability rate[e] (%)	100.0	100.0

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
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[f] The total number of patients expected to have completed at least a baseline questionnaire.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 85 Day 1	Expected forms[a] (n)	76	32
		Received forms[b] (n)	57	23
		Evaluable forms[c] (n)	57	23
		Compliance rate[d] (%)	75.0	71.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 88 Day 1	Expected forms[a] (n)	68	29
		Received forms[b] (n)	47	22
		Evaluable forms[c] (n)	47	22
		Compliance rate[d] (%)	69.1	75.9
		Evaluability rate[e] (%)	100.0	100.0
	Week 91 Day 1	Expected forms[a] (n)	63	23
		Received forms[b] (n)	43	19
		Evaluable forms[c] (n)	43	19
		Compliance rate[d] (%)	68.3	82.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 94 Day 1	Expected forms[a] (n)	57	21
		Received forms[b] (n)	36	14
		Evaluable forms[c] (n)	36	14
		Compliance rate[d] (%)	63.2	66.7
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 97 Day 1	Expected forms[a] (n)	48	18
		Received forms[b] (n)	33	13
		Evaluable forms[c] (n)	33	13
		Compliance rate[d] (%)	68.8	72.2
		Evaluability rate[e] (%)	100.0	100.0
	Week 100 Day 1	Expected forms[a] (n)	45	14
		Received forms[b] (n)	30	11
		Evaluable forms[c] (n)	30	11
		Compliance rate[d] (%)	66.7	78.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 103 Day 1	Expected forms[a] (n)	42	13
		Received forms[b] (n)	29	7
		Evaluable forms[c] (n)	29	7
		Compliance rate[d] (%)	69.0	53.8
		Evaluability rate[e] (%)	100.0	100.0
	Week 106 Day 1	Expected forms[a] (n)	36	11
		Received forms[b] (n)	23	9
		Evaluable forms[c] (n)	23	9
		Compliance rate[d] (%)	63.9	81.8
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 109 Day 1	Expected forms[a] (n)	30	7
		Received forms[b] (n)	23	4
		Evaluable forms[c] (n)	23	4
		Compliance rate[d] (%)	76.7	57.1
		Evaluability rate[e] (%)	100.0	100.0
	Week 112 Day 1	Expected forms[a] (n)	25	6
		Received forms[b] (n)	19	4
		Evaluable forms[c] (n)	19	4
		Compliance rate[d] (%)	76.0	66.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 115 Day 1	Expected forms[a] (n)	22	6
		Received forms[b] (n)	15	4
		Evaluable forms[c] (n)	15	4
		Compliance rate[d] (%)	68.2	66.7
		Evaluability rate[e] (%)	100.0	100.0
	Week 118 Day 1	Expected forms[a] (n)	21	4
		Received forms[b] (n)	15	4
		Evaluable forms[c] (n)	15	4
		Compliance rate[d] (%)	71.4	100.0
		Evaluability rate[e] (%)	100.0	100.0

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
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[e] The number of evaluable forms divided by the number of received forms multiplied by 100.
[f] The total number of patients expected to have completed at least a baseline questionnaire.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 121 Day 1	Expected forms[a] (n)	18	2
		Received forms[b] (n)	11	2
		Evaluable forms[c] (n)	11	2
		Compliance rate[d] (%)	61.1	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 124 Day 1	Expected forms[a] (n)	16	2
		Received forms[b] (n)	12	2
		Evaluable forms[c] (n)	12	2
		Compliance rate[d] (%)	75.0	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 127 Day 1	Expected forms[a] (n)	13	2
		Received forms[b] (n)	9	2
		Evaluable forms[c] (n)	9	2
		Compliance rate[d] (%)	69.2	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 130 Day 1	Expected forms[a] (n)	12	2
		Received forms[b] (n)	7	2
		Evaluable forms[c] (n)	7	2
		Compliance rate[d] (%)	58.3	100.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 133 Day 1	Expected forms[a] (n)	9	2
		Received forms[b] (n)	7	2
		Evaluable forms[c] (n)	7	2
		Compliance rate[d] (%)	77.8	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 136 Day 1	Expected forms[a] (n)	8	2
		Received forms[b] (n)	6	2
		Evaluable forms[c] (n)	6	2
		Compliance rate[d] (%)	75.0	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 139 Day 1	Expected forms[a] (n)	6	2
		Received forms[b] (n)	3	2
		Evaluable forms[c] (n)	3	2
		Compliance rate[d] (%)	50.0	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 142 Day 1	Expected forms[a] (n)	4	1
		Received forms[b] (n)	3	1
		Evaluable forms[c] (n)	3	1
		Compliance rate[d] (%)	75.0	100.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 145 Day 1	Expected forms[a] (n)	4	1
		Received forms[b] (n)	3	1
		Evaluable forms[c] (n)	3	1
		Compliance rate[d] (%)	75.0	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 148 Day 1	Expected forms[a] (n)	4	1
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	50.0	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 151 Day 1	Expected forms[a] (n)	3	1
		Received forms[b] (n)	2	1
		Evaluable forms[c] (n)	2	1
		Compliance rate[d] (%)	66.7	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 154 Day 1	Expected forms[a] (n)	2	1
		Received forms[b] (n)	1	1
		Evaluable forms[c] (n)	1	1
		Compliance rate[d] (%)	50.0	100.0
		Evaluability rate[e] (%)	100.0	100.0

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 157 Day 1	Expected forms[a] (n)	2	1
		Received forms[b] (n)	1	1
		Evaluable forms[c] (n)	1	1
		Compliance rate[d] (%)	50.0	100.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 160 Day 1	Expected forms[a] (n)	2	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	50.0	
		Evaluability rate[e] (%)	100.0	
	Week 163 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Week 166 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	

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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PGI-TT Questionnaire	Week 169 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Week 172 Day 1	Expected forms[a] (n)	1	0
		Received forms[b] (n)	1	0
		Evaluable forms[c] (n)	1	0
		Compliance rate[d] (%)	100.0	
		Evaluability rate[e] (%)	100.0	
	Overall patient compliance	Expected forms[f] (n)	436	430
		Evaluable forms[g] (n)	252	282
		Compliance rate[h] (%)	57.8	65.6

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[c] A questionnaire that is expected to be completed, has a completion date and at least one subscale that is non-missing.
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Table 14.2.9.1.2
Compliance with PRO assessments over time and overall
ITT population

Questionnaire	Time point	Measure	T-DXd (N=436)	Chemotherapy (N=430)
PATIENT GLOBAL IMPRESSION OF BENEFIT/RISK	Week 13 Day 1	Expected forms[a] (n)	402	323
		Received forms[b] (n)	299	237
		Evaluable forms[c] (n)	299	237
		Compliance rate[d] (%)	74.4	73.4
		Evaluability rate[e] (%)	100.0	100.0
	Week 16 Day 1	Expected forms[a] (n)	384	296
		Received forms[b] (n)	285	212
		Evaluable forms[c] (n)	285	212
		Compliance rate[d] (%)	74.2	71.6
		Evaluability rate[e] (%)	100.0	100.0
	Week 19 Day 1	Expected forms[a] (n)	377	285
		Received forms[b] (n)	279	208
		Evaluable forms[c] (n)	279	208
		Compliance rate[d] (%)	74.0	73.0
		Evaluability rate[e] (%)	100.0	100.0
	Week 22 Day 1	Expected forms[a] (n)	362	262
		Received forms[b] (n)	279	191
		Evaluable forms[c] (n)	279	191
		Compliance rate[d] (%)	77.1	72.9
		Evaluability rate[e] (%)	100.0	100.0

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Anhang 4-G 4. Analysen DESTINY-Breast06: Sicherheit – SAF

Anhang 4-G 4.1 Gesamtraten unerwünschter Ereignisse

Tabelle 2.15.1 Unerwünschte Ereignisse – SAF

Daiichi Sankyo Europe GmbH
Data Intelligence - Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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Final
Statistical analyses for AMNOG (HTA Germany)

Table 2.15.1 Adverse events - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Adverse Events	429 (98.8)	0.1 [0.1; 0.1]	397 (95.2)	0.3 [0.2; 0.3]	1.6872 [1.4656; 1.9428] <.0001	<.0001
Serious Adverse Events	88 (20.3)	NE [NE; NE]	67 (16.1)	NE [23.1; NE]	0.9494 [0.6888; 1.3147] 0.7525	0.7530
Adverse Events with CTCAE grade 3 or higher	229 (52.8)	10.3 [6.8; 13.1]	185 (44.4)	11.0 [6.2; NE]	1.0146 [0.8346; 1.2348] 0.8848	0.8919
Adverse Events leading to discontinuation of study medication	62 (14.3)	NE [NE; NE]	39 (9.4)	NE [NE; NE]	1.1420 [0.7651; 1.7244] 0.5206	0.5207

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP*. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test*.
*: The following parameters were analysed using a stratified Cox proportional hazards model (hazard ratio) and a stratified log-rank test (two-sided p-value): Adverse Events. Otherwise unstratified analyses have been conducted.
CI: confidence interval; HR: hazard ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 17DEC2024 7:13; Program name: T.2.15.1_TEAE_SAF.sas; Output name: T.2.15.1_TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.15.2 Unerwünschte Ereignisse – Subgruppenanalyse – SAF

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Adverse events						
Age at randomization						0.1583
<65 years of age	300 / 301 (99.7)	0.1 [0.1, 0.1]	271 / 285 (95.1)	0.2 [0.2, 0.3]	1.7605 [1.4877, 2.0843] <.0001	
>=65 years of age	129 / 133 (97.0)	0.1 [0.1, 0.1]	126 / 132 (95.5)	0.3 [0.2, 0.4]	1.4686 [1.1458, 1.8826] 0.0024	
Race						0.1134
Asian	153 / 153 (100)	0.1 [0.1, 0.1]	138 / 147 (93.9)	0.3 [0.2, 0.4]	2.2387 [1.7604, 2.8512] <.0001	
White	227 / 231 (98.3)	0.1 [0.1, 0.1]	214 / 223 (96.0)	0.2 [0.1, 0.3]	1.4310 [1.1843, 1.7296] 0.0002	
Other	49 / 50 (98.0)	0.1 [0.1, 0.1]	45 / 47 (95.7)	0.3 [0.1, 0.4]	1.5703 [1.0374, 2.3816] 0.0338	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 19AUG2024 5:23; Program name: T.2.15.2_TEAE_SAF_SUB.sas; Output name: T.2.15.2_TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0910
Asia	148 / 148 (100)	0.1 [0.1, 0.1]	135 / 144 (93.8)	0.3 [0.2, 0.4]	2.1919 [1.7218, 2.7932] <.0001	
Europe	223 / 227 (98.2)	0.1 [0.1, 0.1]	198 / 206 (96.1)	0.2 [0.1, 0.3]	1.4010 [1.1549, 1.7009] 0.0007	
Rest of the World	58 / 59 (98.3)	0.1 [0.1, 0.1]	64 / 67 (95.5)	0.3 [0.1, 0.5]	1.7686 [1.2213, 2.5576] 0.0023	
HER2 IHC expression						0.1526
IHC 1+	237 / 239 (99.2)	0.1 [0.1, 0.1]	216 / 226 (95.6)	0.3 [0.2, 0.3]	1.6648 [1.3801, 2.0093] <.0001	
IHC 2+/ISH-	116 / 116 (100)	0.1 [0.1, 0.1]	109 / 115 (94.8)	0.2 [0.1, 0.3]	2.0067 [1.5309, 2.6333] <.0001	
IHC >0 <1+	73 / 76 (96.1)	0.1 [0.1, 0.1]	70 / 74 (94.6)	0.2 [0.1, 0.3]	1.3592 [0.9749, 1.8962] 0.0789	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3305
Yes	388 / 393 (98.7)	0.1 [0.1, 0.1]	358 / 377 (95.0)	0.2 [0.2, 0.3]	1.6890 [1.4590, 1.9559] <.0001	
No	41 / 41 (100)	0.2 [0.1, 0.3]	39 / 40 (97.5)	0.3 [0.2, 0.6]	1.4341 [0.9169, 2.2450] 0.1246	
Prior Taxane Use In The Non-Metastatic Setting						0.3596
Yes	176 / 177 (99.4)	0.1 [0.1, 0.1]	163 / 172 (94.8)	0.3 [0.2, 0.3]	1.8478 [1.4823, 2.3049] <.0001	
No	253 / 257 (98.4)	0.1 [0.1, 0.1]	234 / 245 (95.5)	0.2 [0.2, 0.3]	1.5687 [1.3101, 1.8791] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3531
1	65 / 65 (100)	0.1 [0.1, 0.1]	77 / 79 (97.5)	0.2 [0.1, 0.3]	2.3191 [1.6165, 3.3302] <.0001	
2	289 / 293 (98.6)	0.1 [0.1, 0.1]	266 / 281 (94.7)	0.3 [0.2, 0.3]	1.5793 [1.3336, 1.8708] <.0001	
>=3	74 / 75 (98.7)	0.1 [0.1, 0.1]	53 / 56 (94.6)	0.2 [0.1, 0.3]	1.5804 [1.1069, 2.2721] 0.0101	
ER/PR status I						0.2669
ER+, PR+	247 / 252 (98.0)	0.1 [0.1, 0.1]	222 / 234 (94.9)	0.3 [0.2, 0.3]	1.5332 [1.2758, 1.8437] <.0001	
ER+, PR-	166 / 166 (100)	0.1 [0.1, 0.1]	163 / 171 (95.3)	0.2 [0.2, 0.3]	1.8615 [1.4872, 2.3315] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 19AUG2024 5:23; Program name: T.2.15.2_TEAE_SAF_SUB.sas; Output name: T.2.15.2_TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.8518
ER <=10%	21 / 21 (100)	0.1 [0.1, 0.2]	13 / 14 (92.9)	0.4 [0.1, 0.6]	1.6974 [0.8297, 3.5794] 0.1802	
ER >10%	358 / 362 (98.9)	0.1 [0.1, 0.1]	326 / 343 (95.0)	0.2 [0.2, 0.3]	1.6344 [1.4032, 1.9044] <.0001	
Positive	50 / 51 (98.0)	0.1 [0.1, 0.1]	58 / 60 (96.7)	0.2 [0.2, 0.3]	2.0955 [1.4047, 3.1170] 0.0003	
Endocrine Resistance						0.4930
Primary	126 / 127 (99.2)	0.1 [0.1, 0.1]	131 / 137 (95.6)	0.2 [0.1, 0.3]	1.7486 [1.3606, 2.2465] <.0001	
Secondary	303 / 307 (98.7)	0.1 [0.1, 0.1]	265 / 279 (95.0)	0.3 [0.2, 0.3]	1.6218 [1.3719, 1.9182] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3332
Capecitabine	263 / 265 (99.2)	0.1 [0.1, 0.1]	235 / 249 (94.4)	0.3 [0.2, 0.3]	1.7935 [1.4982, 2.1484] <.0001	
Nab-Paclitaxel	101 / 103 (98.1)	0.1 [0.1, 0.1]	98 / 101 (97.0)	0.3 [0.2, 0.4]	1.4128 [1.0667, 1.8715] 0.0174	
Paclitaxel	65 / 66 (98.5)	0.1 [0.1, 0.1]	64 / 67 (95.5)	0.2 [0.1, 0.3]	1.7210 [1.2031, 2.4635] 0.0026	
Prior anthracycline use						0.8449
Yes	196 / 197 (99.5)	0.1 [0.1, 0.1]	188 / 198 (94.9)	0.2 [0.2, 0.3]	1.6552 [1.3484, 2.0325] <.0001	
No	233 / 237 (98.3)	0.1 [0.1, 0.1]	209 / 219 (95.4)	0.3 [0.2, 0.3]	1.6575 [1.3712, 2.0050] <.0001	
Liver metastases						0.8350
Yes	290 / 294 (98.6)	0.1 [0.1, 0.1]	260 / 275 (94.5)	0.2 [0.2, 0.3]	1.6221 [1.3685, 1.9237] <.0001	
No	139 / 140 (99.3)	0.1 [0.1, 0.1]	137 / 142 (96.5)	0.3 [0.2, 0.3]	1.7303 [1.3597, 2.2024] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 19AUG2024 5:23; Program name: T.2.15.2_TEAE_SAF_SUB.sas; Output name: T.2.15.2_TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0545
0	248 / 251 (98.8)	0.1 [0.1, 0.1]	234 / 246 (95.1)	0.3 [0.2, 0.3]	1.8633 [1.5523, 2.2373] <.0001	
>=1	176 / 178 (98.9)	0.1 [0.1, 0.1]	155 / 163 (95.1)	0.2 [0.1, 0.2]	1.3683 [1.1006, 1.7028] 0.0042	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Serious Adverse events						
Age at randomization						0.9516
<65 years of age	52 / 301 (17.3)	NE [29.3, NE]	37 / 285 (13.0)	NE [NE, NE]	0.9637 [0.6290, 1.4900] 0.8660	
>=65 years of age	36 / 133 (27.1)	NE [23.9, NE]	30 / 132 (22.7)	23.1 [23.1, NE]	0.9559 [0.5851, 1.5712] 0.8570	
Race						0.1009
Asian	32 / 153 (20.9)	NE [NE, NE]	16 / 147 (10.9)	NE [NE, NE]	1.5756 [0.8739, 2.9556] 0.1370	
White	48 / 231 (20.8)	NE [29.3, NE]	43 / 223 (19.3)	23.3 [23.1, NE]	0.7952 [0.5233, 1.2112] 0.2817	
Other	8 / 50 (16.0)	NE [NE, NE]	8 / 47 (17.0)	NE [8.1, NE]	0.6737 [0.2358, 1.8950] 0.4480	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 19AUG2024 5:23; Program name: T.2.15.2_TEAE_SAF_SUB.sas; Output name: T.2.15.2_TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0818
Asia	35 / 148 (23.6)	NE [NE, NE]	18 / 144 (12.5)	NE [NE, NE]	1.5473 [0.8843, 2.8017] 0.1321	
Europe	43 / 227 (18.9)	NE [NE, NE]	40 / 206 (19.4)	NE [NE, NE]	0.7373 [0.4760, 1.1441] 0.1700	
Rest of the World	10 / 59 (16.9)	29.3 [29.3, NE]	9 / 67 (13.4)	23.3 [23.1, NE]	0.7731 [0.2980, 2.0043] 0.5894	
HER2 IHC expression						0.6983
IHC 1+	47 / 239 (19.7)	NE [NE, NE]	37 / 226 (16.4)	NE [23.1, NE]	0.9554 [0.6194, 1.4846] 0.8374	
IHC 2+/ISH-	22 / 116 (19.0)	NE [23.9, NE]	18 / 115 (15.7)	NE [NE, NE]	0.7969 [0.4177, 1.5326] 0.4893	
IHC >0 <1+	19 / 76 (25.0)	NE [18.9, NE]	12 / 74 (16.2)	NE [23.3, NE]	1.2316 [0.6017, 2.6211] 0.5729	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8716
Yes	79 / 393 (20.1)	NE [29.3, NE]	59 / 377 (15.6)	NE [23.1, NE]	0.9634 [0.6854, 1.3613] 0.8308	
No	9 / 41 (22.0)	NE [NE, NE]	8 / 40 (20.0)	23.3 [NE, NE]	0.8664 [0.3258, 2.3356] 0.7658	
Prior Taxane Use In The Non-Metastatic Setting						0.4962
Yes	29 / 177 (16.4)	NE [NE, NE]	25 / 172 (14.5)	NE [NE, NE]	0.8420 [0.4882, 1.4610] 0.5352	
No	59 / 257 (23.0)	NE [29.3, NE]	42 / 245 (17.1)	23.3 [23.1, NE]	1.0182 [0.6836, 1.5289] 0.9302	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3041
1	9 / 65 (13.8)	NE [NE, NE]	14 / 79 (17.7)	NE [13.7, NE]	0.5790 [0.2362, 1.3464] 0.2073	
2	62 / 293 (21.2)	NE [29.3, NE]	46 / 281 (16.4)	NE [23.1, NE]	0.9458 [0.6438, 1.3997] 0.7793	
>=3	17 / 75 (22.7)	NE [NE, NE]	7 / 56 (12.5)	NE [NE, NE]	1.6196 [0.6981, 4.1935] 0.2801	
ER/PR status I						0.6913
ER+, PR+	50 / 252 (19.8)	NE [NE, NE]	39 / 234 (16.7)	NE [23.1, NE]	0.9098 [0.5963, 1.3976] 0.6610	
ER+, PR-	32 / 166 (19.3)	NE [29.3, NE]	24 / 171 (14.0)	NE [NE, NE]	1.0009 [0.5843, 1.7338] 0.9970	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7094
ER <=10%	6 / 21 (28.6)	NE [5.5, NE]	3 / 14 (21.4)	NE [2.1, NE]	0.8584 [0.2213, 4.1352] 0.8315	
ER >10%	70 / 362 (19.3)	NE [29.3, NE]	55 / 343 (16.0)	NE [23.1, NE]	0.8892 [0.6210, 1.2784] 0.5216	
Positive	12 / 51 (23.5)	NE [15.4, NE]	9 / 60 (15.0)	NE [NE, NE]	1.3071 [0.5512, 3.2127] 0.5454	
Endocrine Resistance						0.7790
Primary	25 / 127 (19.7)	NE [NE, NE]	20 / 137 (14.6)	NE [NE, NE]	1.0150 [0.5597, 1.8629] 0.9605	
Secondary	63 / 307 (20.5)	NE [29.3, NE]	47 / 279 (16.8)	NE [23.1, NE]	0.9188 [0.6276, 1.3535] 0.6645	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0985
Capecitabine	50 / 265 (18.9)	NE [29.3, NE]	44 / 249 (17.7)	NE [23.1, NE]	0.8143 [0.5412, 1.2293] 0.3240	
Nab-Paclitaxel	24 / 103 (23.3)	NE [23.9, NE]	11 / 101 (10.9)	NE [NE, NE]	1.6003 [0.7874, 3.4485] 0.2038	
Paclitaxel	14 / 66 (21.2)	NE [NE, NE]	12 / 67 (17.9)	NE [NE, NE]	0.8697 [0.3907, 1.9525] 0.7288	
Prior anthracycline use						0.9568
Yes	40 / 197 (20.3)	NE [NE, NE]	31 / 198 (15.7)	NE [NE, NE]	1.0159 [0.6329, 1.6447] 0.9493	
No	48 / 237 (20.3)	NE [29.3, NE]	36 / 219 (16.4)	23.3 [23.1, NE]	0.8995 [0.5811, 1.4033] 0.6357	
Liver metastases						0.3608
Yes	55 / 294 (18.7)	NE [29.3, NE]	44 / 275 (16.0)	NE [NE, NE]	0.8683 [0.5809, 1.3044] 0.4925	
No	33 / 140 (23.6)	NE [23.9, NE]	23 / 142 (16.2)	NE [23.1, NE]	1.1305 [0.6628, 1.9595] 0.6554	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0595
0	41 / 251 (16.3)	NE [29.3, NE]	42 / 246 (17.1)	NE [23.1, NE]	0.6895 [0.4428, 1.0715] 0.0958	
>=1	46 / 178 (25.8)	NE [NE, NE]	24 / 163 (14.7)	NE [NE, NE]	1.3830 [0.8485, 2.3112] 0.2000	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Adverse events with CTCAE grade 3 or higher						
Age at randomization						0.3020
<65 years of age	154 / 301 (51.2)	11.1 [6.4, 15.4]	114 / 285 (40.0)	23.5 [8.3, NE]	1.1046 [0.8659, 1.4130] 0.4259	
>=65 years of age	75 / 133 (56.4)	8.1 [4.4, 13.7]	71 / 132 (53.8)	5.5 [2.2, 13.1]	0.8721 [0.6279, 1.2120] 0.4090	
Race						0.0333
Asian	93 / 153 (60.8)	5.0 [3.8, 11.1]	59 / 147 (40.1)	23.5 [7.2, NE]	1.4174 [1.0240, 1.9772] 0.0364	
White	114 / 231 (49.4)	12.0 [8.7, 20.2]	110 / 223 (49.3)	5.9 [3.9, 14.4]	0.8071 [0.6189, 1.0527] 0.1112	
Other	22 / 50 (44.0)	22.8 [5.5, NE]	16 / 47 (34.0)	NE [5.5, NE]	1.0623 [0.5489, 2.0901] 0.8582	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0456
Asia	92 / 148 (62.2)	4.9 [3.2, 10.0]	60 / 144 (41.7)	23.5 [6.5, NE]	1.3923 [1.0065, 1.9396] 0.0467	
Europe	112 / 227 (49.3)	13.1 [8.1, NE]	94 / 206 (45.6)	11.0 [4.1, NE]	0.9031 [0.6853, 1.1927] 0.4694	
Rest of the World	25 / 59 (42.4)	22.8 [8.9, NE]	31 / 67 (46.3)	13.1 [4.6, NE]	0.6483 [0.3698, 1.1194] 0.1183	
HER2 IHC expression						0.8008
IHC 1+	122 / 239 (51.0)	11.1 [6.8, 14.8]	101 / 226 (44.7)	11.0 [5.5, NE]	0.9841 [0.7547, 1.2859] 0.9044	
IHC 2+/ISH-	64 / 116 (55.2)	9.4 [5.4, 15.0]	48 / 115 (41.7)	NE [5.1, NE]	1.1180 [0.7665, 1.6405] 0.5665	
IHC >0 <1+	41 / 76 (53.9)	8.1 [2.8, 22.8]	36 / 74 (48.6)	7.8 [2.1, NE]	0.9592 [0.6116, 1.5109] 0.8574	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1134
Yes	204 / 393 (51.9)	10.9 [6.8, 14.8]	170 / 377 (45.1)	9.9 [5.1, NE]	0.9730 [0.7923, 1.1962] 0.7890	
No	25 / 41 (61.0)	10.3 [4.2, 12.0]	15 / 40 (37.5)	14.4 [8.3, NE]	1.6281 [0.8673, 3.1631] 0.1346	
Prior Taxane Use In The Non-Metastatic Setting						0.9148
Yes	97 / 177 (54.8)	5.7 [3.5, 15.0]	80 / 172 (46.5)	7.8 [3.3, NE]	1.0326 [0.7667, 1.3943] 0.8393	
No	132 / 257 (51.4)	11.3 [8.4, 14.6]	105 / 245 (42.9)	14.4 [5.6, NE]	1.0066 [0.7772, 1.3065] 0.9662	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3135
1	35 / 65 (53.8)	5.5 [2.1, 22.8]	31 / 79 (39.2)	16.3 [5.9, NE]	1.3939 [0.8528, 2.2854] 0.1826	
2	148 / 293 (50.5)	11.7 [8.9, 15.4]	124 / 281 (44.1)	13.1 [5.1, NE]	0.9191 [0.7227, 1.1715] 0.4945	
>=3	45 / 75 (60.0)	7.2 [1.4, 14.0]	29 / 56 (51.8)	6.2 [1.6, NE]	1.0217 [0.6413, 1.6522] 0.9715	
ER/PR status I						0.9534
ER+, PR+	129 / 252 (51.2)	11.1 [6.9, 15.0]	102 / 234 (43.6)	14.4 [5.9, NE]	1.0009 [0.7711, 1.3025] 0.9969	
ER+, PR-	90 / 166 (54.2)	10.0 [4.2, 20.2]	79 / 171 (46.2)	11.0 [4.6, NE]	0.9827 [0.7222, 1.3387] 0.9034	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2430
ER <=10%	11 / 21 (52.4)	5.5 [1.4, NE]	4 / 14 (28.6)	NE [2.2, NE]	1.8530 [0.6319, 6.6980] 0.2949	
ER >10%	191 / 362 (52.8)	10.9 [6.4, 14.6]	146 / 343 (42.6)	14.4 [7.0, NE]	1.0730 [0.8640, 1.3358] 0.5294	
Positive	27 / 51 (52.9)	9.4 [4.9, 21.2]	35 / 60 (58.3)	3.2 [1.3, 7.2]	0.6959 [0.4150, 1.1542] 0.1610	
Endocrine Resistance						0.3796
Primary	72 / 127 (56.7)	5.5 [3.5, 13.7]	61 / 137 (44.5)	11.0 [5.6, NE]	1.1585 [0.8233, 1.6365] 0.3953	
Secondary	157 / 307 (51.1)	11.8 [8.9, 15.4]	124 / 279 (44.4)	14.4 [5.1, NE]	0.9589 [0.7562, 1.2187] 0.7213	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0064
Capecitabine	138 / 265 (52.1)	11.1 [6.9, 14.6]	107 / 249 (43.0)	14.4 [5.9, NE]	1.0348 [0.8027, 1.3376] 0.7971	
Nab-Paclitaxel	58 / 103 (56.3)	8.4 [3.7, 15.0]	38 / 101 (37.6)	NE [7.8, NE]	1.4127 [0.9398, 2.1477] 0.0990	
Paclitaxel	33 / 66 (50.0)	8.7 [3.9, NE]	40 / 67 (59.7)	1.8 [0.7, 4.9]	0.6243 [0.3873, 0.9986] 0.0477	
Prior anthracycline use						0.2497
Yes	108 / 197 (54.8)	6.9 [4.4, 14.0]	98 / 198 (49.5)	5.9 [2.6, NE]	0.9197 [0.6983, 1.2131] 0.5482	
No	121 / 237 (51.1)	11.9 [8.5, 21.2]	87 / 219 (39.7)	16.3 [7.2, NE]	1.1198 [0.8488, 1.4831] 0.4301	
Liver metastases						0.2165
Yes	151 / 294 (51.4)	11.1 [6.4, 14.6]	127 / 275 (46.2)	7.2 [5.1, 16.3]	0.9334 [0.7355, 1.1868] 0.5665	
No	78 / 140 (55.7)	9.7 [5.4, 15.4]	58 / 142 (40.8)	23.5 [6.5, NE]	1.1913 [0.8474, 1.6837] 0.3152	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.6561
0	125 / 251 (49.8)	12.0 [9.0, 22.8]	101 / 246 (41.1)	14.4 [7.2, NE]	1.0277 [0.7887, 1.3421] 0.8474	
>=1	101 / 178 (56.7)	6.4 [4.2, 10.3]	80 / 163 (49.1)	5.1 [2.2, NE]	0.9787 [0.7291, 1.3180] 0.8858	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Adverse events leading to discontinuation of study medication						
Age at randomization						0.7414
<65 years of age	38 / 301 (12.6)	NE [29.3, NE]	23 / 285 (8.1)	NE [NE, NE]	1.0337 [0.6126, 1.7790] 0.9026	
>=65 years of age	24 / 133 (18.0)	NE [NE, NE]	16 / 132 (12.1)	NE [NE, NE]	1.3299 [0.7116, 2.5529] 0.3761	
Race						0.0002
Asian	26 / 153 (17.0)	NE [NE, NE]	7 / 147 (4.8)	NE [NE, NE]	2.8764 [1.3119, 7.2133] 0.0098	
White	33 / 231 (14.3)	NE [27.2, NE]	22 / 223 (9.9)	NE [NE, NE]	1.0532 [0.6109, 1.8469] 0.8530	
Other	3 / 50 (6.0)	NE [NE, NE]	10 / 47 (21.3)	NE [9.5, NE]	0.1661 [0.0361, 0.5648] 0.0031	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0065
Asia	25 / 148 (16.9)	NE [NE, NE]	6 / 144 (4.2)	NE [NE, NE]	3.3067 [1.4432, 8.9256] 0.0055	
Europe	32 / 227 (14.1)	NE [27.2, NE]	25 / 206 (12.1)	NE [NE, NE]	0.8340 [0.4912, 1.4296] 0.5018	
Rest of the World	5 / 59 (8.5)	29.3 [29.3, NE]	8 / 67 (11.9)	NE [NE, NE]	0.4009 [0.1054, 1.2959] 0.1294	
HER2 IHC expression						0.7115
IHC 1+	36 / 239 (15.1)	NE [27.2, NE]	21 / 226 (9.3)	NE [NE, NE]	1.2648 [0.7406, 2.2133] 0.3964	
IHC 2+/ISH-	20 / 116 (17.2)	NE [29.3, NE]	12 / 115 (10.4)	NE [NE, NE]	1.0398 [0.5090, 2.2139] 0.9168	
IHC >0 <1+	6 / 76 (7.9)	NE [NE, NE]	6 / 74 (8.1)	NE [NE, NE]	0.8193 [0.2552, 2.6295] 0.7306	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0811
Yes	53 / 393 (13.5)	NE [29.3, NE]	37 / 377 (9.8)	NE [NE, NE]	1.0161 [0.6667, 1.5640] 0.9418	
No	9 / 41 (22.0)	NE [NE, NE]	2 / 40 (5.0)	NE [NE, NE]	3.7330 [0.9586, 24.5308] 0.0711	
Prior Taxane Use In The Non-Metastatic Setting						0.7214
Yes	19 / 177 (10.7)	NE [NE, NE]	13 / 172 (7.6)	NE [NE, NE]	1.1149 [0.5529, 2.3187] 0.7638	
No	43 / 257 (16.7)	NE [27.2, NE]	26 / 245 (10.6)	NE [NE, NE]	1.1742 [0.7225, 1.9444] 0.5228	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6461
1	6 / 65 (9.2)	NE [NE, NE]	8 / 79 (10.1)	NE [NE, NE]	0.8402 [0.2765, 2.4167] 0.7469	
2	41 / 293 (14.0)	NE [29.3, NE]	23 / 281 (8.2)	NE [NE, NE]	1.2438 [0.7489, 2.1152] 0.4068	
>=3	15 / 75 (20.0)	NE [NE, NE]	8 / 56 (14.3)	NE [NE, NE]	1.1458 [0.4960, 2.8538] 0.7563	
ER/PR status I						0.4922
ER+, PR+	34 / 252 (13.5)	NE [27.2, NE]	23 / 234 (9.8)	NE [NE, NE]	1.0183 [0.5996, 1.7597] 0.9468	
ER+, PR-	26 / 166 (15.7)	NE [29.3, NE]	15 / 171 (8.8)	NE [NE, NE]	1.3633 [0.7260, 2.6514] 0.3428	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7064
ER <=10%	2 / 21 (9.5)	NE [NE, NE]	1 / 14 (7.1)	NE [NE, NE]	1.0466 [0.0992, 22.6631] 0.9702	
ER >10%	53 / 362 (14.6)	NE [NE, NE]	30 / 343 (8.7)	NE [NE, NE]	1.2505 [0.8003, 1.9888] 0.3331	
Positive	7 / 51 (13.7)	NE [24.8, NE]	8 / 60 (13.3)	NE [NE, NE]	0.7794 [0.2704, 2.1924] 0.6333	
Endocrine Resistance						0.5671
Primary	17 / 127 (13.4)	NE [24.8, NE]	10 / 137 (7.3)	NE [NE, NE]	1.3844 [0.6376, 3.1622] 0.4179	
Secondary	45 / 307 (14.7)	NE [29.3, NE]	29 / 279 (10.4)	NE [NE, NE]	1.0453 [0.6559, 1.6919] 0.8535	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						<.0001
Capecitabine	39 / 265 (14.7)	NE [29.3, NE]	15 / 249 (6.0)	NE [NE, NE]	1.8272 [1.0254, 3.4329] 0.0454	
Nab-Paclitaxel	19 / 103 (18.4)	NE [NE, NE]	7 / 101 (6.9)	NE [NE, NE]	2.3368 [1.0220, 6.0019] 0.0493	
Paclitaxel	4 / 66 (6.1)	NE [NE, NE]	17 / 67 (25.4)	NE [7.1, NE]	0.1571 [0.0448, 0.4303] 0.0002	
Prior anthracycline use						0.5832
Yes	26 / 197 (13.2)	NE [NE, NE]	19 / 198 (9.6)	NE [NE, NE]	1.0827 [0.6002, 1.9902] 0.7927	
No	36 / 237 (15.2)	NE [27.2, NE]	20 / 219 (9.1)	NE [NE, NE]	1.2125 [0.7042, 2.1454] 0.4946	
Liver metastases						0.5617
Yes	40 / 294 (13.6)	NE [29.3, NE]	26 / 275 (9.5)	NE [NE, NE]	1.0447 [0.6348, 1.7460] 0.8646	
No	22 / 140 (15.7)	NE [NE, NE]	13 / 142 (9.2)	NE [NE, NE]	1.3144 [0.6679, 2.6923] 0.4372	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.15.2 Adverse events - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.6923
0	31 / 251 (12.4)	NE [29.3, NE]	19 / 246 (7.7)	NE [NE, NE]	1.2065 [0.6826, 2.1858] 0.5243	
>=1	31 / 178 (17.4)	NE [NE, NE]	20 / 163 (12.3)	NE [NE, NE]	1.0375 [0.5914, 1.8607] 0.8988	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Tabelle 2.15.3 Unerwünschte Ereignisse – Subgruppenanalyse – Interaktions-p-Wert <0,05 – SAF

Table 2.15.3 Adverse events - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Adverse events with CTCAE grade 3 or higher						
Race						0.0333
Asian	93 / 153 (60.8)	5.0 [3.8, 11.1]	59 / 147 (40.1)	23.5 [7.2, NE]	1.4174 [1.0240, 1.9772] 0.0364	
White	114 / 231 (49.4)	12.0 [8.7, 20.2]	110 / 223 (49.3)	5.9 [3.9, 14.4]	0.8071 [0.6189, 1.0527] 0.1112	
Other	22 / 50 (44.0)	22.8 [5.5, NE]	16 / 47 (34.0)	NE [5.5, NE]	1.0623 [0.5489, 2.0901] 0.8582	
Region						0.0456
Asia	92 / 148 (62.2)	4.9 [3.2, 10.0]	60 / 144 (41.7)	23.5 [6.5, NE]	1.3923 [1.0065, 1.9396] 0.0467	
Europe	112 / 227 (49.3)	13.1 [8.1, NE]	94 / 206 (45.6)	11.0 [4.1, NE]	0.9031 [0.6853, 1.1927] 0.4694	
Rest of the World	25 / 59 (42.4)	22.8 [8.9, NE]	31 / 67 (46.3)	13.1 [4.6, NE]	0.6483 [0.3698, 1.1194] 0.1183	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.15.3 Adverse events - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0064
Capecitabine	138 / 265 (52.1)	11.1 [6.9, 14.6]	107 / 249 (43.0)	14.4 [5.9, NE]	1.0348 [0.8027, 1.3376] 0.7971	
Nab-Paclitaxel	58 / 103 (56.3)	8.4 [3.7, 15.0]	38 / 101 (37.6)	NE [7.8, NE]	1.4127 [0.9398, 2.1477] 0.0990	
Paclitaxel	33 / 66 (50.0)	8.7 [3.9, NE]	40 / 67 (59.7)	1.8 [0.7, 4.9]	0.6243 [0.3873, 0.9986] 0.0477	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 19AUG2024 5:29; Program name: T.2.15.3_TEAE_SAF_SUB_SIG.sas; Output name: T.2.15.3_TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.15.3 Adverse events - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Adverse events leading to discontinuation of study medication						
Race						0.0002
Asian	26 / 153 (17.0)	NE [NE, NE]	7 / 147 (4.8)	NE [NE, NE]	2.8764 [1.3119, 7.2133] 0.0098	
White	33 / 231 (14.3)	NE [27.2, NE]	22 / 223 (9.9)	NE [NE, NE]	1.0532 [0.6109, 1.8469] 0.8530	
Other	3 / 50 (6.0)	NE [NE, NE]	10 / 47 (21.3)	NE [9.5, NE]	0.1661 [0.0361, 0.5648] 0.0031	
Region						0.0065
Asia	25 / 148 (16.9)	NE [NE, NE]	6 / 144 (4.2)	NE [NE, NE]	3.3067 [1.4432, 8.9256] 0.0055	
Europe	32 / 227 (14.1)	NE [27.2, NE]	25 / 206 (12.1)	NE [NE, NE]	0.8340 [0.4912, 1.4296] 0.5018	
Rest of the World	5 / 59 (8.5)	29.3 [29.3, NE]	8 / 67 (11.9)	NE [NE, NE]	0.4009 [0.1054, 1.2959] 0.1294	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 19AUG2024 5:29; Program name: T.2.15.3_TEAE_SAF_SUB_SIG.sas; Output name: T.2.15.3_TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

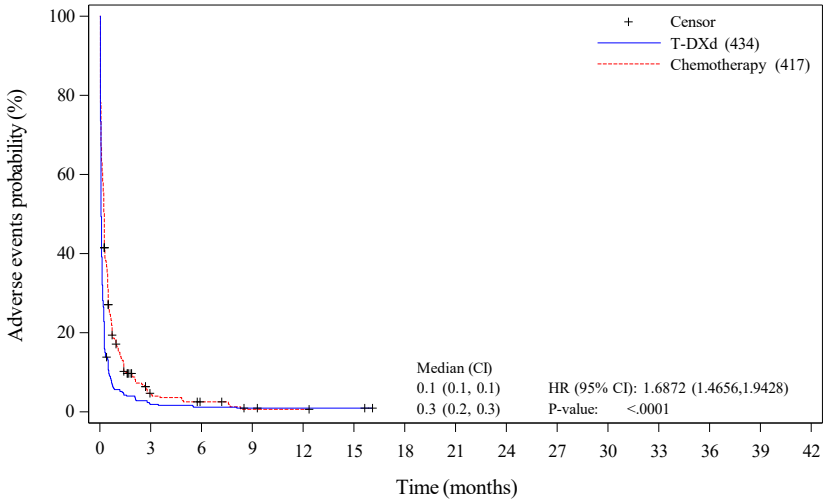
Table 2.15.3 Adverse events - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						<.0001
Capecitabine	39 / 265 (14.7)	NE [29.3, NE]	15 / 249 (6.0)	NE [NE, NE]	1.8272 [1.0254, 3.4329] 0.0454	
Nab-Paclitaxel	19 / 103 (18.4)	NE [NE, NE]	7 / 101 (6.9)	NE [NE, NE]	2.3368 [1.0220, 6.0019] 0.0493	
Paclitaxel	4 / 66 (6.1)	NE [NE, NE]	17 / 67 (25.4)	NE [7.1, NE]	0.1571 [0.0448, 0.4303] 0.0002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Abbildung 2.15.1 Unerwünschte Ereignisse – Kaplan-Meier-Plot – SAF

Figure 2.15.1 Adverse events - Kaplan-Meier plot - Safety Analysis Set
Adverse Events



Patients still at risk:

T-DXd(434)	434	8	5	3	2	2	0
Chemotherapy (417)	417	13	5	1	1	0	

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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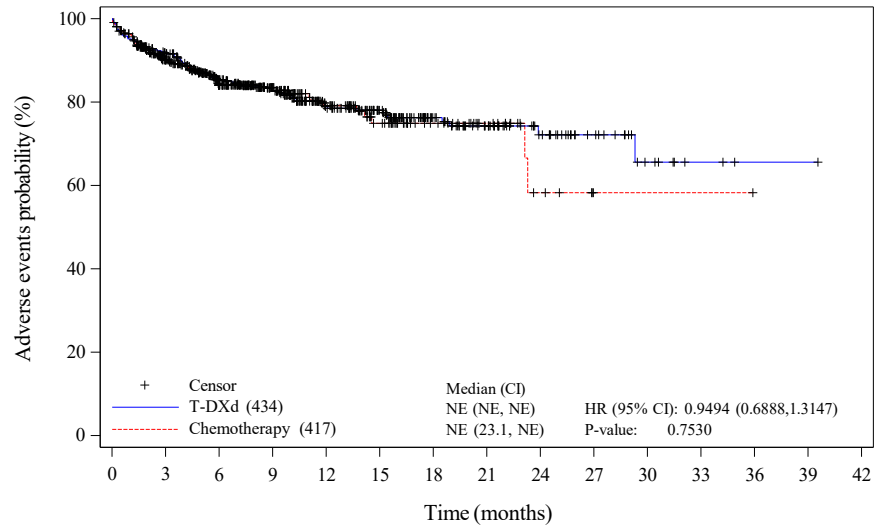
Figure 2.15.1 Adverse events - Kaplan-Meier plot - Safety Analysis Set
Serious Adverse Events



Patients still at risk:

T-DXd(434)	434	373	308	256	183	140	80	56	33	19	8	3	1	1	0
Chemotherapy (417)	417	300	202	126	75	48	28	17	6	1	1	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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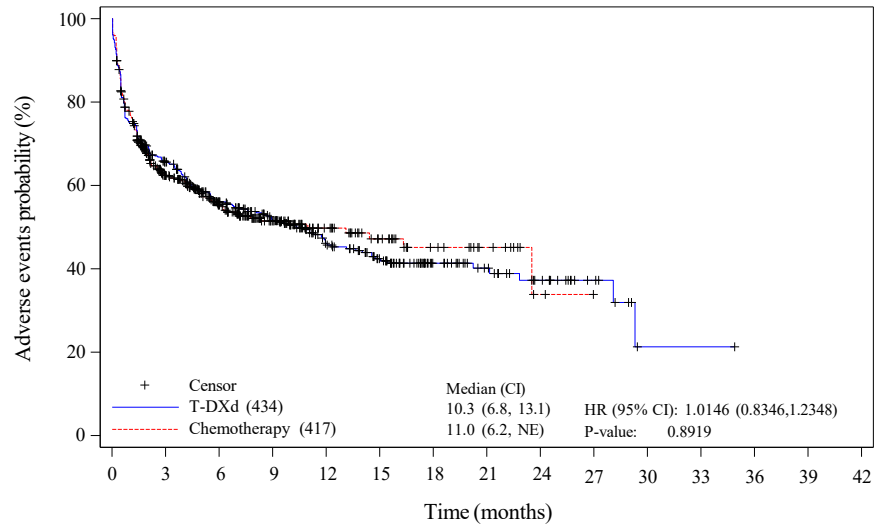
Figure 2.15.1 Adverse events - Kaplan-Meier plot - Safety Analysis Set
Adverse Events with CTCAE grade 3 or higher



Patients still at risk:

T-DXd(434)	434	265	203	163	109	81	45	32	20	9	1	1	0
Chemotherapy (417)	417	204	131	76	47	30	17	10	2	0			

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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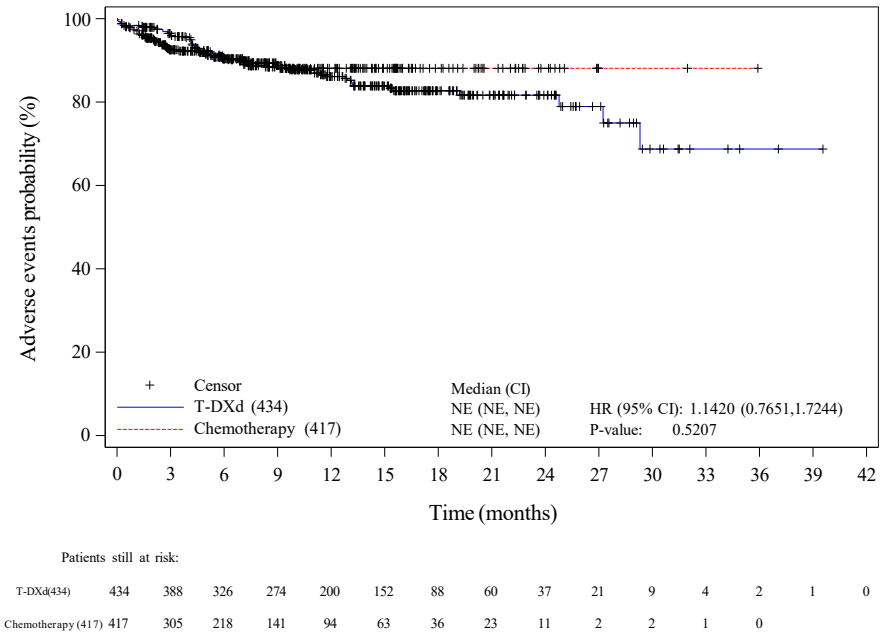
Figure 2.15.1 Adverse events - Kaplan-Meier plot - Safety Analysis Set
Adverse Events leading to discontinuation of study medication



Patients still at risk:

T-DXd(434)	434	388	326	274	200	152	88	60	37	21	9	4	2	1	0
Chemotherapy (417)	417	305	218	141	94	63	36	23	11	2	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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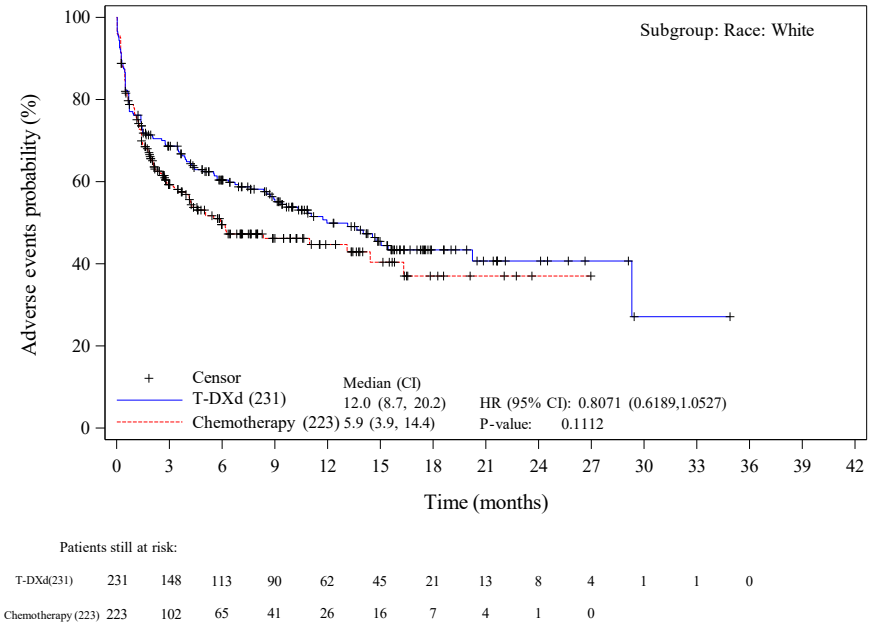
Abbildung 2.15.2 Unerwünschte Ereignisse – Kaplan-Meier-Plot – Analyse nach Subgruppe – SAF

Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events with CTCAE grade 3 or higher



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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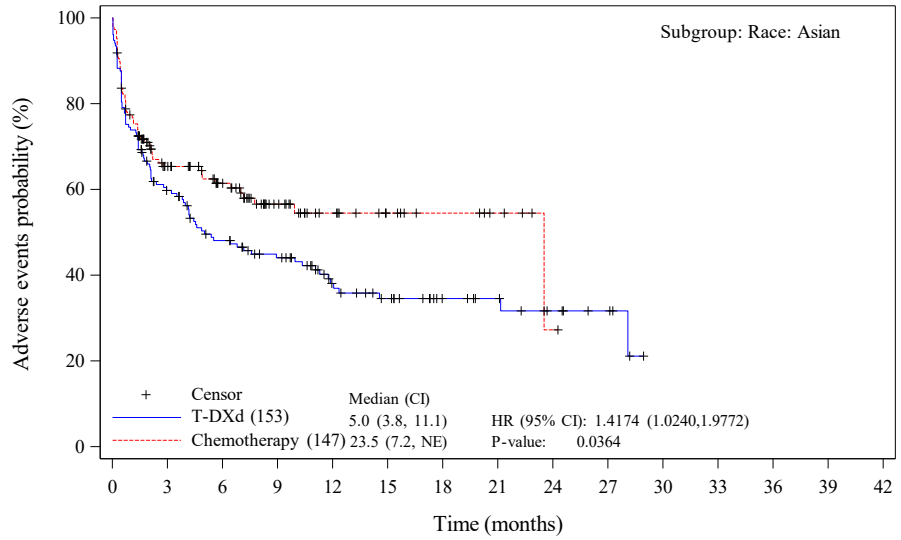
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events with CTCAE grade 3 or higher



Patients still at risk:

T-DXd(153)	153	85	64	52	34	26	16	13	8	5	0
Chemotherapy (147)	147	77	57	32	19	12	8	5	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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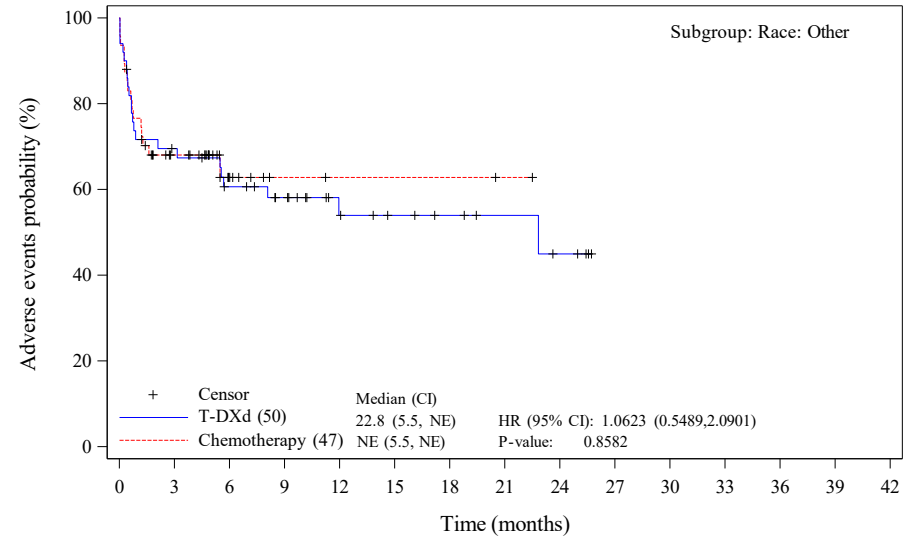
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events with CTCAE grade 3 or higher



Patients still at risk:

T-DXd(50)	50	32	26	21	13	10	8	6	4	0
Chemotherapy (47)	47	25	9	3	2	2	2	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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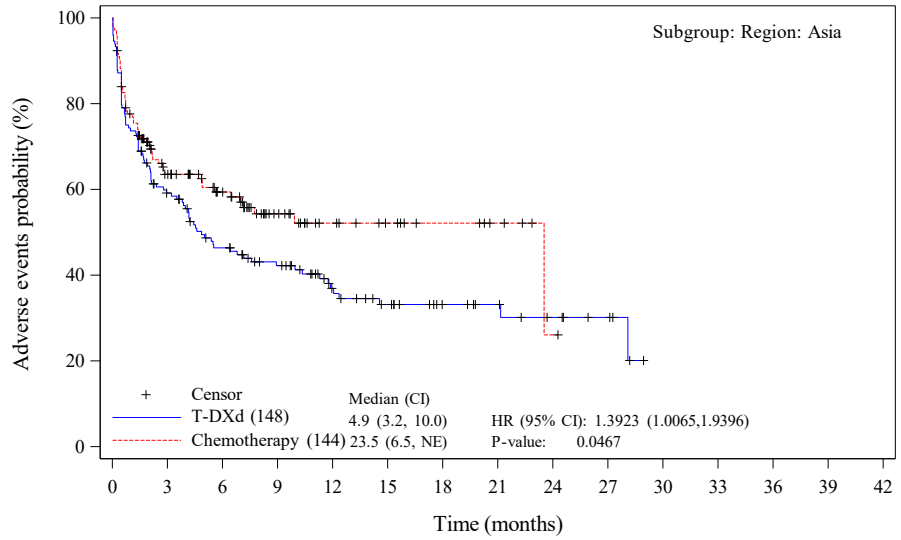
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events with CTCAE grade 3 or higher



Patients still at risk:

T-DXd(148)	148	82	60	48	31	23	15	12	8	5	0
Chemotherapy (144)	144	73	53	29	17	12	8	5	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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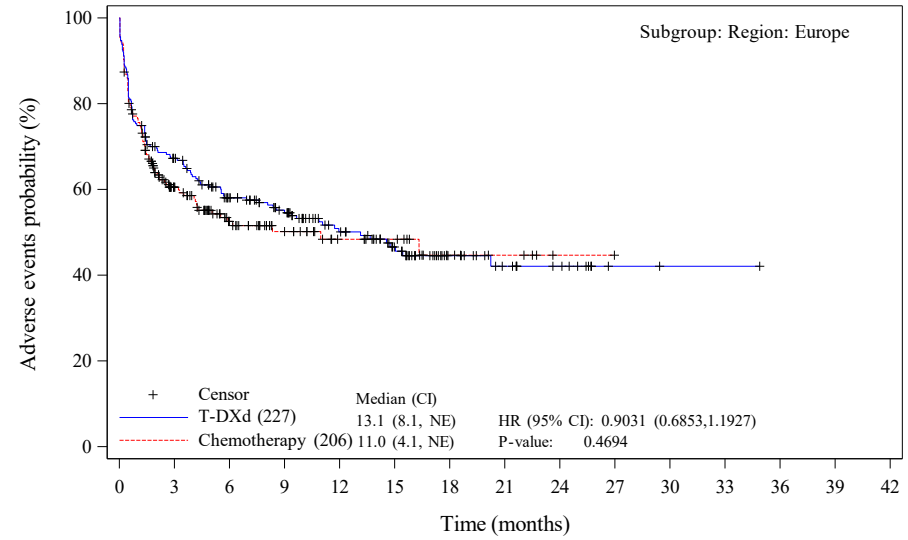
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events with CTCAE grade 3 or higher



Patients still at risk:

T-DXd(227)	227	144	110	90	63	47	24	15	10	2	1	1	0
Chemotherapy (206)	206	94	54	36	23	17	8	5	1	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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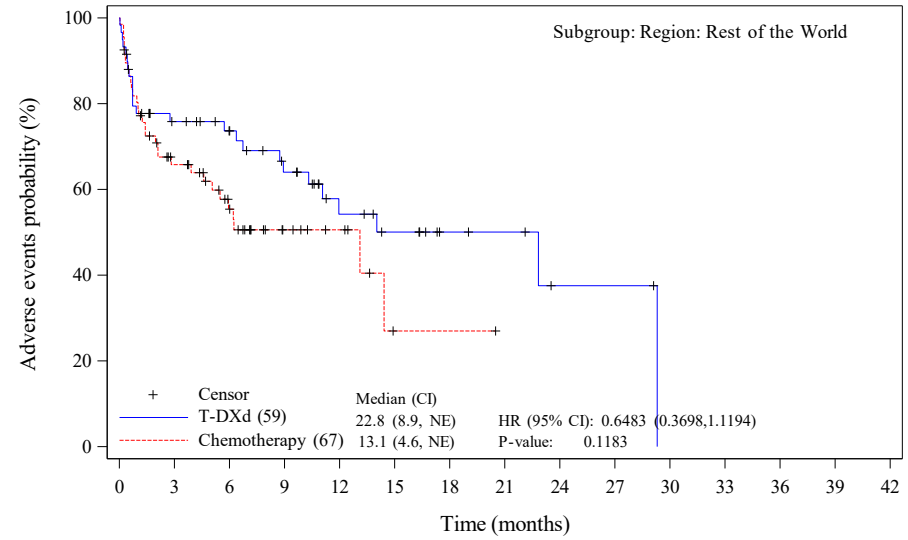
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events with CTCAE grade 3 or higher



Patients still at risk:

T-DXd(59)	59	39	33	25	15	11	6	5	2	2	0
Chemotherapy (67)	67	37	24	11	7	1	1	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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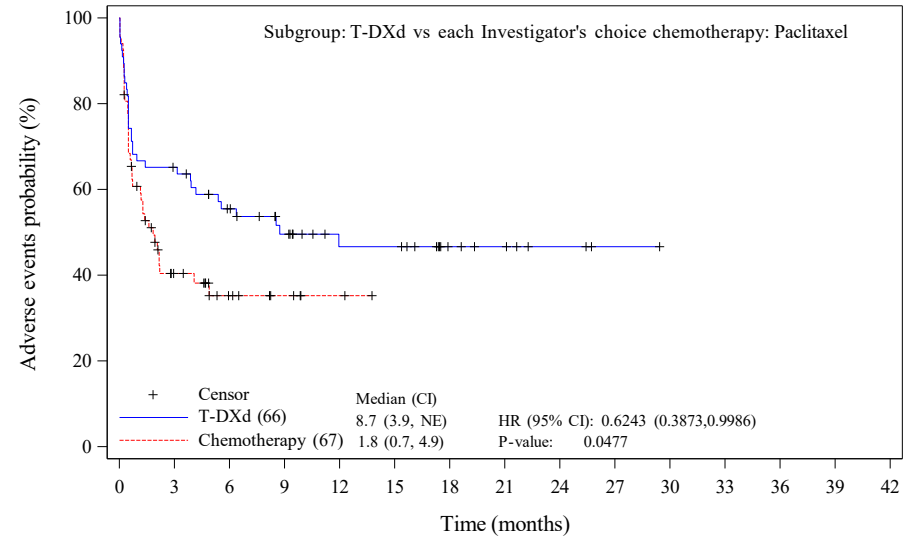
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events with CTCAE grade 3 or higher



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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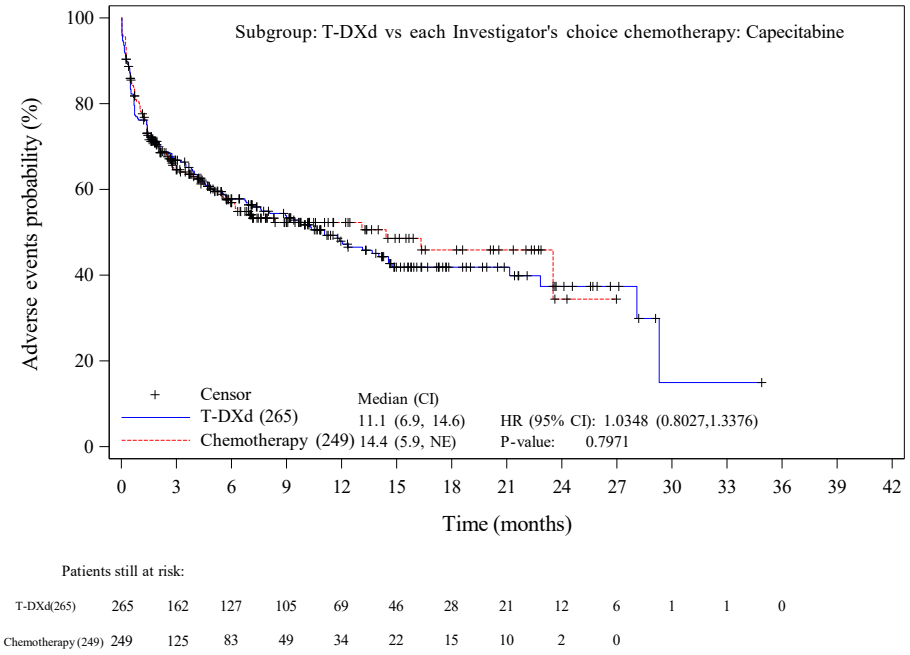
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events with CTCAE grade 3 or higher



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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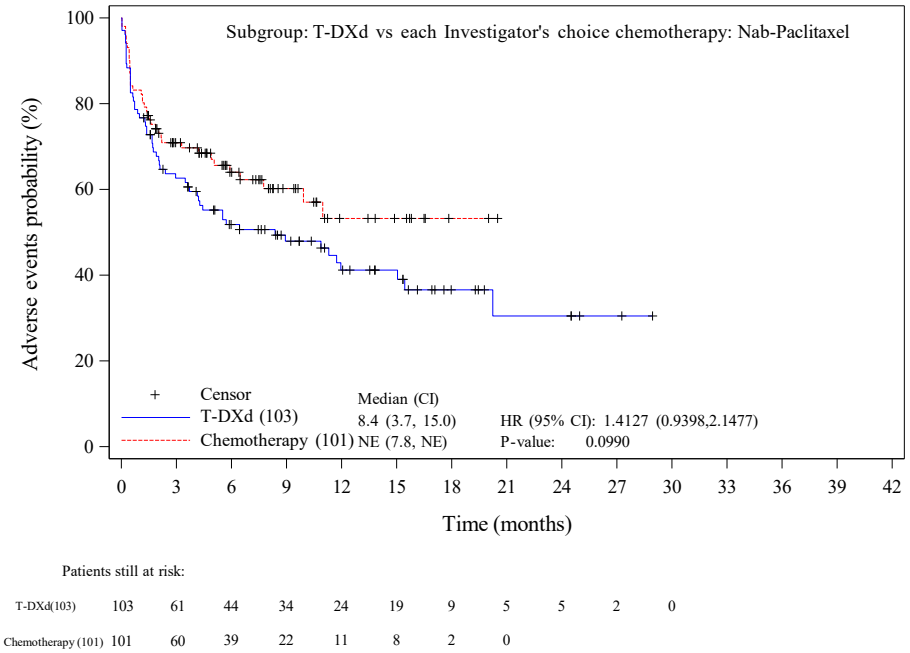
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events with CTCAE grade 3 or higher



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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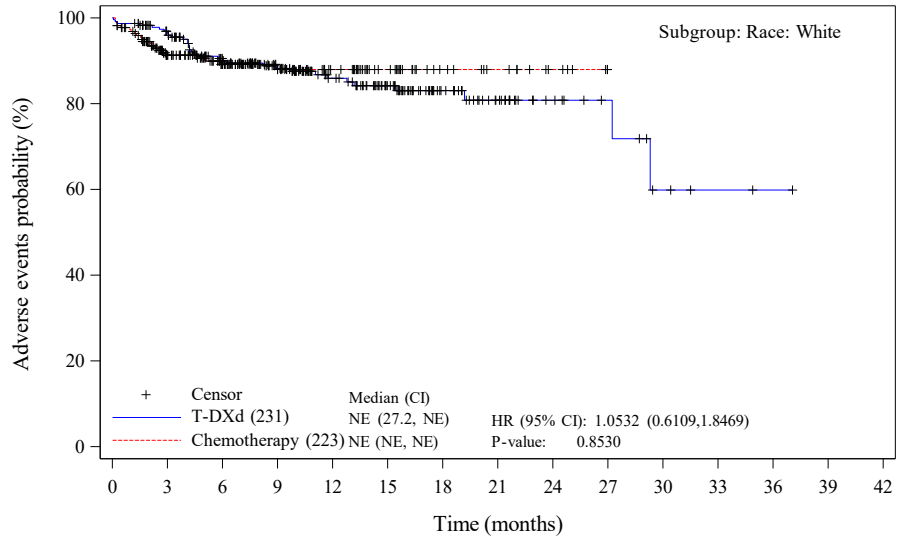
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events leading to discontinuation of study medication



Patients still at risk:

T-DXd(231)	231	208	168	139	103	77	44	27	14	9	4	2	1	0
Chemotherapy (223)	223	154	113	74	50	33	17	12	6	0				

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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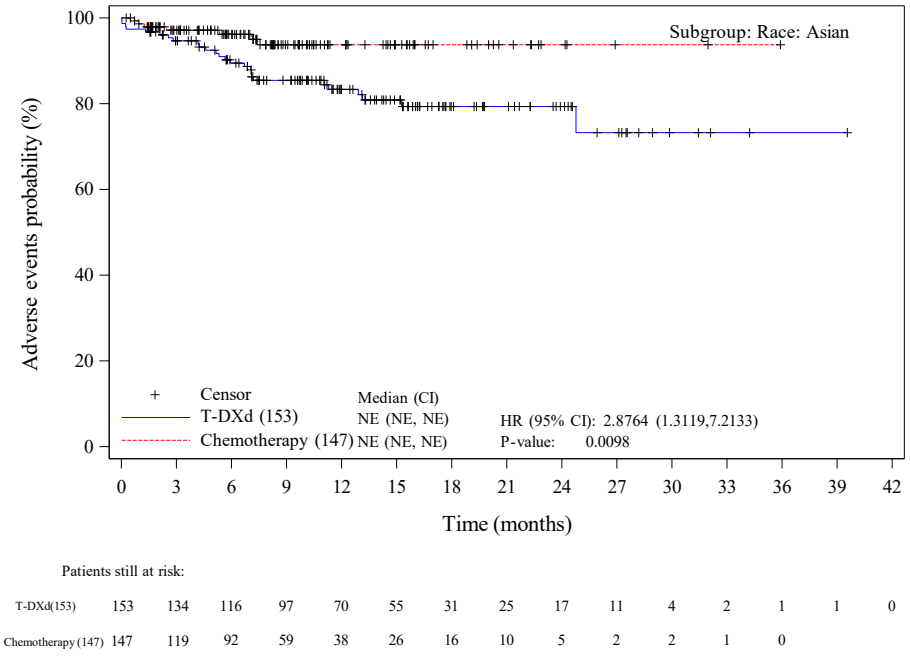
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events leading to discontinuation of study medication



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
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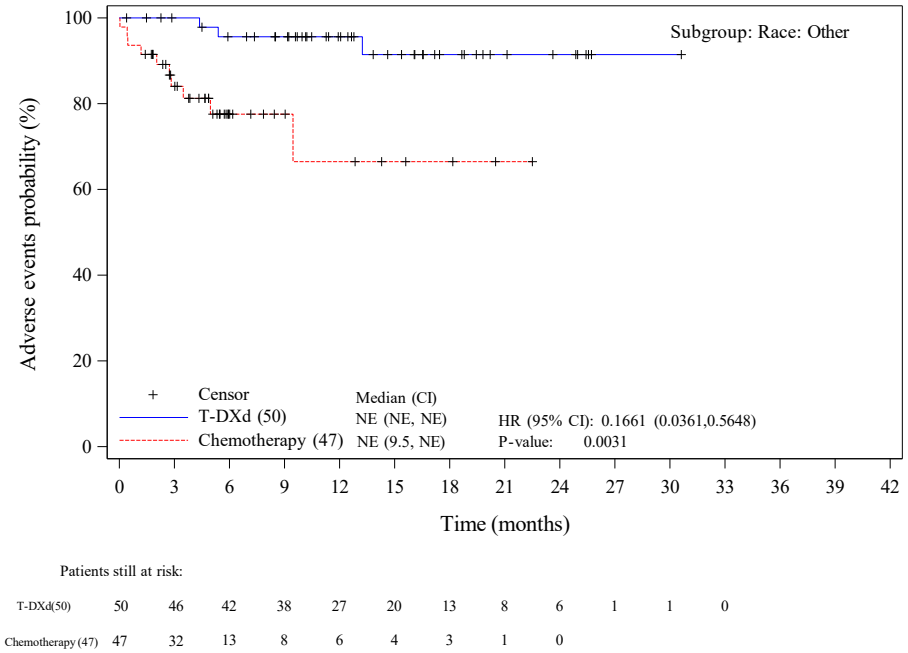
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events leading to discontinuation of study medication



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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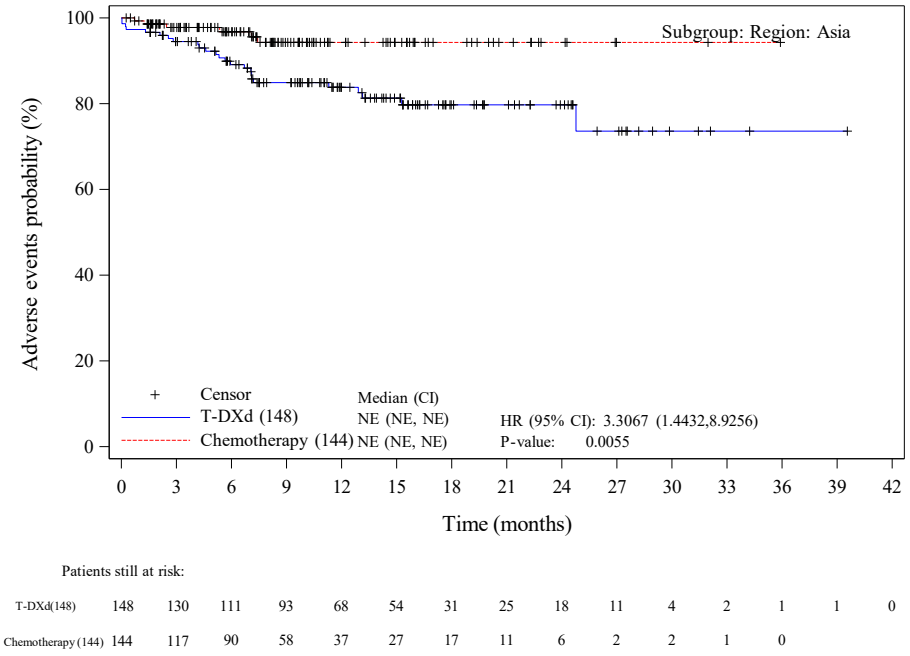
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events leading to discontinuation of study medication



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
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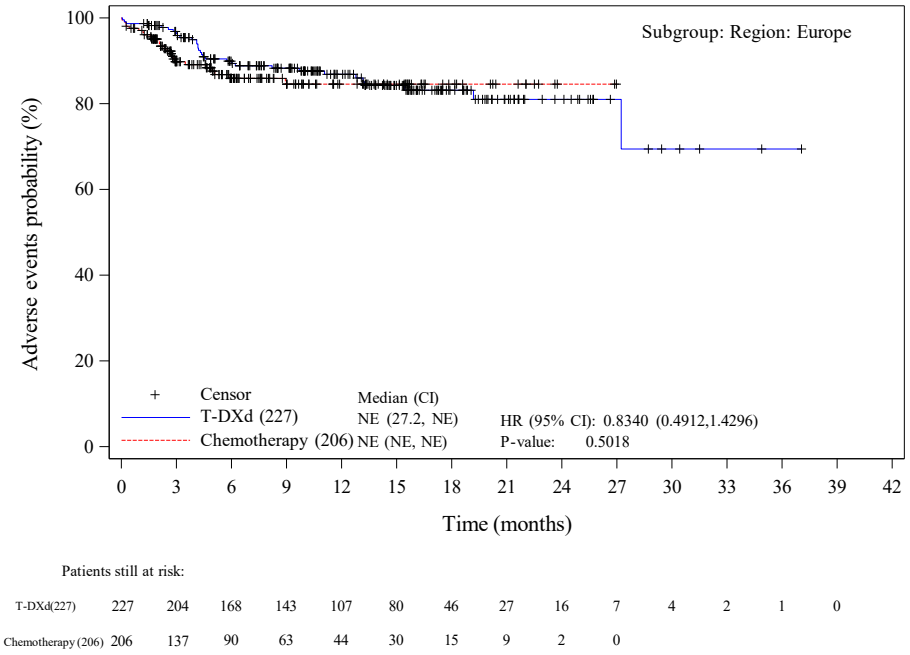
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events leading to discontinuation of study medication



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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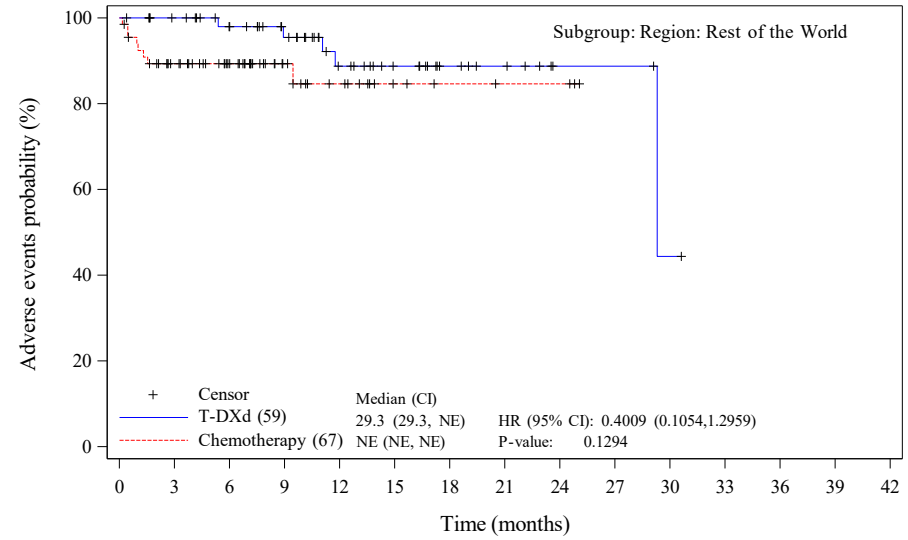
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events leading to discontinuation of study medication



Patients still at risk:

T-DXd(59)	59	54	47	38	25	18	11	8	3	3	1	0
Chemotherapy (67)	67	51	38	20	13	6	4	3	3	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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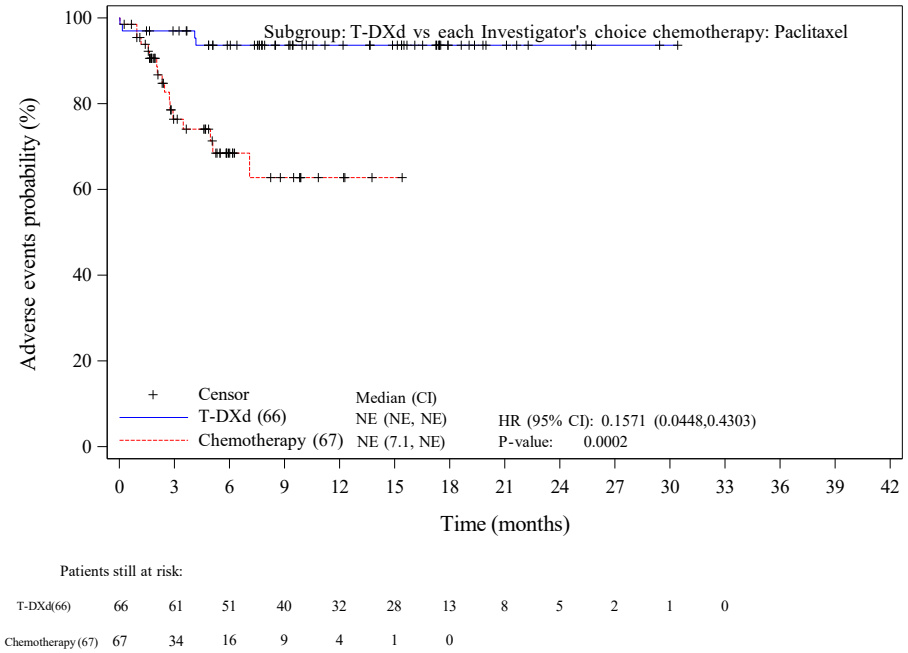
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events leading to discontinuation of study medication



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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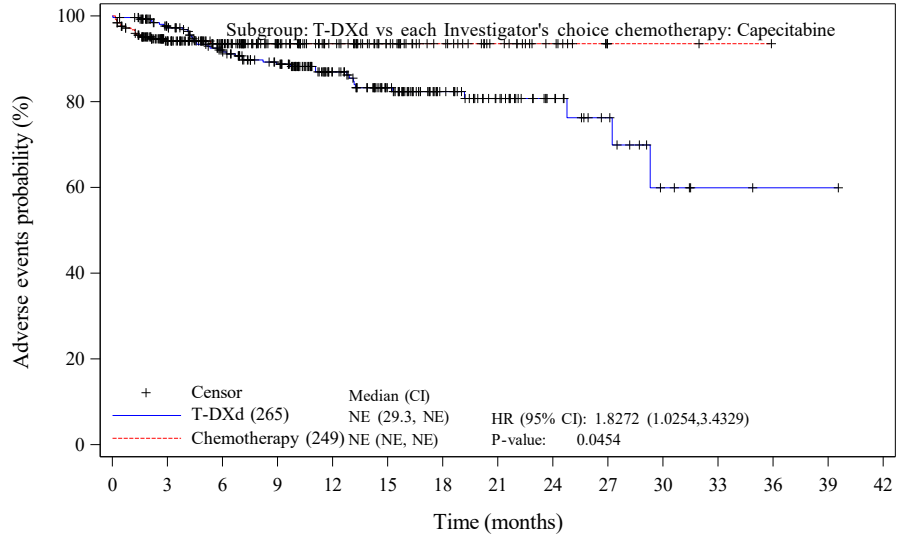
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events leading to discontinuation of study medication



Patients still at risk:

T-DXd(265)	265	237	204	176	124	93	57	39	22	13	5	2	1	1	0
Chemotherapy (249)	249	184	137	97	69	47	31	20	11	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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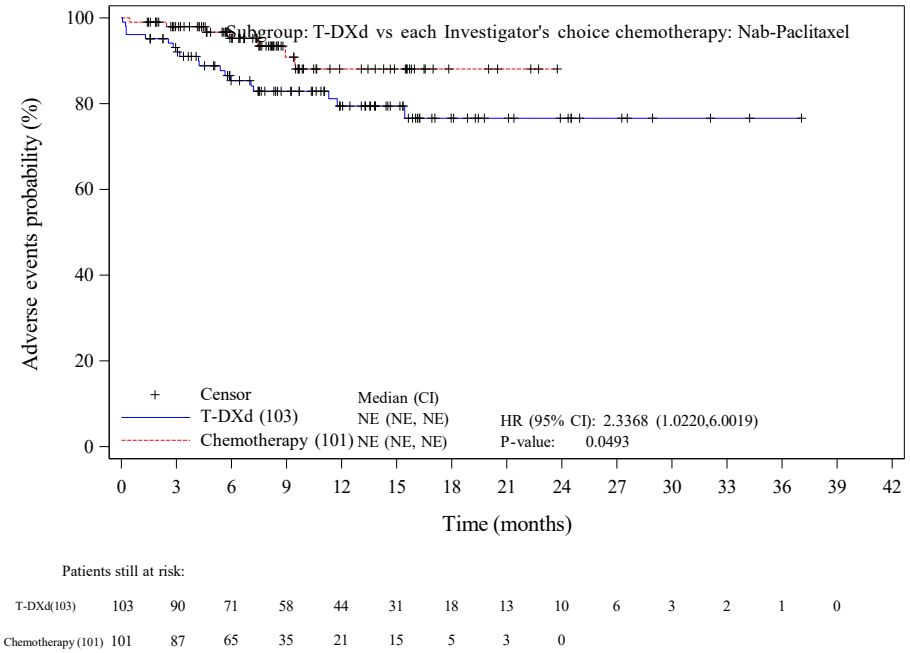
Figure 2.15.2 Treatment-emergent adverse events - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
Adverse Events leading to discontinuation of study medication



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval
NE: Not estimable

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Anhang 4-G 4.2 Unerwünschte Ereignisse von besonderem Interesse

Tabelle 2.19.1 Unerwünschte Ereignisse von besonderem Interesse – SAF

Daiichi Sankyo Europe GmbH
Data Intelligence - Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

Page 1 of 1
Final
Statistical analyses for AMNOG (HTA Germany)

Table 2.19.1 Adverse Events of Special Interest - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
AESI of adjudicated drug-related ILD/pneumonitis	49 (11.3)	NE [NE; NE]	1 (0.2)	NE [NE; NE]	33.1097 [7.2464; 586.8168] 0.0005	<.0001
Serious AESI of adjudicated drug-related ILD/pneumonitis	11 (2.5)	NE [NE; NE]	0 (0.0)	NE [NE; NE]	NE [NE; NE]	0.0068
CTCAE grade 3 or higher AESI of adjudicated drug-related ILD/pneumonitis	6 (1.4)	NE [NE; NE]	0 (0.0)	NE [NE; NE]	NE [NE; NE]	0.0515
AESI of ILD/pneumonitis	52 (12.0)	NE [NE; NE]	1 (0.2)	NE [NE; NE]	35.1463 [7.7111; 622.7351] 0.0004	<.0001
Serious AESI of ILD/pneumonitis	11 (2.5)	NE [NE; NE]	0 (0.0)	NE [NE; NE]	NE [NE; NE]	0.0068
CTCAE grade 3 or higher AESI of ILD/pneumonitis	6 (1.4)	NE [NE; NE]	0 (0.0)	NE [NE; NE]	NE [NE; NE]	0.0515
AESI of LVEF decrease	35 (8.1)	NE [NE; NE]	16 (3.8)	NE [NE; NE]	1.4952 [0.8383; 2.7844] 0.1857	0.1830
Serious AESI of LVEF decrease	0 (0.0)	NE [NE; NE]	2 (0.5)	NE [NE; NE]	NE [NE; NE]	0.1139
CTCAE grade 3 or higher AESI of LVEF decrease	3 (0.7)	NE [NE; NE]	3 (0.7)	NE [NE; NE]	0.7421 [0.1363; 4.0361] 0.7163	0.7153

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from Cox proportional hazards model with treatment as the only categorical variable in the model.Inclusion of stratification factors is following the pooling strategy described in study SAP. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: confidence interval; HR: hazard ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Tabelle 2.19.2 Unerwünschte Ereignisse von besonderem Interesse – Subgruppenanalyse – SAF

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
AESI of adjudicated drug-related ILD/pneumonitis						
Age at randomization						0.3593
<65 years of age	35 / 301 (11.6)	NE [27.4, NE]	1 / 285 (0.4)	NE [NE, NE]	20.7618 [4.4600, 369.5236] <.0001	
>=65 years of age	14 / 133 (10.5)	NE [NE, NE]	0 / 132 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Race						0.4239
Asian	19 / 153 (12.4)	NE [NE, NE]	1 / 147 (0.7)	NE [NE, NE]	15.1295 [3.1336, 271.9049] 0.0004	
White	23 / 231 (10.0)	NE [24.9, NE]	0 / 223 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Other	7 / 50 (14.0)	NE [21.4, NE]	0 / 47 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4301
Asia	19 / 148 (12.8)	NE [NE, NE]	1 / 144 (0.7)	NE [NE, NE]	15.3618 [3.1823, 276.0648] 0.0004	
Europe	25 / 227 (11.0)	NE [27.4, NE]	0 / 206 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Rest of the World	5 / 59 (8.5)	NE [23.2, NE]	0 / 67 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
HER2 IHC expression						0.4548
IHC 1+	22 / 239 (9.2)	NE [NE, NE]	1 / 226 (0.4)	NE [NE, NE]	15.2791 [3.1922, 273.9717] 0.0004	
IHC 2+/ISH-	16 / 116 (13.8)	NE [23.2, NE]	0 / 115 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
IHC >0 <1+	11 / 76 (14.5)	NE [NE, NE]	0 / 74 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6656
Yes	45 / 393 (11.5)	NE [NE, NE]	1 / 377 (0.3)	NE [NE, NE]	29.9025 [6.5195, 530.3184] <.0001	
No	4 / 41 (9.8)	NE [NE, NE]	0 / 40 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Prior Taxane Use In The Non-Metastatic Setting						0.1767
Yes	20 / 177 (11.3)	NE [NE, NE]	1 / 172 (0.6)	NE [NE, NE]	13.1835 [2.7213, 237.1884] 0.0012	
No	29 / 257 (11.3)	NE [NE, NE]	0 / 245 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1743
1	8 / 65 (12.3)	NE [NE, NE]	0 / 79 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
2	31 / 293 (10.6)	NE [NE, NE]	0 / 281 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
>=3	10 / 75 (13.3)	NE [21.4, NE]	1 / 56 (1.8)	NE [NE, NE]	4.9101 [0.9129, 90.8166] 0.0958	
ER/PR status I						0.2362
ER+, PR+	24 / 252 (9.5)	NE [27.4, NE]	1 / 234 (0.4)	NE [NE, NE]	14.8193 [3.1162, 265.2707] 0.0005	
ER+, PR-	22 / 166 (13.3)	NE [NE, NE]	0 / 171 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.8167
ER <=10%	2 / 21 (9.5)	NE [15.1, NE]	0 / 14 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
ER >10%	41 / 362 (11.3)	NE [NE, NE]	1 / 343 (0.3)	NE [NE, NE]	26.6065 [5.7733, 472.3470] <.0001	
Positive	6 / 51 (11.8)	NE [NE, NE]	0 / 60 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Endocrine Resistance						0.4132
Primary	13 / 127 (10.2)	NE [27.4, NE]	0 / 137 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Secondary	36 / 307 (11.7)	NE [NE, NE]	1 / 279 (0.4)	NE [NE, NE]	23.4269 [5.0588, 416.3796] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 19JAN2025 7:50; Program name: T.2.19.2_ADJILD_SAF_SUB.sas; Output name: T.2.19.2_ADJILD_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0928
Capecitabine	32 / 265 (12.1)	NE [27.4, NE]	0 / 249 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Nab-Paclitaxel	11 / 103 (10.7)	NE [NE, NE]	0 / 101 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Paclitaxel	6 / 66 (9.1)	NE [NE, NE]	1 / 67 (1.5)	NE [NE, NE]	3.7813 [0.6142, 72.3862] 0.1920	
Prior anthracycline use						0.2465
Yes	24 / 197 (12.2)	NE [27.4, NE]	0 / 198 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
No	25 / 237 (10.5)	NE [NE, NE]	1 / 219 (0.5)	NE [NE, NE]	17.0733 [3.6067, 305.2286] 0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.3311
Yes	32 / 294 (10.9)	NE [27.4, NE]	1 / 275 (0.4)	NE [NE, NE]	19.9211 [4.2615, 354.9457] <.0001	
No	17 / 140 (12.1)	NE [NE, NE]	0 / 142 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
ECOG						0.3093
0	27 / 251 (10.8)	NE [NE, NE]	1 / 246 (0.4)	NE [NE, NE]	19.8558 [4.2178, 354.4423] <.0001	
>=1	21 / 178 (11.8)	NE [27.4, NE]	0 / 163 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Serious AESI of adjudicated drug-related ILD/pneumonitis						
Prior CDK4/6 inhibitor use						0.9996
Yes	11 / 393 (2.8)	NE [NE, NE]	0 / 377 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
No	0 / 41 (0.0)	NE [NE, NE]	0 / 40 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
AESI of ILD/pneumonitis						
Age at randomization						0.3548
<65 years of age	37 / 301 (12.3)	NE [27.4, NE]	1 / 285 (0.4)	NE [NE, NE]	21.5969 [4.6534, 384.0863] <.0001	
>=65 years of age	15 / 133 (11.3)	NE [NE, NE]	0 / 132 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Race						0.4429
Asian	21 / 153 (13.7)	NE [NE, NE]	1 / 147 (0.7)	NE [NE, NE]	16.7447 [3.4976, 300.2527] 0.0002	
White	24 / 231 (10.4)	NE [24.9, NE]	0 / 223 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Other	7 / 50 (14.0)	NE [21.4, NE]	0 / 47 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 19JAN2025 7:50; Program name: T.2.19.2_ADJILD_SAF_SUB.sas; Output name: T.2.19.2_ADJILD_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4503
Asia	21 / 148 (14.2)	NE [NE, NE]	1 / 144 (0.7)	NE [NE, NE]	17.0282 [3.5576, 305.3163] 0.0002	
Europe	26 / 227 (11.5)	NE [27.4, NE]	0 / 206 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Rest of the World	5 / 59 (8.5)	NE [23.2, NE]	0 / 67 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
HER2 IHC expression						0.4702
IHC 1+	24 / 239 (10.0)	NE [NE, NE]	1 / 226 (0.4)	NE [NE, NE]	16.7886 [3.5320, 300.4784] 0.0002	
IHC 2+/ISH-	17 / 116 (14.7)	NE [23.2, NE]	0 / 115 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
IHC >0 <1+	11 / 76 (14.5)	NE [NE, NE]	0 / 74 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6759
Yes	48 / 393 (12.2)	NE [NE, NE]	1 / 377 (0.3)	NE [NE, NE]	31.9143 [6.9773, 565.7270] <.0001	
No	4 / 41 (9.8)	NE [NE, NE]	0 / 40 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Prior Taxane Use In The Non-Metastatic Setting						0.1724
Yes	21 / 177 (11.9)	NE [27.4, NE]	1 / 172 (0.6)	NE [NE, NE]	13.6241 [2.8244, 244.8321] 0.0009	
No	31 / 257 (12.1)	NE [NE, NE]	0 / 245 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 19JAN2025 7:50; Program name: T.2.19.2_ADJILD_SAF_SUB.sas; Output name: T.2.19.2_ADJILD_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1646
1	8 / 65 (12.3)	NE [NE, NE]	0 / 79 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
2	34 / 293 (11.6)	NE [NE, NE]	0 / 281 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
>=3	10 / 75 (13.3)	NE [21.4, NE]	1 / 56 (1.8)	NE [NE, NE]	4.9101 [0.9129, 90.8166] 0.0958	
ER/PR status I						0.2288
ER+, PR+	25 / 252 (9.9)	NE [27.4, NE]	1 / 234 (0.4)	NE [NE, NE]	15.7984 [3.3319, 282.5718] 0.0003	
ER+, PR-	24 / 166 (14.5)	NE [NE, NE]	0 / 171 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7982
ER <=10%	2 / 21 (9.5)	NE [15.1, NE]	0 / 14 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
ER >10%	43 / 362 (11.9)	NE [NE, NE]	1 / 343 (0.3)	NE [NE, NE]	27.5627 [5.9939, 489.0783] <.0001	
Positive	7 / 51 (13.7)	NE [NE, NE]	0 / 60 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Endocrine Resistance						0.4305
Primary	13 / 127 (10.2)	NE [27.4, NE]	0 / 137 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Secondary	39 / 307 (12.7)	NE [NE, NE]	1 / 279 (0.4)	NE [NE, NE]	25.4438 [5.5161, 451.7855] <.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0868
Capecitabine	35 / 265 (13.2)	NE [27.4, NE]	0 / 249 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Nab-Paclitaxel	11 / 103 (10.7)	NE [NE, NE]	0 / 101 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
Paclitaxel	6 / 66 (9.1)	NE [NE, NE]	1 / 67 (1.5)	NE [NE, NE]	3.7813 [0.6142, 72.3862] 0.1920	
Prior anthracycline use						0.2399
Yes	26 / 197 (13.2)	NE [27.4, NE]	0 / 198 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
No	26 / 237 (11.0)	NE [NE, NE]	1 / 219 (0.5)	NE [NE, NE]	18.0667 [3.8272, 322.7474] 0.0001	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.2979
Yes	32 / 294 (10.9)	NE [27.4, NE]	1 / 275 (0.4)	NE [NE, NE]	19.9211 [4.2615, 354.9457] <.0001	
No	20 / 140 (14.3)	NE [NE, NE]	0 / 142 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
ECOG						0.3233
0	29 / 251 (11.6)	NE [NE, NE]	1 / 246 (0.4)	NE [NE, NE]	21.4811 [4.5840, 382.9858] <.0001	
>=1	21 / 178 (11.8)	NE [27.4, NE]	0 / 163 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Serious AESI of ILD/pneumonitis						
Prior CDK4/6 inhibitor use						0.9996
Yes	11 / 393 (2.8)	NE [NE, NE]	0 / 377 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
No	0 / 41 (0.0)	NE [NE, NE]	0 / 40 (0.0)	NE [NE, NE]	NE [NE; NE] NE	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
AESI of LVEF decrease						
Age at randomization						0.2924
<65 years of age	25 / 301 (8.3)	NE [NE, NE]	8 / 285 (2.8)	NE [NE, NE]	1.9752 [0.9236, 4.7079] 0.0907	
>=65 years of age	10 / 133 (7.5)	NE [NE, NE]	8 / 132 (6.1)	NE [NE, NE]	1.0362 [0.4081, 2.7184] 0.9407	
Race						0.6672
Asian	11 / 153 (7.2)	NE [NE, NE]	4 / 147 (2.7)	NE [NE, NE]	2.0923 [0.7132, 7.5655] 0.1971	
White	21 / 231 (9.1)	NE [NE, NE]	10 / 223 (4.5)	NE [NE, NE]	1.4190 [0.6812, 3.1605] 0.3630	
Other	3 / 50 (6.0)	NE [NE, NE]	2 / 47 (4.3)	NE [8.0, NE]	0.8607 [0.1330, 6.8557] 0.8742	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.3634
Asia	11 / 148 (7.4)	NE [NE, NE]	3 / 144 (2.1)	NE [NE, NE]	2.8313 [0.8812, 12.5407] 0.0956	
Europe	19 / 227 (8.4)	NE [NE, NE]	8 / 206 (3.9)	NE [NE, NE]	1.4661 [0.6589, 3.5777] 0.3661	
Rest of the World	5 / 59 (8.5)	NE [22.9, NE]	5 / 67 (7.5)	NE [14.0, NE]	0.7913 [0.2171, 2.8782] 0.7138	
HER2 IHC expression						0.3478
IHC 1+	21 / 239 (8.8)	NE [NE, NE]	7 / 226 (3.1)	NE [NE, NE]	2.2460 [0.9984, 5.7150] 0.0578	
IHC 2+/ISH-	9 / 116 (7.8)	NE [22.9, NE]	7 / 115 (6.1)	NE [NE, NE]	0.7033 [0.2560, 2.0094] 0.4915	
IHC >0 <1+	4 / 76 (5.3)	NE [NE, NE]	2 / 74 (2.7)	NE [16.8, NE]	1.4317 [0.2775, 10.3745] 0.6782	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6311
Yes	32 / 393 (8.1)	NE [NE, NE]	15 / 377 (4.0)	NE [NE, NE]	1.4236 [0.7808, 2.7148] 0.2605	
No	3 / 41 (7.3)	NE [NE, NE]	1 / 40 (2.5)	NE [NE, NE]	2.6198 [0.3344, 53.0214] 0.3869	
Prior Taxane Use In The Non-Metastatic Setting						0.1166
Yes	12 / 177 (6.8)	NE [NE, NE]	9 / 172 (5.2)	NE [NE, NE]	0.9650 [0.4049, 2.3813] 0.9358	
No	23 / 257 (8.9)	NE [NE, NE]	7 / 245 (2.9)	NE [NE, NE]	2.2348 [1.0053, 5.6490] 0.0567	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4530
1	5 / 65 (7.7)	NE [NE, NE]	5 / 79 (6.3)	NE [NE, NE]	1.0474 [0.2904, 3.7765] 0.9418	
2	27 / 293 (9.2)	NE [NE, NE]	9 / 281 (3.2)	NE [NE, NE]	1.9611 [0.9531, 4.4365] 0.0766	
>=3	3 / 75 (4.0)	NE [NE, NE]	2 / 56 (3.6)	NE [NE, NE]	0.9044 [0.1492, 6.8909] 0.9126	
ER/PR status I						0.7741
ER+, PR+	19 / 252 (7.5)	NE [NE, NE]	8 / 234 (3.4)	NE [NE, NE]	1.5508 [0.6998, 3.7736] 0.2959	
ER+, PR-	14 / 166 (8.4)	NE [NE, NE]	8 / 171 (4.7)	NE [NE, NE]	1.2805 [0.5410, 3.2399] 0.5815	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2390
ER <=10%	1 / 21 (4.8)	NE [NE, NE]	0 / 14 (0.0)	NE [NE, NE]	NE [NE; NE] NE	
ER >10%	31 / 362 (8.6)	NE [NE, NE]	11 / 343 (3.2)	NE [NE, NE]	1.8971 [0.9780, 3.9657] 0.0655	
Positive	3 / 51 (5.9)	NE [NE, NE]	5 / 60 (8.3)	NE [NE, NE]	0.5455 [0.1116, 2.2301] 0.4006	
Endocrine Resistance						0.9939
Primary	10 / 127 (7.9)	NE [NE, NE]	5 / 137 (3.6)	NE [NE, NE]	1.5954 [0.5633, 5.1459] 0.3918	
Secondary	25 / 307 (8.1)	NE [NE, NE]	11 / 279 (3.9)	NE [NE, NE]	1.4630 [0.7347, 3.1096] 0.2931	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1632
Capecitabine	20 / 265 (7.5)	NE [NE, NE]	13 / 249 (5.2)	NE [NE, NE]	1.0539 [0.5281, 2.1781] 0.8827	
Nab-Paclitaxel	11 / 103 (10.7)	NE [NE, NE]	2 / 101 (2.0)	NE [NE, NE]	4.8331 [1.2897, 31.3328] 0.0241	
Paclitaxel	4 / 66 (6.1)	NE [21.9, NE]	1 / 67 (1.5)	NE [NE, NE]	1.7316 [0.2151, 35.4436] 0.6336	
Prior anthracycline use						0.1229
Yes	18 / 197 (9.1)	NE [NE, NE]	12 / 198 (6.1)	NE [NE, NE]	1.1401 [0.5513, 2.4420] 0.7278	
No	17 / 237 (7.2)	NE [NE, NE]	4 / 219 (1.8)	NE [NE, NE]	2.6301 [0.9690, 9.1662] 0.0716	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.19.2 Adverse Events of Special Interest - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.8889
Yes	22 / 294 (7.5)	NE [NE, NE]	9 / 275 (3.3)	NE [NE, NE]	1.4879 [0.7011, 3.4319] 0.3173	
No	13 / 140 (9.3)	NE [NE, NE]	7 / 142 (4.9)	NE [NE, NE]	1.5142 [0.6184, 4.0389] 0.3742	
ECOG						0.3757
0	21 / 251 (8.4)	NE [NE, NE]	8 / 246 (3.3)	NE [NE, NE]	1.8582 [0.8511, 4.4853] 0.1319	
>=1	12 / 178 (6.7)	NE [NE, NE]	7 / 163 (4.3)	NE [NE, NE]	1.1371 [0.4531, 3.0770] 0.7892	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Tabelle 2.19.3 Unerwünschte Ereignisse von besonderem Interesse – Subgruppenanalyse – Interaktions-p-Wert <0,05 – SAF

Table 2.19.3 Adverse Events of Special Interest – Subgroup Analysis - interaction p-value < 0.05 - Full Analysis Set

No output displayed as p-value >= 0.05 for all subgroups.

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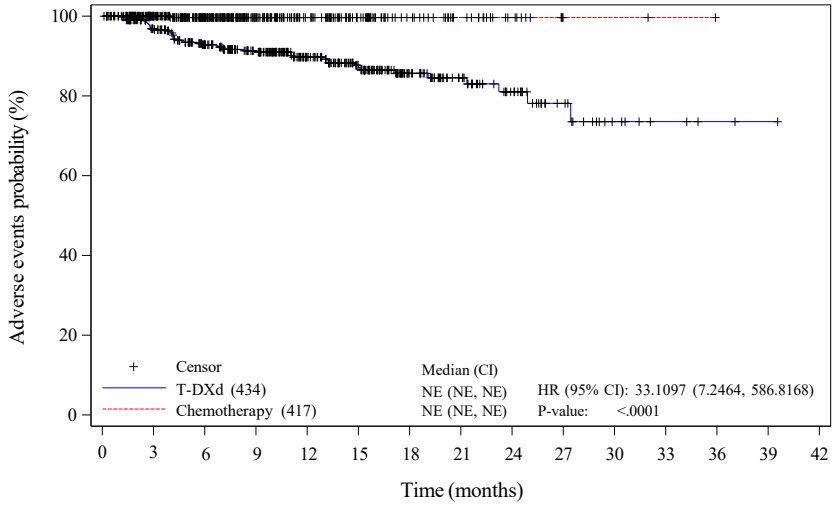
Abbildung 2.19.1 Unerwünschte Ereignisse von besonderem Interesse – Kaplan-Meier-Plot – SAF

Figure 2.19.1 Adverse Events of Special Interest - Kaplan-Meier plot - Safety Analysis Set
AESI of adjudicated drug-related ILD/pneumonitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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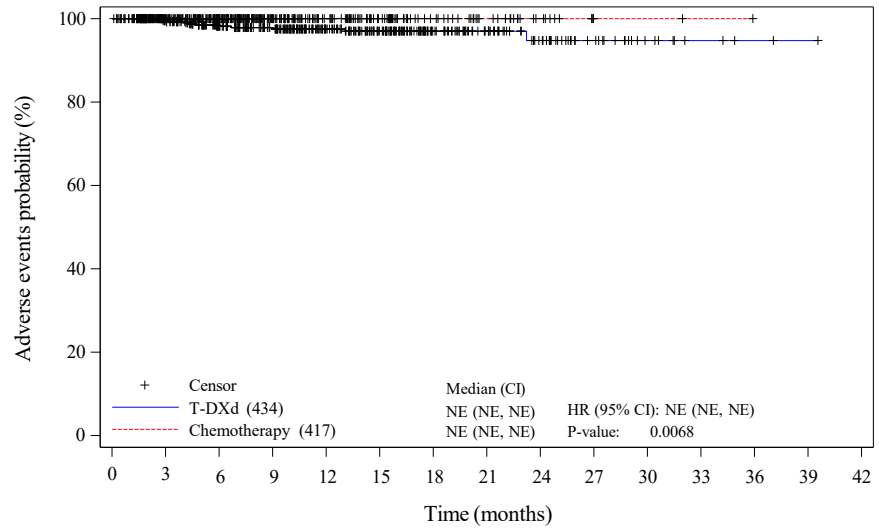
Figure 2.19.1 Adverse Events of Special Interest - Kaplan-Meier plot - Safety Analysis Set
Serious AESI of adjudicated drug-related ILD/pneumonitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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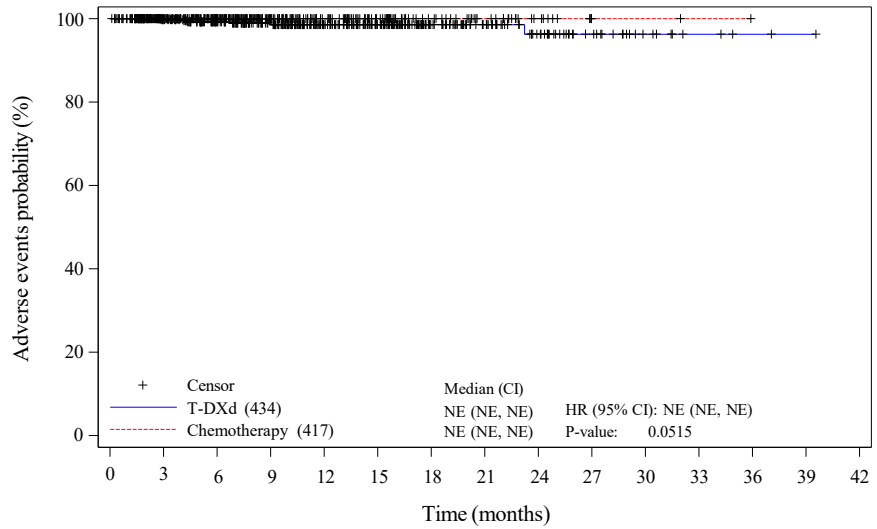
Figure 2.19.1 Adverse Events of Special Interest - Kaplan-Meier plot - Safety Analysis Set
CTCAE grade 3 or higher AESI of adjudicated drug-related ILD/pneumonitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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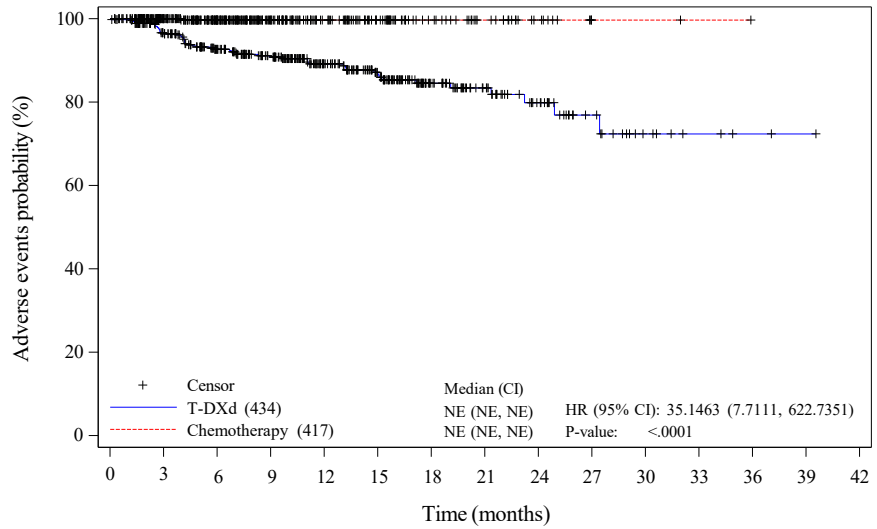
Figure 2.19.1 Adverse Events of Special Interest - Kaplan-Meier plot - Safety Analysis Set
AESI of ILD/pneumonitis



Patients still at risk:

T-DXd(434)	434	385	320	268	194	146	84	57	35	18	8	4	2	1	0
Chemotherapy (417)	417	319	229	144	94	63	36	23	11	2	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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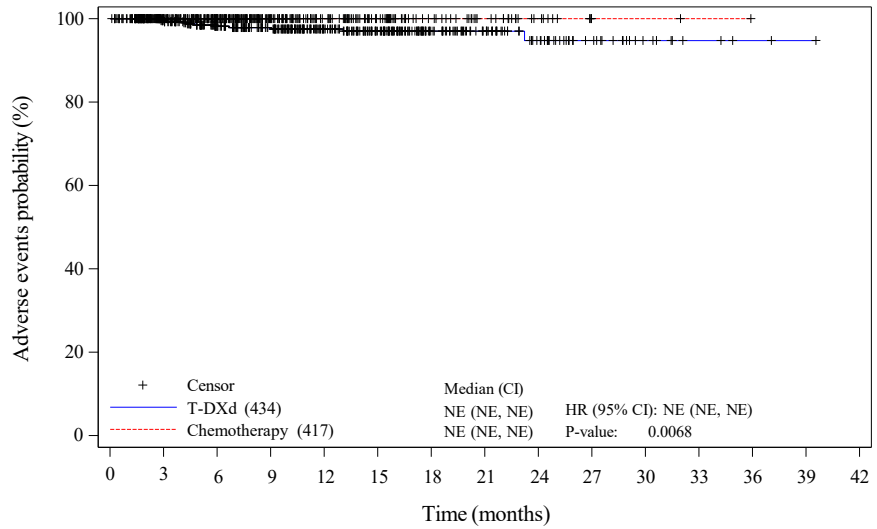
Figure 2.19.1 Adverse Events of Special Interest - Kaplan-Meier plot - Safety Analysis Set
Serious AESI of ILD/pneumonitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

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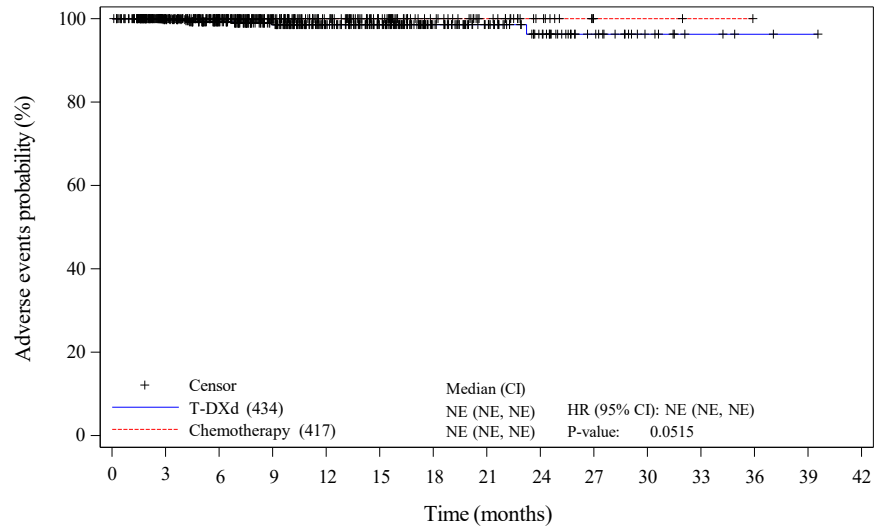
Figure 2.19.1 Adverse Events of Special Interest - Kaplan-Meier plot - Safety Analysis Set
CTCAE grade 3 or higher AESI of ILD/pneumonitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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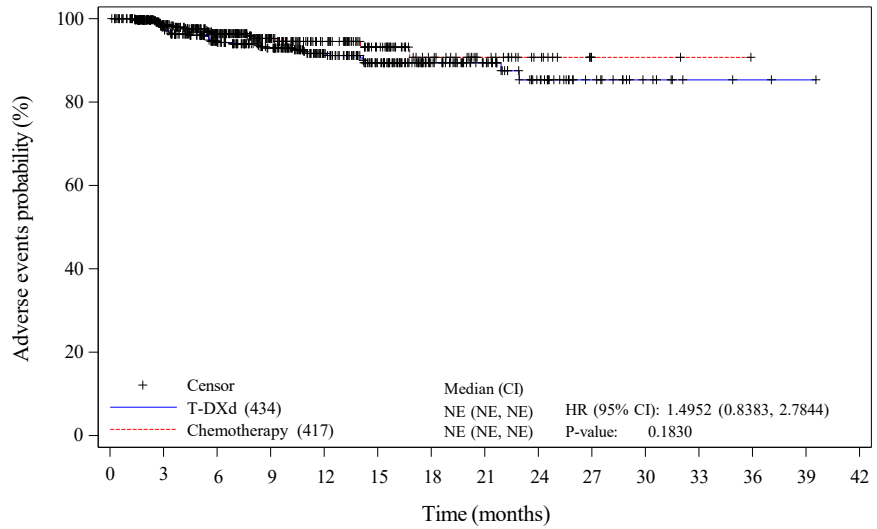
Figure 2.19.1 Adverse Events of Special Interest - Kaplan-Meier plot - Safety Analysis Set
AESI of LVEF decrease



Patients still at risk:

T-DXd(434)	434	388	317	261	187	138	83	57	33	17	8	3	2	1	0
Chemotherapy (417)	417	316	222	139	91	59	33	21	11	2	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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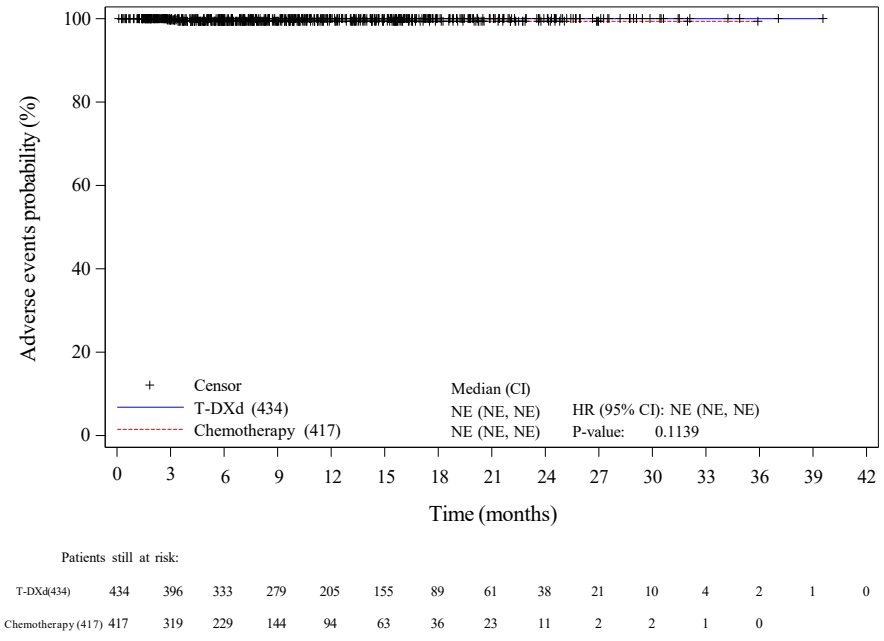
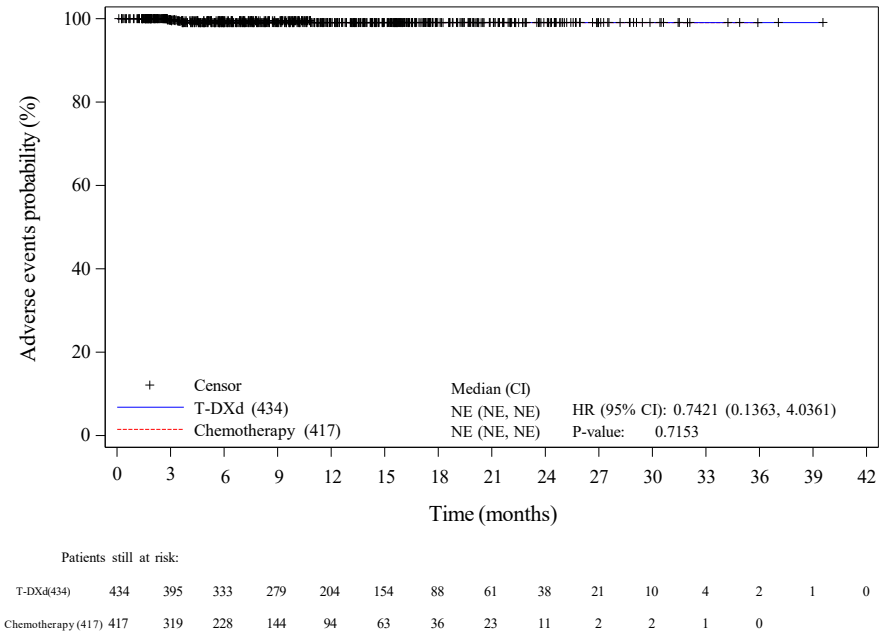
Figure 2.19.1 Adverse Events of Special Interest - Kaplan-Meier plot - Safety Analysis Set
Serious AESI of LVEF decrease



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C0 0001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 13DEC2024 11:54; Program name: F.2.19.1_ADJILD_SAF.sas; Output name: F.2.19.1_ADJILD_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.19.1 Adverse Events of Special Interest - Kaplan-Meier plot - Safety Analysis Set
CTCAE grade 3 or higher AESI of LVEF decrease



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. Inclusion of stratification factors is following the pooling strategy described in study SAP.
CI: Confidence interval; NE: Not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C0 0001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 13DEC2024 11:54; Program name: F.2.19.1_ADJILD_SAF.sas; Output name: F.2.19.1_ADJILD_SAF.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.19.2 Unerwünschte Ereignisse von besonderem Interesse – Kaplan-Meier-Plot – Analyse nach Subgruppe – SAF

Daiichi Sankyo Europe GmbH
Data Intelligence - Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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Final
Statistical analyses for AMNOG (HTA Germany)

Figure 2.19.2 Adverse Events of Special Interest - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set

No output displayed as p-value >= 0.05 for all subgroups.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 19AUG2024 9:57; Program name: F.2.19.2_ADJILD_SAF_SUB.sas; Output name: F.2.19.2_ADJILD_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Anhang 4-G 4.3 Unerwünschte Ereignisse nach SOC und PT

Tabelle 2.28.1 Unerwünschte Ereignisse nach SOC und PT mit Inzidenz ≥10 % in mindestens einem Arm – SAF

Table 2.28.1 Adverse events by SOC and PT with incidence ≥ 10% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders						
All (any PT)	376 (86.6)	0.1 [0.1; 0.1]	256 (61.4)	2.0 [1.2; 3.0]	2.2866 [1.9491; 2.6871] <.0001	<.0001
PT: Nausea	303 (69.8)	0.2 [0.1; 0.3]	126 (30.2)	NE [NE; NE]	3.4031 [2.7691; 4.2077] <.0001	<.0001
PT: Diarrhoea	148 (34.1)	NE [22.5; NE]	114 (27.3)	NE [21.0; NE]	1.0380 [0.8117; 1.3309] 0.7669	0.7669
PT: Vomiting	146 (33.6)	NE [NE; NE]	49 (11.8)	NE [NE; NE]	3.0522 [2.2247; 4.2605] <.0001	<.0001
PT: Constipation	137 (31.6)	NE [NE; NE]	62 (14.9)	NE [NE; NE]	2.0786 [1.5464; 2.8270] <.0001	<.0001
PT: Stomatitis	57 (13.1)	NE [NE; NE]	37 (8.9)	NE [NE; NE]	1.2099 [0.7998; 1.8514] 0.3719	0.3691

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model (unstratified). Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.28.1 Adverse events by SOC and PT with incidence ≥ 10% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Dyspepsia	50 (11.5)	NE [NE; NE]	20 (4.8)	NE [NE; NE]	2.0828 [1.2576; 3.5877] 0.0058	0.0048
PT: Abdominal pain	45 (10.4)	NE [NE; NE]	35 (8.4)	NE [NE; NE]	1.0878 [0.6997; 1.7060] 0.7102	0.7097
SOC: Investigations						
All (any PT)	281 (64.7)	4.2 [2.8; 5.5]	151 (36.2)	23.3 [13.1; 26.2]	1.8584 [1.5272; 2.2705] <.0001	<.0001
PT: Aspartate aminotransferase increased	117 (27.0)	NE [27.7; NE]	44 (10.6)	NE [NE; NE]	2.3750 [1.6908; 3.3967] <.0001	<.0001
PT: Neutrophil count decreased	99 (22.8)	NE [NE; NE]	66 (15.8)	NE [NE; NE]	1.2938 [0.9480; 1.7768] 0.1073	0.1091
PT: Alanine aminotransferase increased	93 (21.4)	NE [NE; NE]	48 (11.5)	NE [NE; NE]	1.7704 [1.2555; 2.5290] 0.0013	0.0012
PT: White blood cell count decreased	79 (18.2)	NE [NE; NE]	53 (12.7)	NE [NE; NE]	1.3086 [0.9261; 1.8639] 0.1307	0.1303

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model (unstratified). Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.28.1 Adverse events by SOC and PT with incidence ≥ 10% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Platelet count decreased	61 (14.1)	NE [NE; NE]	15 (3.6)	NE [26.2; NE]	3.4582 [2.0160; 6.3255] <.0001	<.0001
PT: Blood alkaline phosphatase increased	48 (11.1)	NE [NE; NE]	17 (4.1)	NE [NE; NE]	2.0811 [1.2165; 3.7359] 0.0099	0.0085
SOC: General disorders and administration site conditions						
All (any PT)	275 (63.4)	3.5 [2.1; 4.7]	230 (55.2)	4.5 [3.2; 6.0]	1.1547 [0.9690; 1.3784] 0.1093	0.1231
PT: Fatigue	117 (27.0)	NE [NE; NE]	83 (19.9)	NE [NE; NE]	1.3263 [1.0021; 1.7633] 0.0497	0.0511
PT: Asthenia	99 (22.8)	NE [NE; NE]	71 (17.0)	NE [NE; NE]	1.2483 [0.9209; 1.7005] 0.1556	0.1588
PT: Pyrexia	52 (12.0)	NE [NE; NE]	30 (7.2)	NE [NE; NE]	1.2272 [0.7840; 1.9546] 0.3777	0.3768
PT: Oedema peripheral	36 (8.3)	NE [NE; NE]	59 (14.1)	NE [NE; NE]	0.4446 [0.2902; 0.6720] 0.0001	0.0001

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model (unstratified). Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.28.1 Adverse events by SOC and PT with incidence ≥ 10% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders						
All (any PT)	250 (57.6)	3.3 [2.1; 5.5]	278 (66.7)	1.9 [1.4; 2.3]	0.7071 [0.5949; 0.8400] 0.0001	0.0001
PT: Alopecia	210 (48.4)	9.7 [3.7; NE]	87 (20.9)	NE [NE; NE]	2.5250 [1.9752; 3.2593] <.0001	<.0001
PT: Palmar-plantar erythrodysaesthesia syndrome	4 (0.9)	NE [NE; NE]	146 (35.0)	NE [12.5; NE]	0.0174 [0.0053; 0.0413] <.0001	<.0001
SOC: Infections and infestations						
All (any PT)	233 (53.7)	10.1 [7.7; 12.0]	161 (38.6)	11.5 [8.1; 13.7]	1.0949 [0.8954; 1.3421] 0.3795	0.3793
PT: COVID-19	106 (24.4)	NE [20.0; NE]	52 (12.5)	NE [NE; NE]	1.4053 [1.0112; 1.9773] 0.0462	0.0454

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model (unstratified). Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.28.1 Adverse events by SOC and PT with incidence ≥ 10% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders						
All (any PT)	209 (48.2)	12.4 [9.9; 15.3]	106 (25.4)	NE [20.4; NE]	1.5584 [1.2357; 1.9771] 0.0002	0.0002
PT: Cough	69 (15.9)	NE [NE; NE]	38 (9.1)	NE [NE; NE]	1.3504 [0.9118; 2.0301] 0.1400	0.1387
PT: Epistaxis	44 (10.1)	NE [NE; NE]	15 (3.6)	NE [NE; NE]	2.0866 [1.1834; 3.8903] 0.0146	0.0126
SOC: Blood and lymphatic system disorders						
All (any PT)	203 (46.8)	14.3 [8.5; NE]	152 (36.5)	NE [NE; NE]	1.1722 [0.9501; 1.4492] 0.1399	0.1445
PT: Anaemia	159 (36.6)	NE [21.5; NE]	107 (25.7)	NE [NE; NE]	1.2861 [1.0070; 1.6489] 0.0452	0.0465
PT: Neutropenia	76 (17.5)	NE [NE; NE]	63 (15.1)	NE [NE; NE]	1.0306 [0.7378; 1.4446] 0.8602	0.8590

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model (unstratified). Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.28.1 Adverse events by SOC and PT with incidence ≥ 10% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders						
All (any PT)	197 (45.4)	14.6 [11.1; NE]	107 (25.7)	NE [NE; NE]	1.7241 [1.3645; 2.1906] <.0001	<.0001
PT: Decreased appetite	114 (26.3)	NE [NE; NE]	48 (11.5)	NE [NE; NE]	2.2716 [1.6320; 3.2140] <.0001	<.0001
PT: Hypokalaemia	56 (12.9)	NE [NE; NE]	15 (3.6)	NE [NE; NE]	2.8471 [1.6479; 5.2339] 0.0003	0.0002
SOC: Nervous system disorders						
All (any PT)	169 (38.9)	NE [14.9; NE]	188 (45.1)	8.5 [5.9; 11.9]	0.7134 [0.5778; 0.8799] 0.0016	0.0015
PT: Headache	74 (17.1)	NE [NE; NE]	42 (10.1)	NE [NE; NE]	1.5429 [1.0597; 2.2757] 0.0257	0.0251
PT: Dysgeusia	51 (11.8)	NE [NE; NE]	24 (5.8)	NE [NE; NE]	1.7927 [1.1145; 2.9668] 0.0188	0.0172
PT: Peripheral sensory neuropathy	12 (2.8)	NE [NE; NE]	49 (11.8)	NE [NE; NE]	0.1949 [0.0987; 0.3548] <.0001	<.0001

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model (unstratified). Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.28.1 Adverse events by SOC and PT with incidence ≥ 10% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Musculoskeletal and connective tissue disorders						
All (any PT)	129 (29.7)	NE [19.3; NE]	133 (31.9)	26.5 [14.3; NE]	0.6953 [0.5435; 0.8892] 0.0038	0.0037
PT: Arthralgia	32 (7.4)	NE [NE; NE]	45 (10.8)	NE [NE; NE]	0.4925 [0.3090; 0.7761] 0.0025	0.0020
SOC: Eye disorders						
All (any PT)	89 (20.5)	NE [NE; NE]	58 (13.9)	NE [NE; NE]	1.1553 [0.8297; 1.6208] 0.3970	0.3972
SOC: Vascular disorders						
All (any PT)	60 (13.8)	NE [NE; NE]	52 (12.5)	NE [NE; NE]	0.9233 [0.6357; 1.3459] 0.6757	0.6767

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model (unstratified). Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.28.1 Adverse events by SOC and PT with incidence ≥ 10% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Psychiatric disorders						
All (any PT)	53 (12.2)	NE [31.3; NE]	32 (7.7)	NE [NE; NE]	1.2846 [0.8307; 2.0179] 0.2667	0.2651
SOC: Injury, poisoning and procedural complications						
All (any PT)	45 (10.4)	NE [NE; NE]	38 (9.1)	NE [NE; NE]	0.8461 [0.5471; 1.3151] 0.4535	0.4535

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model (unstratified). Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Tabelle 2.28.2 Unerwünschte Ereignisse nach SOC und PT mit Inzidenz ≥10 % in mindestens einem Arm – Subgruppenanalyse – SAF

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: All (any PT)						
Age at randomization						0.0174
<65 years of age	269 / 301 (89.4)	0.1 [0.1; 0.1]	174 / 285 (61.1)	2.1 [1.2; 3.3]	2.5850 [2.1324; 3.1424] <.0001	
>=65 years of age	107 / 133 (80.5)	0.2 [0.1; 0.4]	82 / 132 (62.1)	1.2 [0.7; 4.3]	1.7520 [1.3144; 2.3438] 0.0001	
Race						0.1319
Asian	134 / 153 (87.6)	0.1 [0.1; 0.2]	82 / 147 (55.8)	4.8 [2.0; 7.3]	3.0634 [2.3226; 4.0641] <.0001	
White	198 / 231 (85.7)	0.1 [0.1; 0.2]	142 / 223 (63.7)	1.3 [0.7; 2.7]	1.9805 [1.5956; 2.4646] <.0001	
Other	44 / 50 (88.0)	0.1 [0.1; 0.2]	32 / 47 (68.1)	0.7 [0.3; 3.0]	1.9684 [1.2481; 3.1382] 0.0040	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2577
Asia	128 / 148 (86.5)	0.1 [0.1; 0.2]	81 / 144 (56.3)	3.4 [1.4; 6.2]	2.8804 [2.1781; 3.8339] <.0001	
Europe	194 / 227 (85.5)	0.1 [0.1; 0.1]	131 / 206 (63.6)	1.2 [0.6; 2.7]	1.9596 [1.5697; 2.4539] <.0001	
Rest of the World	54 / 59 (91.5)	0.1 [0.1; 0.2]	44 / 67 (65.7)	1.6 [0.7; 4.6]	2.4843 [1.6553; 3.7527] <.0001	
HER2 IHC expression						0.8672
IHC 1+	198 / 239 (82.8)	0.1 [0.1; 0.2]	132 / 226 (58.4)	2.7 [1.2; 5.6]	2.1996 [1.7634; 2.7526] <.0001	
IHC 2+/ISH-	106 / 116 (91.4)	0.1 [0.1; 0.1]	77 / 115 (67.0)	1.3 [0.5; 3.3]	2.4897 [1.8530; 3.3615] <.0001	
IHC >0 <1+	69 / 76 (90.8)	0.1 [0.1; 0.2]	46 / 74 (62.2)	1.1 [0.5; 5.6]	2.3051 [1.5855; 3.3822] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8750
Yes	342 / 393 (87.0)	0.1 [0.1; 0.1]	234 / 377 (62.1)	1.4 [1.0; 2.8]	2.2681 [1.9187; 2.6860] <.0001	
No	34 / 41 (82.9)	0.2 [0.1; 1.0]	22 / 40 (55.0)	6.2 [2.1; NE]	2.5757 [1.5083; 4.4901] 0.0005	
Prior Taxane Use In The Non-Metastatic Setting						0.5347
Yes	152 / 177 (85.9)	0.1 [0.1; 0.2]	102 / 172 (59.3)	2.7 [1.3; 5.6]	2.4353 [1.8928; 3.1468] <.0001	
No	224 / 257 (87.2)	0.1 [0.1; 0.1]	154 / 245 (62.9)	1.3 [0.7; 2.8]	2.1819 [1.7755; 2.6883] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1118
1	59 / 65 (90.8)	0.1 [0.1; 0.2]	48 / 79 (60.8)	2.7 [1.1; 6.2]	3.1756 [2.1419; 4.7305] <.0001	
2	254 / 293 (86.7)	0.1 [0.1; 0.1]	169 / 281 (60.1)	2.1 [1.1; 3.3]	2.2502 [1.8513; 2.7421] <.0001	
>=3	62 / 75 (82.7)	0.2 [0.1; 0.2]	39 / 56 (69.6)	0.7 [0.3; 5.1]	1.6871 [1.1312; 2.5458] 0.0114	
ER/PR status I						0.8185
ER+, PR+	213 / 252 (84.5)	0.1 [0.1; 0.2]	136 / 234 (58.1)	2.8 [1.2; 4.8]	2.2315 [1.7985; 2.7781] <.0001	
ER+, PR-	148 / 166 (89.2)	0.1 [0.1; 0.2]	113 / 171 (66.1)	1.4 [0.6; 2.5]	2.3293 [1.8203; 2.9894] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4065
ER <=10%	17 / 21 (81.0)	0.1 [0.1; 2.1]	9 / 14 (64.3)	1.1 [0.2; NE]	1.9131 [0.8651; 4.5236] 0.1379	
ER >10%	314 / 362 (86.7)	0.1 [0.1; 0.2]	201 / 343 (58.6)	2.7 [1.4; 4.7]	2.4392 [2.0419; 2.9207] <.0001	
Positive	45 / 51 (88.2)	0.1 [0.1; 0.1]	46 / 60 (76.7)	0.4 [0.2; 1.1]	1.8446 [1.2109; 2.8086] 0.0051	
Endocrine Resistance						0.5601
Primary	109 / 127 (85.8)	0.1 [0.1; 0.1]	83 / 137 (60.6)	2.1 [0.8; 5.2]	2.3929 [1.7943; 3.2039] <.0001	
Secondary	267 / 307 (87.0)	0.1 [0.1; 0.2]	172 / 279 (61.6)	2.0 [1.1; 3.3]	2.2490 [1.8556; 2.7331] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0781
Capecitabine	239 / 265 (90.2)	0.1 [0.1; 0.1]	174 / 249 (69.9)	1.1 [0.7; 1.4]	2.0672 [1.6981; 2.5215] <.0001	
Nab-Paclitaxel	78 / 103 (75.7)	0.2 [0.1; 0.9]	47 / 101 (46.5)	8.9 [5.1; NE]	2.4741 [1.7263; 3.5841] <.0001	
Paclitaxel	59 / 66 (89.4)	0.1 [0.1; 0.1]	35 / 67 (52.2)	3.9 [0.6; NE]	3.2987 [2.1635; 5.1019] <.0001	
Prior anthracycline use						0.8418
Yes	172 / 197 (87.3)	0.1 [0.1; 0.2]	120 / 198 (60.6)	2.5 [1.2; 5.2]	2.3562 [1.8638; 2.9886] <.0001	
No	204 / 237 (86.1)	0.1 [0.1; 0.1]	136 / 219 (62.1)	1.3 [0.7; 2.9]	2.2264 [1.7906; 2.7771] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5625
Yes	256 / 294 (87.1)	0.1 [0.1; 0.1]	165 / 275 (60.0)	2.1 [1.2; 3.4]	2.3398 [1.9227; 2.8555] <.0001	
No	120 / 140 (85.7)	0.1 [0.1; 0.2]	91 / 142 (64.1)	1.6 [1.0; 4.6]	2.1799 [1.6570; 2.8778] <.0001	
ECOG						0.0592
0	221 / 251 (88.0)	0.1 [0.1; 0.1]	148 / 246 (60.2)	2.5 [1.4; 4.3]	2.6064 [2.1143; 3.2236] <.0001	
>=1	150 / 178 (84.3)	0.2 [0.1; 0.2]	102 / 163 (62.6)	1.0 [0.6; 3.0]	1.9106 [1.4852; 2.4677] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Nausea						
Age at randomization						0.5410
<65 years of age	222 / 301 (73.8)	0.1 [0.1; 0.2]	91 / 285 (31.9)	NE [NE; NE]	3.5210 [2.7641; 4.5230] <.0001	
>=65 years of age	81 / 133 (60.9)	1.4 [0.3; 3.9]	35 / 132 (26.5)	NE [NE; NE]	3.1603 [2.1427; 4.7598] <.0001	
Race						0.1072
Asian	101 / 153 (66.0)	0.3 [0.1; 0.8]	30 / 147 (20.4)	NE [NE; NE]	4.8575 [3.2666; 7.4412] <.0001	
White	166 / 231 (71.9)	0.2 [0.1; 0.3]	77 / 223 (34.5)	NE [NE; NE]	2.9994 [2.2951; 3.9547] <.0001	
Other	36 / 50 (72.0)	0.1 [0.1; 0.8]	19 / 47 (40.4)	NE [2.8; NE]	2.6727 [1.5454; 4.7707] 0.0004	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.3086
Asia	95 / 148 (64.2)	0.3 [0.2; 1.6]	31 / 144 (21.5)	NE [NE; NE]	4.3651 [2.9395; 6.6636] <.0001	
Europe	161 / 227 (70.9)	0.2 [0.1; 0.3]	71 / 206 (34.5)	NE [NE; NE]	2.9369 [2.2289; 3.9099] <.0001	
Rest of the World	47 / 59 (79.7)	0.2 [0.1; 0.2]	24 / 67 (35.8)	NE [4.7; NE]	3.7798 [2.3176; 6.3241] <.0001	
HER2 IHC expression						0.8505
IHC 1+	158 / 239 (66.1)	0.3 [0.2; 1.4]	64 / 226 (28.3)	NE [NE; NE]	3.2610 [2.4493; 4.3959] <.0001	
IHC 2+/ISH-	87 / 116 (75.0)	0.1 [0.1; 0.3]	40 / 115 (34.8)	NE [9.4; NE]	3.3852 [2.3385; 4.9848] <.0001	
IHC >0 <1+	55 / 76 (72.4)	0.2 [0.1; 0.3]	21 / 74 (28.4)	NE [11.8; NE]	4.0040 [2.4516; 6.7899] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1082
Yes	280 / 393 (71.2)	0.2 [0.1; 0.2]	122 / 377 (32.4)	NE [NE; NE]	3.2810 [2.6561; 4.0770] <.0001	
No	23 / 41 (56.1)	2.4 [0.3; NE]	4 / 40 (10.0)	NE [NE; NE]	7.6411 [2.9305; 26.1174] <.0001	
Prior Taxane Use In The Non-Metastatic Setting						0.2924
Yes	118 / 177 (66.7)	0.3 [0.1; 0.9]	42 / 172 (24.4)	NE [NE; NE]	3.8432 [2.7205; 5.5359] <.0001	
No	185 / 257 (72.0)	0.2 [0.1; 0.3]	84 / 245 (34.3)	NE [NE; NE]	3.1829 [2.4647; 4.1445] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0216
1	53 / 65 (81.5)	0.1 [0.1; 0.2]	22 / 79 (27.8)	NE [NE; NE]	5.6259 [3.4349; 9.5236] <.0001	
2	203 / 293 (69.3)	0.2 [0.1; 0.3]	82 / 281 (29.2)	NE [NE; NE]	3.4011 [2.6397; 4.4246] <.0001	
>=3	46 / 75 (61.3)	0.8 [0.2; 3.9]	22 / 56 (39.3)	14.0 [1.8; NE]	1.9980 [1.2160; 3.3853] 0.0067	
ER/PR status I						0.6188
ER+, PR+	172 / 252 (68.3)	0.2 [0.1; 0.3]	71 / 234 (30.3)	NE [NE; NE]	3.2859 [2.5006; 4.3650] <.0001	
ER+, PR-	118 / 166 (71.1)	0.2 [0.1; 0.8]	50 / 171 (29.2)	NE [NE; NE]	3.6178 [2.6112; 5.0862] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5797
ER <=10%	12 / 21 (57.1)	1.0 [0.1; NE]	5 / 14 (35.7)	NE [0.3; NE]	1.9171 [0.7093; 6.0405] 0.2280	
ER >10%	250 / 362 (69.1)	0.2 [0.2; 0.3]	96 / 343 (28.0)	NE [NE; NE]	3.6070 [2.8587; 4.5914] <.0001	
Positive	41 / 51 (80.4)	0.1 [0.1; 0.1]	25 / 60 (41.7)	NE [3.9; NE]	3.5019 [2.1216; 5.8935] <.0001	
Endocrine Resistance						0.7965
Primary	91 / 127 (71.7)	0.1 [0.1; 0.2]	44 / 137 (32.1)	NE [11.8; NE]	3.4272 [2.3985; 4.9713] <.0001	
Secondary	212 / 307 (69.1)	0.2 [0.2; 0.6]	82 / 279 (29.4)	NE [NE; NE]	3.4070 [2.6500; 4.4261] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.1894
Capecitabine	192 / 265 (72.5)	0.2 [0.1; 0.3]	87 / 249 (34.9)	NE [NE; NE]	2.9938 [2.3292; 3.8793] <.0001	
Nab-Paclitaxel	60 / 103 (58.3)	1.0 [0.1; NE]	19 / 101 (18.8)	NE [NE; NE]	4.2849 [2.6008; 7.3897] <.0001	
Paclitaxel	51 / 66 (77.3)	0.1 [0.1; 0.3]	20 / 67 (29.9)	NE [6.7; NE]	4.5514 [2.7409; 7.8546] <.0001	
Prior anthracycline use						0.8221
Yes	134 / 197 (68.0)	0.3 [0.2; 0.8]	54 / 198 (27.3)	NE [NE; NE]	3.4787 [2.5486; 4.8169] <.0001	
No	169 / 237 (71.3)	0.1 [0.1; 0.2]	72 / 219 (32.9)	NE [NE; NE]	3.3472 [2.5474; 4.4434] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.8342
Yes	208 / 294 (70.7)	0.2 [0.1; 0.3]	84 / 275 (30.5)	NE [NE; NE]	3.4212 [2.6631; 4.4367] <.0001	
No	95 / 140 (67.9)	0.2 [0.1; 0.8]	42 / 142 (29.6)	NE [NE; NE]	3.3501 [2.3419; 4.8739] <.0001	
ECOG						0.9725
0	176 / 251 (70.1)	0.2 [0.1; 0.3]	76 / 246 (30.9)	NE [NE; NE]	3.4797 [2.6658; 4.5854] <.0001	
>=1	124 / 178 (69.7)	0.2 [0.1; 0.6]	46 / 163 (28.2)	NE [NE; NE]	3.4726 [2.4907; 4.9266] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Vomiting						
Age at randomization						0.2248
<65 years of age	114 / 301 (37.9)	NE [NE; NE]	34 / 285 (11.9)	NE [NE; NE]	3.4286 [2.3636; 5.1063] <.0001	
>=65 years of age	32 / 133 (24.1)	NE [NE; NE]	15 / 132 (11.4)	NE [23.6; NE]	2.1593 [1.1886; 4.1062] 0.0119	
Race						0.0922
Asian	51 / 153 (33.3)	NE [NE; NE]	10 / 147 (6.8)	NE [23.6; NE]	5.4884 [2.9110; 11.4833] <.0001	
White	80 / 231 (34.6)	NE [NE; NE]	33 / 223 (14.8)	NE [NE; NE]	2.4176 [1.6264; 3.6764] <.0001	
Other	15 / 50 (30.0)	NE [NE; NE]	6 / 47 (12.8)	NE [NE; NE]	2.4374 [0.9886; 6.8448] 0.0588	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0439
Asia	48 / 148 (32.4)	NE [NE; NE]	8 / 144 (5.6)	NE [23.6; NE]	6.4820 [3.2460; 14.8275] <.0001	
Europe	73 / 227 (32.2)	NE [NE; NE]	29 / 206 (14.1)	NE [NE; NE]	2.3914 [1.5725; 3.7349] <.0001	
Rest of the World	25 / 59 (42.4)	18.6 [6.2; NE]	12 / 67 (17.9)	NE [NE; NE]	2.3710 [1.2113; 4.9047] 0.0119	
HER2 IHC expression						0.8741
IHC 1+	74 / 239 (31.0)	NE [NE; NE]	24 / 226 (10.6)	NE [23.6; NE]	3.1518 [2.0191; 5.1006] <.0001	
IHC 2+/ISH-	45 / 116 (38.8)	NE [14.9; NE]	17 / 115 (14.8)	NE [NE; NE]	2.7182 [1.5843; 4.8876] 0.0003	
IHC >0 <1+	27 / 76 (35.5)	NE [15.2; NE]	8 / 74 (10.8)	NE [NE; NE]	3.4433 [1.6350; 8.1257] 0.0011	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9681
Yes	132 / 393 (33.6)	NE [NE; NE]	44 / 377 (11.7)	NE [NE; NE]	3.0478 [2.1846; 4.3354] <.0001	
No	14 / 41 (34.1)	NE [8.5; NE]	5 / 40 (12.5)	NE [NE; NE]	3.0759 [1.1764; 9.5200] 0.0230	
Prior Taxane Use In The Non-Metastatic Setting						0.4815
Yes	52 / 177 (29.4)	NE [NE; NE]	20 / 172 (11.6)	NE [23.6; NE]	2.6164 [1.5860; 4.4893] 0.0002	
No	94 / 257 (36.6)	NE [NE; NE]	29 / 245 (11.8)	NE [NE; NE]	3.3668 [2.2500; 5.1946] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3608
1	22 / 65 (33.8)	NE [18.6; NE]	9 / 79 (11.4)	NE [NE; NE]	3.3931 [1.6090; 7.7876] 0.0011	
2	101 / 293 (34.5)	NE [NE; NE]	30 / 281 (10.7)	NE [23.6; NE]	3.3721 [2.2726; 5.1561] <.0001	
>=3	23 / 75 (30.7)	NE [NE; NE]	10 / 56 (17.9)	NE [NE; NE]	1.8133 [0.8848; 3.9973] 0.1131	
ER/PR status I						0.2773
ER+, PR+	79 / 252 (31.3)	NE [NE; NE]	20 / 234 (8.5)	NE [23.6; NE]	3.8771 [2.4230; 6.5088] <.0001	
ER+, PR-	61 / 166 (36.7)	NE [NE; NE]	25 / 171 (14.6)	NE [NE; NE]	2.7363 [1.7388; 4.4382] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1741
ER <=10%	8 / 21 (38.1)	NE [0.2; NE]	4 / 14 (28.6)	NE [0.4; NE]	1.4206 [0.4466; 5.3306] 0.5877	
ER >10%	122 / 362 (33.7)	NE [NE; NE]	35 / 343 (10.2)	NE [NE; NE]	3.5610 [2.4732; 5.2628] <.0001	
Positive	16 / 51 (31.4)	NE [7.4; NE]	10 / 60 (16.7)	23.6 [23.6; NE]	1.9391 [0.8910; 4.4308] 0.0948	
Endocrine Resistance						0.9896
Primary	39 / 127 (30.7)	NE [NE; NE]	15 / 137 (10.9)	NE [NE; NE]	3.0871 [1.7365; 5.7843] 0.0001	
Secondary	107 / 307 (34.9)	NE [NE; NE]	34 / 279 (12.2)	NE [23.6; NE]	3.0143 [2.0720; 4.4992] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.1280
Capecitabine	87 / 265 (32.8)	NE [NE; NE]	35 / 249 (14.1)	NE [NE; NE]	2.4343 [1.6592; 3.6503] <.0001	
Nab-Paclitaxel	36 / 103 (35.0)	NE [NE; NE]	7 / 101 (6.9)	NE [NE; NE]	5.7464 [2.7193; 14.1049] <.0001	
Paclitaxel	23 / 66 (34.8)	NE [NE; NE]	7 / 67 (10.4)	NE [NE; NE]	3.5470 [1.6005; 8.9458] 0.0017	
Prior anthracycline use						0.1939
Yes	56 / 197 (28.4)	NE [NE; NE]	24 / 198 (12.1)	NE [23.6; NE]	2.3748 [1.4893; 3.9064] 0.0003	
No	90 / 237 (38.0)	NE [NE; NE]	25 / 219 (11.4)	NE [NE; NE]	3.6884 [2.4066; 5.8668] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5895
Yes	94 / 294 (32.0)	NE [NE; NE]	32 / 275 (11.6)	NE [NE; NE]	2.8530 [1.9312; 4.3275] <.0001	
No	52 / 140 (37.1)	NE [NE; NE]	17 / 142 (12.0)	NE [23.6; NE]	3.4860 [2.0591; 6.2099] <.0001	
ECOG						0.0628
0	88 / 251 (35.1)	NE [NE; NE]	23 / 246 (9.3)	NE [NE; NE]	4.0762 [2.6220; 6.6036] <.0001	
>=1	58 / 178 (32.6)	NE [NE; NE]	25 / 163 (15.3)	23.6 [23.6; NE]	2.2109 [1.3996; 3.5984] 0.0007	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Constipation						
Age at randomization						0.4687
<65 years of age	101 / 301 (33.6)	NE [NE; NE]	41 / 285 (14.4)	NE [NE; NE]	2.2381 [1.5668; 3.2562] <.0001	
>=65 years of age	36 / 133 (27.1)	NE [NE; NE]	21 / 132 (15.9)	NE [NE; NE]	1.7485 [1.0300; 3.0452] 0.0400	
Race						0.3641
Asian	53 / 153 (34.6)	NE [NE; NE]	19 / 147 (12.9)	NE [NE; NE]	2.8565 [1.7222; 4.9484] <.0001	
White	71 / 231 (30.7)	NE [NE; NE]	37 / 223 (16.6)	NE [NE; NE]	1.7707 [1.1966; 2.6641] 0.0045	
Other	13 / 50 (26.0)	NE [23.5; NE]	6 / 47 (12.8)	NE [NE; NE]	1.5118 [0.5712; 4.4210] 0.4177	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7770
Asia	47 / 148 (31.8)	NE [NE; NE]	20 / 144 (13.9)	NE [NE; NE]	2.3718 [1.4271; 4.0939] 0.0009	
Europe	69 / 227 (30.4)	NE [NE; NE]	28 / 206 (13.6)	NE [NE; NE]	2.1125 [1.3754; 3.3367] 0.0007	
Rest of the World	21 / 59 (35.6)	23.5 [9.7; NE]	14 / 67 (20.9)	NE [11.0; NE]	1.6804 [0.8577; 3.3926] 0.1339	
HER2 IHC expression						0.1892
IHC 1+	71 / 239 (29.7)	NE [NE; NE]	29 / 226 (12.8)	NE [NE; NE]	2.2799 [1.4955; 3.5676] 0.0001	
IHC 2+/ISH-	43 / 116 (37.1)	NE [13.9; NE]	16 / 115 (13.9)	NE [NE; NE]	2.6577 [1.5247; 4.8705] 0.0006	
IHC >0 <1+	23 / 76 (30.3)	NE [23.5; NE]	17 / 74 (23.0)	NE [11.9; NE]	1.2678 [0.6792; 2.4132] 0.4618	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5217
Yes	124 / 393 (31.6)	NE [NE; NE]	54 / 377 (14.3)	NE [NE; NE]	2.1616 [1.5784; 3.0021] <.0001	
No	13 / 41 (31.7)	NE [9.6; NE]	8 / 40 (20.0)	NE [NE; NE]	1.5446 [0.6503; 3.9056] 0.3282	
Prior Taxane Use In The Non-Metastatic Setting						0.0236
Yes	55 / 177 (31.1)	NE [NE; NE]	35 / 172 (20.3)	NE [NE; NE]	1.4729 [0.9662; 2.2746] 0.0741	
No	82 / 257 (31.9)	NE [23.5; NE]	27 / 245 (11.0)	NE [NE; NE]	2.8627 [1.8776; 4.5056] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.8411
1	21 / 65 (32.3)	NE [11.1; NE]	14 / 79 (17.7)	NE [NE; NE]	1.8883 [0.9624; 3.8146] 0.0644	
2	93 / 293 (31.7)	NE [NE; NE]	38 / 281 (13.5)	NE [NE; NE]	2.2273 [1.5382; 3.2897] <.0001	
>=3	23 / 75 (30.7)	NE [NE; NE]	10 / 56 (17.9)	NE [NE; NE]	1.7927 [0.8772; 3.9442] 0.1188	
ER/PR status I						0.8982
ER+, PR+	75 / 252 (29.8)	NE [NE; NE]	30 / 234 (12.8)	NE [NE; NE]	2.2338 [1.4775; 3.4647] 0.0001	
ER+, PR-	57 / 166 (34.3)	NE [23.5; NE]	28 / 171 (16.4)	NE [NE; NE]	2.0818 [1.3335; 3.3261] 0.0013	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7183
ER <=10%	4 / 21 (19.0)	NE [13.6; NE]	2 / 14 (14.3)	NE [2.6; NE]	0.8973 [0.1675; 6.6246] 0.9025	
ER >10%	112 / 362 (30.9)	NE [NE; NE]	47 / 343 (13.7)	NE [NE; NE]	2.1765 [1.5577; 3.0922] <.0001	
Positive	21 / 51 (41.2)	NE [0.9; NE]	13 / 60 (21.7)	NE [NE; NE]	2.1728 [1.1000; 4.4576] 0.0253	
Endocrine Resistance						0.9929
Primary	44 / 127 (34.6)	NE [NE; NE]	23 / 137 (16.8)	NE [NE; NE]	2.1439 [1.3063; 3.6137] 0.0026	
Secondary	93 / 307 (30.3)	NE [NE; NE]	39 / 279 (14.0)	NE [NE; NE]	2.0742 [1.4379; 3.0519] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0726
Capecitabine	99 / 265 (37.4)	NE [23.5; NE]	41 / 249 (16.5)	NE [NE; NE]	2.3378 [1.6366; 3.4010] <.0001	
Nab-Paclitaxel	21 / 103 (20.4)	NE [NE; NE]	17 / 101 (16.8)	NE [NE; NE]	1.0999 [0.5797; 2.1181] 0.7693	
Paclitaxel	17 / 66 (25.8)	NE [NE; NE]	4 / 67 (6.0)	NE [NE; NE]	4.1511 [1.5205; 14.5068] 0.0060	
Prior anthracycline use						0.0335
Yes	61 / 197 (31.0)	NE [NE; NE]	38 / 198 (19.2)	NE [NE; NE]	1.5628 [1.0452; 2.3661] 0.0306	
No	76 / 237 (32.1)	NE [23.5; NE]	24 / 219 (11.0)	NE [NE; NE]	2.9155 [1.8707; 4.7130] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.3008
Yes	93 / 294 (31.6)	NE [NE; NE]	45 / 275 (16.4)	NE [NE; NE]	1.8622 [1.3107; 2.6852] 0.0006	
No	44 / 140 (31.4)	NE [NE; NE]	17 / 142 (12.0)	NE [NE; NE]	2.6201 [1.5244; 4.7170] 0.0005	
ECOG						0.1458
0	86 / 251 (34.3)	NE [NE; NE]	34 / 246 (13.8)	NE [NE; NE]	2.5463 [1.7276; 3.8393] <.0001	
>=1	50 / 178 (28.1)	NE [NE; NE]	27 / 163 (16.6)	NE [NE; NE]	1.5278 [0.9615; 2.4802] 0.0766	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Dyspepsia						
Age at randomization						0.4821
<65 years of age	33 / 301 (11.0)	NE [NE; NE]	14 / 285 (4.9)	NE [NE; NE]	1.8383 [0.9989; 3.5650] 0.0549	
>=65 years of age	17 / 133 (12.8)	NE [NE; NE]	6 / 132 (4.5)	NE [20.6; NE]	2.7143 [1.1263; 7.5286] 0.0288	
Race						0.0171
Asian	7 / 153 (4.6)	NE [NE; NE]	9 / 147 (6.1)	NE [NE; NE]	0.6639 [0.2366; 1.7865] 0.4144	
White	41 / 231 (17.7)	NE [NE; NE]	10 / 223 (4.5)	NE [NE; NE]	3.5711 [1.8604; 7.5562] 0.0001	
Other	2 / 50 (4.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	1.2054 [0.1036; 27.2290] 0.8832	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1167
Asia	8 / 148 (5.4)	NE [NE; NE]	8 / 144 (5.6)	NE [NE; NE]	0.8419 [0.3082; 2.2987] 0.7318	
Europe	33 / 227 (14.5)	NE [NE; NE]	9 / 206 (4.4)	NE [NE; NE]	2.8939 [1.4411; 6.4475] 0.0032	
Rest of the World	9 / 59 (15.3)	NE [NE; NE]	3 / 67 (4.5)	NE [20.6; NE]	2.8367 [0.8330; 12.9017] 0.1066	
HER2 IHC expression						0.6552
IHC 1+	24 / 239 (10.0)	NE [NE; NE]	12 / 226 (5.3)	NE [NE; NE]	1.6648 [0.8457; 3.4565] 0.1478	
IHC 2+/ISH-	17 / 116 (14.7)	NE [NE; NE]	5 / 115 (4.3)	NE [NE; NE]	2.7697 [1.0858; 8.4741] 0.0385	
IHC >0 <1+	9 / 76 (11.8)	NE [NE; NE]	3 / 74 (4.1)	NE [NE; NE]	2.6068 [0.7760; 11.7642] 0.1360	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0240
Yes	50 / 393 (12.7)	NE [NE; NE]	18 / 377 (4.8)	NE [NE; NE]	2.3021 [1.3656; 4.0608] 0.0019	
No	0 / 41 (0.0)	NE [NE; NE]	2 / 40 (5.0)	NE [NE; NE]	NE [NE; NE] NE	
Prior Taxane Use In The Non-Metastatic Setting						0.5199
Yes	19 / 177 (10.7)	NE [NE; NE]	6 / 172 (3.5)	NE [NE; NE]	2.5997 [1.0912; 7.1717] 0.0356	
No	31 / 257 (12.1)	NE [NE; NE]	14 / 245 (5.7)	NE [NE; NE]	1.8511 [1.0019; 3.5970] 0.0532	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1131
1	3 / 65 (4.6)	NE [NE; NE]	5 / 79 (6.3)	NE [NE; NE]	0.6190 [0.1264; 2.5365] 0.5090	
2	38 / 293 (13.0)	NE [NE; NE]	14 / 281 (5.0)	NE [NE; NE]	2.2211 [1.2284; 4.2540] 0.0092	
>=3	9 / 75 (12.0)	NE [NE; NE]	1 / 56 (1.8)	NE [NE; NE]	6.3174 [1.1833; 116.5747] 0.0448	
ER/PR status I						0.0632
ER+, PR+	25 / 252 (9.9)	NE [NE; NE]	5 / 234 (2.1)	NE [NE; NE]	3.8379 [1.5918; 11.3968] 0.0032	
ER+, PR-	21 / 166 (12.7)	NE [NE; NE]	14 / 171 (8.2)	NE [NE; NE]	1.3708 [0.6998; 2.7672] 0.3631	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3199
ER <=10%	2 / 21 (9.5)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER >10%	43 / 362 (11.9)	NE [NE; NE]	15 / 343 (4.4)	NE [NE; NE]	2.3204 [1.3153; 4.3266] 0.0041	
Positive	5 / 51 (9.8)	NE [NE; NE]	5 / 60 (8.3)	NE [NE; NE]	1.1042 [0.3064; 3.9774] 0.8759	
Endocrine Resistance						0.8150
Primary	10 / 127 (7.9)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	1.8151 [0.6384; 5.8699] 0.2736	
Secondary	40 / 307 (13.0)	NE [NE; NE]	15 / 279 (5.4)	NE [NE; NE]	2.1282 [1.1993; 3.9834] 0.0110	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.3553
Capecitabine	34 / 265 (12.8)	NE [NE; NE]	10 / 249 (4.0)	NE [NE; NE]	2.8020 [1.4343; 5.9949] 0.0029	
Nab-Paclitaxel	9 / 103 (8.7)	NE [NE; NE]	6 / 101 (5.9)	NE [NE; NE]	1.4492 [0.5224; 4.3241] 0.4798	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	4 / 67 (6.0)	NE [NE; NE]	1.4831 [0.4399; 5.7282] 0.5328	
Prior anthracycline use						0.7124
Yes	24 / 197 (12.2)	NE [NE; NE]	9 / 198 (4.5)	NE [NE; NE]	2.3377 [1.1203; 5.3319] 0.0262	
No	26 / 237 (11.0)	NE [NE; NE]	11 / 219 (5.0)	NE [NE; NE]	1.8925 [0.9571; 4.0049] 0.0727	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5168
Yes	35 / 294 (11.9)	NE [NE; NE]	15 / 275 (5.5)	NE [NE; NE]	1.8250 [1.0126; 3.4541] 0.0494	
No	15 / 140 (10.7)	NE [NE; NE]	5 / 142 (3.5)	NE [NE; NE]	2.8006 [1.0814; 8.6294] 0.0379	
ECOG						0.5221
0	34 / 251 (13.5)	NE [NE; NE]	15 / 246 (6.1)	NE [NE; NE]	1.9705 [1.0917; 3.7327] 0.0264	
>=1	15 / 178 (8.4)	NE [NE; NE]	4 / 163 (2.5)	NE [NE; NE]	2.8861 [1.0385; 10.1764] 0.0504	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: All (any PT)						
Age at randomization						0.1010
<65 years of age	208 / 301 (69.1)	2.8 [2.1; 4.9]	100 / 285 (35.1)	23.5 [16.8; NE]	2.0777 [1.6398; 2.6513] <.0001	
>=65 years of age	73 / 133 (54.9)	7.4 [4.2; 15.0]	51 / 132 (38.6)	23.3 [9.6; NE]	1.4412 [1.0088; 2.0740] 0.0454	
Race						0.0559
Asian	125 / 153 (81.7)	0.7 [0.5; 1.4]	81 / 147 (55.1)	3.7 [1.8; 11.0]	1.7022 [1.2886; 2.2608] 0.0002	
White	130 / 231 (56.3)	6.5 [4.9; 10.4]	65 / 223 (29.1)	23.3 [16.8; NE]	1.9285 [1.4368; 2.6149] <.0001	
Other	26 / 50 (52.0)	9.9 [2.6; NE]	5 / 47 (10.6)	NE [NE; NE]	5.4295 [2.2559; 16.1096] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0895
Asia	121 / 148 (81.8)	0.7 [0.5; 2.1]	81 / 144 (56.3)	3.7 [1.8; 11.0]	1.6627 [1.2563; 2.2120] 0.0004	
Europe	133 / 227 (58.6)	5.5 [4.5; 9.6]	49 / 206 (23.8)	NE [16.8; NE]	2.4889 [1.8064; 3.4863] <.0001	
Rest of the World	27 / 59 (45.8)	12.4 [5.6; NE]	21 / 67 (31.3)	23.3 [9.2; NE]	1.5086 [0.8482; 2.7291] 0.1635	
HER2 IHC expression						0.1823
IHC 1+	157 / 239 (65.7)	3.6 [2.3; 5.5]	92 / 226 (40.7)	13.1 [7.3; NE]	1.6517 [1.2793; 2.1449] 0.0001	
IHC 2+/ISH-	69 / 116 (59.5)	6.4 [2.8; 11.2]	36 / 115 (31.3)	NE [11.3; NE]	1.8244 [1.2263; 2.7609] 0.0033	
IHC >0 <1+	53 / 76 (69.7)	2.8 [0.7; 5.6]	23 / 74 (31.1)	23.3 [16.8; NE]	3.0855 [1.8736; 5.2886] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3095
Yes	252 / 393 (64.1)	4.5 [2.8; 5.5]	130 / 377 (34.5)	23.5 [14.0; NE]	1.9331 [1.5672; 2.3962] <.0001	
No	29 / 41 (70.7)	2.8 [0.8; 12.4]	21 / 40 (52.5)	9.2 [0.6; NE]	1.4790 [0.8403; 2.6556] 0.1724	
Prior Taxane Use In The Non-Metastatic Setting						0.4138
Yes	120 / 177 (67.8)	2.6 [1.3; 4.4]	63 / 172 (36.6)	NE [9.3; NE]	2.0726 [1.5338; 2.8282] <.0001	
No	161 / 257 (62.6)	5.2 [3.5; 6.9]	88 / 245 (35.9)	23.3 [11.3; 23.7]	1.7284 [1.3360; 2.2510] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.9919
1	42 / 65 (64.6)	2.6 [0.8; 5.5]	31 / 79 (39.2)	NE [4.8; NE]	1.8967 [1.1935; 3.0463] 0.0063	
2	185 / 293 (63.1)	4.9 [2.8; 7.4]	98 / 281 (34.9)	23.3 [11.3; 26.2]	1.8376 [1.4416; 2.3572] <.0001	
>=3	53 / 75 (70.7)	3.3 [2.1; 5.7]	22 / 56 (39.3)	23.5 [5.5; NE]	1.9158 [1.1794; 3.2208] 0.0089	
ER/PR status I						0.9314
ER+, PR+	161 / 252 (63.9)	4.8 [2.8; 5.7]	82 / 234 (35.0)	23.3 [23.3; 26.2]	1.8689 [1.4371; 2.4497] <.0001	
ER+, PR-	113 / 166 (68.1)	2.8 [1.4; 4.9]	68 / 171 (39.8)	11.3 [8.3; NE]	1.8190 [1.3465; 2.4749] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2298
ER <=10%	12 / 21 (57.1)	5.5 [0.5; NE]	5 / 14 (35.7)	NE [0.4; NE]	1.4196 [0.5197; 4.5005] 0.5143	
ER >10%	238 / 362 (65.7)	3.7 [2.7; 5.2]	119 / 343 (34.7)	23.3 [14.0; 26.2]	2.0158 [1.6211; 2.5206] <.0001	
Positive	31 / 51 (60.8)	5.1 [2.1; 12.4]	27 / 60 (45.0)	9.3 [2.6; NE]	1.2490 [0.7449; 2.1066] 0.3961	
Endocrine Resistance						0.3134
Primary	81 / 127 (63.8)	2.8 [0.8; 5.7]	55 / 137 (40.1)	NE [5.3; NE]	1.6473 [1.1718; 2.3329] 0.0040	
Secondary	200 / 307 (65.1)	4.8 [2.8; 5.6]	96 / 279 (34.4)	23.3 [13.1; 26.2]	1.9943 [1.5680; 2.5547] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0109
Capecitabine	174 / 265 (65.7)	4.2 [2.7; 5.5]	77 / 249 (30.9)	23.3 [14.0; 26.2]	2.4287 [1.8647; 3.1944] <.0001	
Nab-Paclitaxel	72 / 103 (69.9)	2.6 [0.6; 4.9]	50 / 101 (49.5)	7.7 [0.9; NE]	1.4526 [1.0144; 2.0962] 0.0412	
Paclitaxel	35 / 66 (53.0)	7.6 [5.1; NE]	24 / 67 (35.8)	NE [3.6; NE]	1.0801 [0.6347; 1.8639] 0.7751	
Prior anthracycline use						0.5420
Yes	126 / 197 (64.0)	3.1 [2.0; 5.7]	75 / 198 (37.9)	16.8 [8.3; NE]	1.7676 [1.3313; 2.3632] 0.0001	
No	155 / 237 (65.4)	4.9 [2.8; 5.6]	76 / 219 (34.7)	23.3 [13.1; 26.2]	1.9742 [1.5052; 2.6121] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.1942
Yes	190 / 294 (64.6)	3.7 [2.7; 5.5]	93 / 275 (33.8)	26.2 [11.3; NE]	2.0524 [1.6061; 2.6420] <.0001	
No	91 / 140 (65.0)	4.9 [2.3; 8.3]	58 / 142 (40.8)	23.3 [7.6; 23.7]	1.5562 [1.1216; 2.1761] 0.0078	
ECOG						0.2589
0	161 / 251 (64.1)	3.7 [2.3; 6.9]	84 / 246 (34.1)	23.3 [14.0; 26.2]	2.0302 [1.5634; 2.6557] <.0001	
>=1	116 / 178 (65.2)	4.2 [2.7; 5.5]	65 / 163 (39.9)	NE [5.6; NE]	1.6030 [1.1872; 2.1834] 0.0022	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Age at randomization						0.7703
<65 years of age	90 / 301 (29.9)	NE [27.7; NE]	34 / 285 (11.9)	NE [NE; NE]	2.3101 [1.5695; 3.4798] <.0001	
>=65 years of age	27 / 133 (20.3)	NE [22.6; NE]	10 / 132 (7.6)	NE [NE; NE]	2.5299 [1.2634; 5.4954] 0.0095	
Race						0.0065
Asian	54 / 153 (35.3)	NE [NE; NE]	28 / 147 (19.0)	NE [NE; NE]	1.8618 [1.1897; 2.9791] 0.0068	
White	49 / 231 (21.2)	NE [22.6; NE]	16 / 223 (7.2)	NE [NE; NE]	2.5781 [1.4948; 4.6900] 0.0007	
Other	14 / 50 (28.0)	NE [19.8; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0108
Asia	52 / 148 (35.1)	NE [NE; NE]	27 / 144 (18.8)	NE [NE; NE]	1.8799 [1.1915; 3.0352] 0.0069	
Europe	60 / 227 (26.4)	27.7 [22.6; NE]	11 / 206 (5.3)	NE [NE; NE]	4.3955 [2.4010; 8.8517] <.0001	
Rest of the World	5 / 59 (8.5)	NE [20.5; NE]	6 / 67 (9.0)	NE [NE; NE]	0.8187 [0.2348; 2.7310] 0.7419	
HER2 IHC expression						0.3783
IHC 1+	66 / 239 (27.6)	NE [22.6; NE]	30 / 226 (13.3)	NE [NE; NE]	1.9504 [1.2777; 3.0484] 0.0021	
IHC 2+/ISH-	28 / 116 (24.1)	NE [27.7; NE]	9 / 115 (7.8)	NE [NE; NE]	2.6626 [1.2980; 6.0111] 0.0086	
IHC >0 <1+	21 / 76 (27.6)	NE [NE; NE]	5 / 74 (6.8)	NE [NE; NE]	4.0409 [1.6451; 12.1132] 0.0024	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3876
Yes	105 / 393 (26.7)	NE [27.7; NE]	37 / 377 (9.8)	NE [NE; NE]	2.5040 [1.7361; 3.6926] <.0001	
No	12 / 41 (29.3)	NE [20.5; NE]	7 / 40 (17.5)	NE [NE; NE]	1.6422 [0.6583; 4.4240] 0.2924	
Prior Taxane Use In The Non-Metastatic Setting						0.8526
Yes	58 / 177 (32.8)	NE [19.8; NE]	23 / 172 (13.4)	NE [NE; NE]	2.2891 [1.4301; 3.7890] 0.0006	
No	59 / 257 (23.0)	NE [27.7; NE]	21 / 245 (8.6)	NE [NE; NE]	2.4841 [1.5320; 4.1881] 0.0002	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.7940
1	18 / 65 (27.7)	NE [19.8; NE]	11 / 79 (13.9)	NE [NE; NE]	2.0590 [0.9846; 4.5063] 0.0549	
2	86 / 293 (29.4)	27.7 [22.6; NE]	30 / 281 (10.7)	NE [NE; NE]	2.5147 [1.6774; 3.8757] <.0001	
>=3	12 / 75 (16.0)	NE [NE; NE]	3 / 56 (5.4)	NE [NE; NE]	2.8486 [0.9041; 12.5069] 0.0903	
ER/PR status I						0.2725
ER+, PR+	63 / 252 (25.0)	27.7 [22.6; NE]	26 / 234 (11.1)	NE [NE; NE]	1.9325 [1.2367; 3.1102] 0.0042	
ER+, PR-	53 / 166 (31.9)	NE [NE; NE]	18 / 171 (10.5)	NE [NE; NE]	3.1838 [1.9021; 5.5867] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5522
ER <=10%	5 / 21 (23.8)	NE [NE; NE]	2 / 14 (14.3)	NE [NE; NE]	1.3623 [0.2925; 9.5333] 0.7112	
ER >10%	105 / 362 (29.0)	NE [27.7; NE]	37 / 343 (10.8)	NE [NE; NE]	2.4962 [1.7303; 3.6820] <.0001	
Positive	7 / 51 (13.7)	NE [NE; NE]	5 / 60 (8.3)	NE [NE; NE]	1.6037 [0.5119; 5.4184] 0.4143	
Endocrine Resistance						0.0719
Primary	36 / 127 (28.3)	NE [NE; NE]	22 / 137 (16.1)	NE [NE; NE]	1.7476 [1.0349; 3.0183] 0.0375	
Secondary	81 / 307 (26.4)	NE [27.7; NE]	22 / 279 (7.9)	NE [NE; NE]	3.0648 [1.9469; 5.0335] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.2156
Capecitabine	65 / 265 (24.5)	NE [NE; NE]	18 / 249 (7.2)	NE [NE; NE]	3.2204 [1.9526; 5.5928] <.0001	
Nab-Paclitaxel	36 / 103 (35.0)	NE [12.3; NE]	21 / 101 (20.8)	NE [NE; NE]	1.6477 [0.9688; 2.8739] 0.0667	
Paclitaxel	16 / 66 (24.2)	27.7 [19.8; NE]	5 / 67 (7.5)	NE [NE; NE]	2.3930 [0.9021; 7.4692] 0.0873	
Prior anthracycline use						0.6371
Yes	57 / 197 (28.9)	NE [20.5; NE]	24 / 198 (12.1)	NE [NE; NE]	2.1532 [1.3513; 3.5409] 0.0013	
No	60 / 237 (25.3)	NE [27.7; NE]	20 / 219 (9.1)	NE [NE; NE]	2.6314 [1.6131; 4.4791] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.4636
Yes	82 / 294 (27.9)	NE [27.7; NE]	27 / 275 (9.8)	NE [NE; NE]	2.5545 [1.6730; 4.0251] <.0001	
No	35 / 140 (25.0)	NE [22.6; NE]	17 / 142 (12.0)	NE [NE; NE]	2.0529 [1.1666; 3.7569] 0.0131	
ECOG						0.9663
0	66 / 251 (26.3)	NE [22.6; NE]	26 / 246 (10.6)	NE [NE; NE]	2.3809 [1.5303; 3.8166] 0.0001	
>=1	49 / 178 (27.5)	NE [27.7; NE]	17 / 163 (10.4)	NE [NE; NE]	2.3925 [1.4033; 4.2835] 0.0015	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Alanine aminotransferase increased						
Age at randomization						0.7970
<65 years of age	77 / 301 (25.6)	NE [NE; NE]	40 / 285 (14.0)	NE [NE; NE]	1.7157 [1.1769; 2.5399] 0.0053	
>=65 years of age	16 / 133 (12.0)	NE [NE; NE]	8 / 132 (6.1)	NE [NE; NE]	1.9020 [0.8358; 4.6955] 0.1315	
Race						0.0077
Asian	50 / 153 (32.7)	NE [NE; NE]	34 / 147 (23.1)	NE [NE; NE]	1.3981 [0.9077; 2.1793] 0.1307	
White	33 / 231 (14.3)	NE [NE; NE]	14 / 223 (6.3)	NE [NE; NE]	2.0648 [1.1268; 3.9916] 0.0206	
Other	10 / 50 (20.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1339
Asia	48 / 148 (32.4)	NE [NE; NE]	33 / 144 (22.9)	NE [NE; NE]	1.4047 [0.9051; 2.2065] 0.1316	
Europe	37 / 227 (16.3)	NE [NE; NE]	10 / 206 (4.9)	NE [NE; NE]	3.0431 [1.5690; 6.4816] 0.0011	
Rest of the World	8 / 59 (13.6)	NE [NE; NE]	5 / 67 (7.5)	NE [NE; NE]	1.7171 [0.5725; 5.6854] 0.3389	
HER2 IHC expression						0.1461
IHC 1+	50 / 239 (20.9)	NE [NE; NE]	33 / 226 (14.6)	NE [NE; NE]	1.3879 [0.8978; 2.1741] 0.1434	
IHC 2+/ISH-	24 / 116 (20.7)	NE [NE; NE]	10 / 115 (8.7)	NE [NE; NE]	2.0969 [1.0280; 4.6123] 0.0454	
IHC >0 <1+	19 / 76 (25.0)	NE [NE; NE]	5 / 74 (6.8)	NE [NE; NE]	3.6448 [1.4643; 11.0008] 0.0060	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8523
Yes	83 / 393 (21.1)	NE [NE; NE]	42 / 377 (11.1)	NE [NE; NE]	1.7845 [1.2379; 2.6118] 0.0020	
No	10 / 41 (24.4)	NE [NE; NE]	6 / 40 (15.0)	NE [NE; NE]	1.6258 [0.6032; 4.7818] 0.3415	
Prior Taxane Use In The Non-Metastatic Setting						0.6066
Yes	46 / 177 (26.0)	NE [NE; NE]	26 / 172 (15.1)	NE [NE; NE]	1.5955 [0.9927; 2.6196] 0.0553	
No	47 / 257 (18.3)	NE [NE; NE]	22 / 245 (9.0)	NE [NE; NE]	1.9769 [1.2060; 3.3439] 0.0073	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1204
1	12 / 65 (18.5)	NE [NE; NE]	12 / 79 (15.2)	NE [NE; NE]	1.1868 [0.5255; 2.6792] 0.6771	
2	71 / 293 (24.2)	NE [NE; NE]	29 / 281 (10.3)	NE [NE; NE]	2.2929 [1.5043; 3.5874] 0.0001	
>=3	9 / 75 (12.0)	NE [NE; NE]	7 / 56 (12.5)	NE [NE; NE]	0.8591 [0.3199; 2.4051] 0.7685	
ER/PR status I						0.1715
ER+, PR+	49 / 252 (19.4)	NE [NE; NE]	29 / 234 (12.4)	NE [NE; NE]	1.4250 [0.9053; 2.2837] 0.1311	
ER+, PR-	43 / 166 (25.9)	NE [NE; NE]	19 / 171 (11.1)	NE [NE; NE]	2.3622 [1.3969; 4.1505] 0.0013	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4161
ER <=10%	4 / 21 (19.0)	NE [NE; NE]	2 / 14 (14.3)	NE [5.6; NE]	1.1152 [0.2161; 8.0816] 0.9002	
ER >10%	83 / 362 (22.9)	NE [NE; NE]	39 / 343 (11.4)	NE [NE; NE]	1.9386 [1.3340; 2.8677] 0.0005	
Positive	6 / 51 (11.8)	NE [NE; NE]	7 / 60 (11.7)	NE [NE; NE]	0.9385 [0.3017; 2.8284] 0.9079	
Endocrine Resistance						0.0236
Primary	26 / 127 (20.5)	NE [NE; NE]	24 / 137 (17.5)	NE [NE; NE]	1.0620 [0.6069; 1.8658] 0.8310	
Secondary	67 / 307 (21.8)	NE [NE; NE]	24 / 279 (8.6)	NE [NE; NE]	2.4660 [1.5692; 4.0106] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0899
Capecitabine	54 / 265 (20.4)	NE [NE; NE]	19 / 249 (7.6)	NE [NE; NE]	2.6026 [1.5708; 4.5052] 0.0002	
Nab-Paclitaxel	29 / 103 (28.2)	NE [20.3; NE]	24 / 101 (23.8)	NE [NE; NE]	1.1229 [0.6533; 1.9487] 0.6677	
Paclitaxel	10 / 66 (15.2)	NE [NE; NE]	5 / 67 (7.5)	NE [NE; NE]	1.8347 [0.6457; 5.9258] 0.2603	
Prior anthracycline use						0.4246
Yes	43 / 197 (21.8)	NE [NE; NE]	26 / 198 (13.1)	NE [NE; NE]	1.5140 [0.9351; 2.4992] 0.0940	
No	50 / 237 (21.1)	NE [NE; NE]	22 / 219 (10.0)	NE [NE; NE]	2.0682 [1.2694; 3.4841] 0.0038	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.2475
Yes	65 / 294 (22.1)	NE [NE; NE]	28 / 275 (10.2)	NE [NE; NE]	2.0134 [1.3055; 3.1888] 0.0017	
No	28 / 140 (20.0)	NE [NE; NE]	20 / 142 (14.1)	NE [NE; NE]	1.4029 [0.7943; 2.5239] 0.2444	
ECOG						0.8763
0	57 / 251 (22.7)	NE [NE; NE]	30 / 246 (12.2)	NE [NE; NE]	1.8148 [1.1752; 2.8601] 0.0076	
>=1	36 / 178 (20.2)	NE [NE; NE]	18 / 163 (11.0)	NE [NE; NE]	1.6856 [0.9686; 3.0399] 0.0682	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Platelet count decreased						
Age at randomization						0.8910
<65 years of age	49 / 301 (16.3)	NE [NE; NE]	12 / 285 (4.2)	NE [26.2; NE]	3.3571 [1.8404; 6.6345] 0.0001	
>=65 years of age	12 / 133 (9.0)	NE [NE; NE]	3 / 132 (2.3)	NE [NE; NE]	3.6382 [1.1511; 16.0022] 0.0332	
Race						0.1073
Asian	48 / 153 (31.4)	NE [21.5; NE]	9 / 147 (6.1)	NE [NE; NE]	5.3154 [2.7391; 11.5968] <.0001	
White	11 / 231 (4.8)	NE [NE; NE]	6 / 223 (2.7)	NE [26.2; NE]	1.3218 [0.4957; 3.8798] 0.5875	
Other	2 / 50 (4.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2593
Asia	49 / 148 (33.1)	NE [21.5; NE]	10 / 144 (6.9)	NE [26.2; NE]	4.9596 [2.6224; 10.3968] <.0001	
Europe	10 / 227 (4.4)	NE [NE; NE]	3 / 206 (1.5)	NE [NE; NE]	2.3313 [0.7025; 10.4902] 0.1906	
Rest of the World	2 / 59 (3.4)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	0.6766 [0.0776; 5.8844] 0.7025	
HER2 IHC expression						0.4485
IHC 1+	35 / 239 (14.6)	NE [NE; NE]	7 / 226 (3.1)	NE [NE; NE]	4.2377 [1.9952; 10.4334] 0.0002	
IHC 2+/ISH-	15 / 116 (12.9)	NE [NE; NE]	6 / 115 (5.2)	NE [NE; NE]	2.2024 [0.8878; 6.2102] 0.0982	
IHC >0 <1+	11 / 76 (14.5)	NE [21.5; NE]	2 / 74 (2.7)	26.2 [26.2; NE]	4.9715 [1.3288; 32.2046] 0.0211	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4399
Yes	49 / 393 (12.5)	NE [NE; NE]	13 / 377 (3.4)	NE [26.2; NE]	3.1995 [1.7853; 6.1634] 0.0001	
No	12 / 41 (29.3)	NE [17.1; NE]	2 / 40 (5.0)	NE [NE; NE]	5.4040 [1.4601; 34.8868] 0.0140	
Prior Taxane Use In The Non-Metastatic Setting						0.7807
Yes	34 / 177 (19.2)	NE [NE; NE]	8 / 172 (4.7)	NE [NE; NE]	3.8896 [1.8898; 9.0558] 0.0002	
No	27 / 257 (10.5)	NE [NE; NE]	7 / 245 (2.9)	NE [26.2; NE]	3.0707 [1.4053; 7.6867] 0.0057	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.7748
1	5 / 65 (7.7)	NE [NE; NE]	2 / 79 (2.5)	NE [NE; NE]	3.0490 [0.6571; 21.2839] 0.1613	
2	45 / 293 (15.4)	NE [NE; NE]	10 / 281 (3.6)	NE [26.2; NE]	3.7182 [1.9485; 7.8398] 0.0001	
>=3	10 / 75 (13.3)	NE [NE; NE]	3 / 56 (5.4)	NE [NE; NE]	2.2787 [0.6942; 10.1861] 0.1997	
ER/PR status I						0.5155
ER+, PR+	29 / 252 (11.5)	NE [NE; NE]	8 / 234 (3.4)	NE [26.2; NE]	2.8596 [1.3643; 6.7322] 0.0064	
ER+, PR-	32 / 166 (19.3)	NE [NE; NE]	7 / 171 (4.1)	NE [NE; NE]	4.4786 [2.0923; 11.0752] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4122
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	1 / 14 (7.1)	NE [NE; NE]	0.6325 [0.0250; 15.9887] 0.7439	
ER >10%	53 / 362 (14.6)	NE [NE; NE]	12 / 343 (3.5)	NE [26.2; NE]	3.6591 [2.0193; 7.1999] <.0001	
Positive	7 / 51 (13.7)	NE [NE; NE]	2 / 60 (3.3)	NE [NE; NE]	3.8472 [0.9279; 25.8458] 0.0715	
Endocrine Resistance						0.6349
Primary	18 / 127 (14.2)	NE [NE; NE]	6 / 137 (4.4)	NE [NE; NE]	2.9788 [1.2436; 8.2390] 0.0157	
Secondary	43 / 307 (14.0)	NE [NE; NE]	9 / 279 (3.2)	NE [26.2; NE]	3.8081 [1.9412; 8.3641] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.3743
Capecitabine	27 / 265 (10.2)	NE [NE; NE]	8 / 249 (3.2)	NE [26.2; NE]	2.8255 [1.3396; 6.6756] 0.0076	
Nab-Paclitaxel	30 / 103 (29.1)	NE [17.5; NE]	7 / 101 (6.9)	NE [NE; NE]	4.1784 [1.9402; 10.3686] 0.0002	
Paclitaxel	4 / 66 (6.1)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
Prior anthracycline use						0.9032
Yes	34 / 197 (17.3)	NE [NE; NE]	9 / 198 (4.5)	NE [NE; NE]	3.4807 [1.7376; 7.7434] 0.0004	
No	27 / 237 (11.4)	NE [NE; NE]	6 / 219 (2.7)	NE [26.2; NE]	3.5538 [1.5632; 9.5524] 0.0029	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.2037
Yes	44 / 294 (15.0)	NE [NE; NE]	8 / 275 (2.9)	NE [26.2; NE]	4.7963 [2.3814; 11.0251] <.0001	
No	17 / 140 (12.1)	NE [NE; NE]	7 / 142 (4.9)	NE [NE; NE]	1.9602 [0.8413; 5.0934] 0.1291	
ECOG						0.9435
0	30 / 251 (12.0)	NE [NE; NE]	7 / 246 (2.8)	NE [26.2; NE]	3.7965 [1.7618; 9.4248] 0.0007	
>=1	31 / 178 (17.4)	NE [NE; NE]	7 / 163 (4.3)	NE [NE; NE]	3.4887 [1.6191; 8.6626] 0.0016	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Blood alkaline phosphatase increased						
Age at randomization						0.2958
<65 years of age	33 / 301 (11.0)	NE [NE; NE]	13 / 285 (4.6)	NE [NE; NE]	1.7031 [0.9105; 3.3793] 0.1045	
>=65 years of age	15 / 133 (11.3)	NE [NE; NE]	4 / 132 (3.0)	NE [NE; NE]	3.3494 [1.2129; 11.7659] 0.0228	
Race						0.3611
Asian	20 / 153 (13.1)	NE [NE; NE]	6 / 147 (4.1)	NE [NE; NE]	2.6048 [1.1036; 7.1477] 0.0337	
White	25 / 231 (10.8)	NE [NE; NE]	11 / 223 (4.9)	NE [NE; NE]	1.7052 [0.8560; 3.6261] 0.1384	
Other	3 / 50 (6.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0824
Asia	19 / 148 (12.8)	NE [NE; NE]	6 / 144 (4.2)	NE [NE; NE]	2.5455 [1.0714; 7.0097] 0.0395	
Europe	26 / 227 (11.5)	NE [NE; NE]	6 / 206 (2.9)	NE [NE; NE]	2.8750 [1.2557; 7.7611] 0.0156	
Rest of the World	3 / 59 (5.1)	NE [NE; NE]	5 / 67 (7.5)	NE [NE; NE]	0.5073 [0.1021; 2.1113] 0.3513	
HER2 IHC expression						0.7112
IHC 1+	30 / 239 (12.6)	NE [NE; NE]	10 / 226 (4.4)	NE [NE; NE]	2.3076 [1.1614; 4.9908] 0.0194	
IHC 2+/ISH-	10 / 116 (8.6)	NE [NE; NE]	5 / 115 (4.3)	NE [NE; NE]	1.2422 [0.4343; 4.0387] 0.6957	
IHC >0 <1+	7 / 76 (9.2)	NE [22.0; NE]	2 / 74 (2.7)	NE [NE; NE]	2.9315 [0.7017; 19.7754] 0.1619	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5291
Yes	43 / 393 (10.9)	NE [NE; NE]	14 / 377 (3.7)	NE [NE; NE]	2.2859 [1.2780; 4.3471] 0.0061	
No	5 / 41 (12.2)	NE [NE; NE]	3 / 40 (7.5)	NE [NE; NE]	1.1897 [0.2872; 5.8700] 0.8138	
Prior Taxane Use In The Non-Metastatic Setting						0.2850
Yes	19 / 177 (10.7)	NE [NE; NE]	9 / 172 (5.2)	NE [NE; NE]	1.4444 [0.6635; 3.3839] 0.3677	
No	29 / 257 (11.3)	NE [NE; NE]	8 / 245 (3.3)	NE [NE; NE]	2.7776 [1.3261; 6.5360] 0.0079	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0841
1	7 / 65 (10.8)	NE [NE; NE]	5 / 79 (6.3)	NE [NE; NE]	1.4267 [0.4522; 4.8480] 0.5440	
2	33 / 293 (11.3)	NE [NE; NE]	12 / 281 (4.3)	NE [NE; NE]	1.9132 [1.0105; 3.8752] 0.0521	
>=3	8 / 75 (10.7)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER/PR status I						0.0894
ER+, PR+	31 / 252 (12.3)	NE [NE; NE]	7 / 234 (3.0)	NE [NE; NE]	3.2267 [1.5007; 8.0018] 0.0032	
ER+, PR-	16 / 166 (9.6)	NE [NE; NE]	10 / 171 (5.8)	NE [NE; NE]	1.2141 [0.5489; 2.8072] 0.6368	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4279
ER <=10%	2 / 21 (9.5)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER >10%	41 / 362 (11.3)	NE [NE; NE]	16 / 343 (4.7)	NE [NE; NE]	1.8063 [1.0289; 3.3298] 0.0438	
Positive	5 / 51 (9.8)	NE [NE; NE]	1 / 60 (1.7)	NE [NE; NE]	5.5067 [0.8867; 105.5406] 0.0799	
Endocrine Resistance						0.0156
Primary	14 / 127 (11.0)	NE [25.2; NE]	11 / 137 (8.0)	NE [NE; NE]	0.9850 [0.4363; 2.2627] 0.9700	
Secondary	34 / 307 (11.1)	NE [NE; NE]	6 / 279 (2.2)	NE [NE; NE]	4.0164 [1.8088; 10.6566] 0.0007	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.5134
Capecitabine	30 / 265 (11.3)	NE [NE; NE]	8 / 249 (3.2)	NE [NE; NE]	2.9473 [1.4142; 6.9136] 0.0045	
Nab-Paclitaxel	13 / 103 (12.6)	NE [25.2; NE]	7 / 101 (6.9)	NE [NE; NE]	1.3283 [0.5302; 3.5915] 0.5524	
Paclitaxel	5 / 66 (7.6)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	1.6334 [0.3386; 11.6625] 0.5620	
Prior anthracycline use						0.0120
Yes	20 / 197 (10.2)	NE [NE; NE]	13 / 198 (6.6)	NE [NE; NE]	1.1883 [0.5917; 2.4668] 0.6326	
No	28 / 237 (11.8)	NE [NE; NE]	4 / 219 (1.8)	NE [NE; NE]	4.9691 [1.9413; 16.8222] 0.0009	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5121
Yes	34 / 294 (11.6)	NE [NE; NE]	13 / 275 (4.7)	NE [NE; NE]	1.8348 [0.9867; 3.6261] 0.0612	
No	14 / 140 (10.0)	NE [NE; NE]	4 / 142 (2.8)	NE [NE; NE]	2.7349 [0.9729; 9.6987] 0.0664	
ECOG						0.0836
0	27 / 251 (10.8)	NE [NE; NE]	6 / 246 (2.4)	NE [NE; NE]	3.2190 [1.4148; 8.6580] 0.0065	
>=1	20 / 178 (11.2)	NE [NE; NE]	11 / 163 (6.7)	NE [NE; NE]	1.3789 [0.6694; 2.9925] 0.3928	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)						
Age at randomization						0.0156
<65 years of age	182 / 301 (60.5)	2.2 [1.4; 3.8]	183 / 285 (64.2)	2.1 [1.4; 2.8]	0.8241 [0.6701; 1.0133] 0.0625	
>=65 years of age	68 / 133 (51.1)	6.3 [3.3; NE]	95 / 132 (72.0)	1.4 [1.2; 2.1]	0.4920 [0.3573; 0.6737] <.0001	
Race						0.3231
Asian	86 / 153 (56.2)	2.8 [1.4; 11.0]	100 / 147 (68.0)	1.4 [1.1; 2.5]	0.6902 [0.5157; 0.9219] 0.0113	
White	130 / 231 (56.3)	3.8 [2.2; 8.5]	150 / 223 (67.3)	2.0 [1.5; 2.5]	0.6666 [0.5251; 0.8450] 0.0007	
Other	34 / 50 (68.0)	2.0 [1.4; 6.2]	28 / 47 (59.6)	2.4 [1.1; 7.4]	0.9678 [0.5835; 1.6170] 0.8914	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.6697
Asia	79 / 148 (53.4)	3.4 [1.4; NE]	95 / 144 (66.0)	1.4 [1.1; 2.8]	0.6754 [0.4992; 0.9112] 0.0094	
Europe	133 / 227 (58.6)	3.5 [2.0; 5.9]	138 / 206 (67.0)	2.1 [1.4; 2.7]	0.7043 [0.5531; 0.8965] 0.0040	
Rest of the World	38 / 59 (64.4)	3.0 [0.9; 6.4]	45 / 67 (67.2)	1.8 [1.1; 2.8]	0.8127 [0.5239; 1.2530] 0.3463	
HER2 IHC expression						0.4657
IHC 1+	131 / 239 (54.8)	3.8 [2.1; 9.5]	150 / 226 (66.4)	1.6 [1.3; 2.4]	0.6671 [0.5262; 0.8446] 0.0007	
IHC 2+/ISH-	74 / 116 (63.8)	2.2 [1.4; 4.4]	82 / 115 (71.3)	1.4 [1.1; 2.1]	0.6668 [0.4843; 0.9164] 0.0116	
IHC >0 <1+	43 / 76 (56.6)	3.7 [0.9; NE]	45 / 74 (60.8)	2.8 [1.9; 4.8]	0.8722 [0.5702; 1.3321] 0.5225	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0864
Yes	226 / 393 (57.5)	3.3 [2.2; 5.5]	255 / 377 (67.6)	1.8 [1.4; 2.1]	0.6701 [0.5588; 0.8031] <.0001	
No	24 / 41 (58.5)	3.5 [0.8; NE]	23 / 40 (57.5)	5.6 [1.4; NE]	1.0669 [0.5997; 1.9024] 0.8401	
Prior Taxane Use In The Non-Metastatic Setting						0.9534
Yes	102 / 177 (57.6)	3.3 [1.6; 7.8]	112 / 172 (65.1)	1.8 [1.4; 2.5]	0.7224 [0.5501; 0.9474] 0.0177	
No	148 / 257 (57.6)	3.3 [2.1; 5.9]	166 / 245 (67.8)	2.0 [1.4; 2.7]	0.6995 [0.5592; 0.8742] 0.0015	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4815
1	43 / 65 (66.2)	1.0 [0.8; 2.7]	59 / 79 (74.7)	1.4 [1.1; 2.5]	0.9075 [0.6077; 1.3440] 0.6141	
2	163 / 293 (55.6)	4.3 [2.6; 9.5]	178 / 281 (63.3)	2.0 [1.4; 2.8]	0.6862 [0.5531; 0.8508] 0.0005	
>=3	43 / 75 (57.3)	3.2 [1.6; 7.8]	40 / 56 (71.4)	1.8 [1.0; 2.8]	0.6667 [0.4328; 1.0293] 0.0632	
ER/PR status I						0.4928
ER+, PR+	138 / 252 (54.8)	5.0 [2.7; 9.5]	151 / 234 (64.5)	2.1 [1.4; 2.5]	0.6505 [0.5145; 0.8216] 0.0003	
ER+, PR-	100 / 166 (60.2)	2.4 [1.4; 4.3]	118 / 171 (69.0)	1.4 [1.2; 2.7]	0.7609 [0.5814; 0.9941] 0.0434	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6874
ER <=10%	10 / 21 (47.6)	8.8 [1.0; NE]	7 / 14 (50.0)	4.8 [0.6; NE]	0.7204 [0.2668; 2.0257] 0.5173	
ER >10%	209 / 362 (57.7)	3.4 [2.1; 5.6]	224 / 343 (65.3)	2.1 [1.4; 2.8]	0.7341 [0.6069; 0.8876] 0.0012	
Positive	31 / 51 (60.8)	2.1 [0.8; 8.5]	47 / 60 (78.3)	1.2 [1.0; 1.8]	0.6046 [0.3773; 0.9548] 0.0312	
Endocrine Resistance						0.9158
Primary	69 / 127 (54.3)	2.1 [1.4; NE]	91 / 137 (66.4)	1.8 [1.1; 2.8]	0.7273 [0.5293; 0.9950] 0.0438	
Secondary	181 / 307 (59.0)	3.5 [2.3; 5.5]	187 / 279 (67.0)	1.9 [1.4; 2.4]	0.6977 [0.5674; 0.8575] 0.0006	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.3880
Capecitabine	163 / 265 (61.5)	2.4 [1.4; 4.0]	172 / 249 (69.1)	2.0 [1.4; 2.5]	0.7460 [0.6001; 0.9269] 0.0075	
Nab-Paclitaxel	45 / 103 (43.7)	NE [3.8; NE]	59 / 101 (58.4)	3.2 [1.1; 8.6]	0.6345 [0.4282; 0.9339] 0.0206	
Paclitaxel	42 / 66 (63.6)	2.0 [1.4; 7.7]	47 / 67 (70.1)	1.0 [0.7; 1.9]	0.5699 [0.3688; 0.8757] 0.0097	
Prior anthracycline use						0.3107
Yes	116 / 197 (58.9)	2.6 [1.5; 7.7]	126 / 198 (63.6)	2.0 [1.4; 2.8]	0.7816 [0.6054; 1.0080] 0.0540	
No	134 / 237 (56.5)	3.7 [2.0; 6.3]	152 / 219 (69.4)	1.8 [1.2; 2.4]	0.6489 [0.5128; 0.8201] 0.0003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5976
Yes	170 / 294 (57.8)	3.2 [1.9; 4.4]	185 / 275 (67.3)	1.6 [1.2; 2.1]	0.6883 [0.5575; 0.8492] 0.0004	
No	80 / 140 (57.1)	3.6 [1.7; 11.0]	93 / 142 (65.5)	2.1 [1.4; 3.5]	0.7403 [0.5465; 1.0003] 0.0490	
ECOG						0.4064
0	144 / 251 (57.4)	3.7 [2.1; 6.4]	170 / 246 (69.1)	1.9 [1.4; 2.4]	0.6674 [0.5328; 0.8348] 0.0004	
>=1	103 / 178 (57.9)	2.6 [1.6; 8.5]	102 / 163 (62.6)	1.9 [1.2; 2.9]	0.7798 [0.5917; 1.0278] 0.0719	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia						
Age at randomization						0.4954
<65 years of age	155 / 301 (51.5)	5.5 [2.2; NE]	61 / 285 (21.4)	NE [NE; NE]	2.6537 [1.9841; 3.5948] <.0001	
>=65 years of age	55 / 133 (41.4)	NE [5.5; NE]	26 / 132 (19.7)	NE [NE; NE]	2.2065 [1.3991; 3.5731] 0.0006	
Race						0.4588
Asian	76 / 153 (49.7)	6.4 [2.1; NE]	35 / 147 (23.8)	NE [NE; NE]	2.2059 [1.4905; 3.3314] 0.0001	
White	108 / 231 (46.8)	NE [4.1; NE]	45 / 223 (20.2)	NE [NE; NE]	2.5257 [1.7976; 3.6119] <.0001	
Other	26 / 50 (52.0)	5.5 [1.4; NE]	7 / 47 (14.9)	NE [NE; NE]	4.0004 [1.8292; 10.0150] 0.0005	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0423
Asia	70 / 148 (47.3)	NE [2.3; NE]	33 / 144 (22.9)	NE [NE; NE]	2.1777 [1.4521; 3.3350] 0.0002	
Europe	109 / 227 (48.0)	9.7 [3.5; NE]	47 / 206 (22.8)	NE [NE; NE]	2.2457 [1.6065; 3.1908] <.0001	
Rest of the World	31 / 59 (52.5)	4.4 [1.0; NE]	7 / 67 (10.4)	NE [NE; NE]	6.1432 [2.8631; 15.2121] <.0001	
HER2 IHC expression						0.4306
IHC 1+	104 / 239 (43.5)	NE [5.5; NE]	48 / 226 (21.2)	NE [NE; NE]	2.2038 [1.5755; 3.1288] <.0001	
IHC 2+/ISH-	64 / 116 (55.2)	2.8 [1.5; NE]	26 / 115 (22.6)	NE [NE; NE]	2.6130 [1.6766; 4.1938] <.0001	
IHC >0 <1+	40 / 76 (52.6)	5.5 [1.0; NE]	13 / 74 (17.6)	NE [NE; NE]	3.4908 [1.9184; 6.7916] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5217
Yes	189 / 393 (48.1)	9.7 [4.1; NE]	79 / 377 (21.0)	NE [NE; NE]	2.4703 [1.9087; 3.2308] <.0001	
No	21 / 41 (51.2)	3.8 [0.8; NE]	8 / 40 (20.0)	NE [NE; NE]	2.9528 [1.3565; 7.1058] 0.0063	
Prior Taxane Use In The Non-Metastatic Setting						0.9131
Yes	87 / 177 (49.2)	7.7 [2.3; NE]	37 / 172 (21.5)	NE [NE; NE]	2.4737 [1.6986; 3.6781] <.0001	
No	123 / 257 (47.9)	11.7 [2.8; NE]	50 / 245 (20.4)	NE [NE; NE]	2.5538 [1.8504; 3.5785] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3060
1	40 / 65 (61.5)	1.4 [0.9; 6.3]	19 / 79 (24.1)	NE [NE; NE]	3.1931 [1.8701; 5.6483] <.0001	
2	131 / 293 (44.7)	NE [6.4; NE]	58 / 281 (20.6)	NE [NE; NE]	2.2490 [1.6604; 3.0860] <.0001	
>=3	38 / 75 (50.7)	4.3 [2.0; NE]	9 / 56 (16.1)	NE [NE; NE]	3.6757 [1.8600; 8.1075] 0.0002	
ER/PR status I						0.6847
ER+, PR+	112 / 252 (44.4)	NE [6.3; NE]	45 / 234 (19.2)	NE [NE; NE]	2.4292 [1.7317; 3.4663] <.0001	
ER+, PR-	87 / 166 (52.4)	3.8 [1.7; NE]	38 / 171 (22.2)	NE [NE; NE]	2.6894 [1.8520; 3.9825] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1737
ER <=10%	8 / 21 (38.1)	NE [1.0; NE]	4 / 14 (28.6)	NE [0.6; NE]	1.1275 [0.3546; 4.2290] 0.8425	
ER >10%	175 / 362 (48.3)	9.7 [3.6; NE]	74 / 343 (21.6)	NE [NE; NE]	2.4350 [1.8645; 3.2150] <.0001	
Positive	27 / 51 (52.9)	4.3 [1.2; NE]	9 / 60 (15.0)	NE [NE; NE]	4.1917 [2.0462; 9.4513] 0.0001	
Endocrine Resistance						0.6141
Primary	63 / 127 (49.6)	5.6 [1.4; NE]	33 / 137 (24.1)	NE [NE; NE]	2.2820 [1.5081; 3.5177] 0.0001	
Secondary	147 / 307 (47.9)	9.7 [4.1; NE]	54 / 279 (19.4)	NE [NE; NE]	2.6705 [1.9681; 3.6784] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						<.0001
Capecitabine	135 / 265 (50.9)	5.5 [2.2; NE]	7 / 249 (2.8)	NE [NE; NE]	23.1606 [11.6856; 54.7105] <.0001	
Nab-Paclitaxel	41 / 103 (39.8)	NE [5.4; NE]	46 / 101 (45.5)	NE [1.1; NE]	0.7691 [0.5031; 1.1717] 0.2220	
Paclitaxel	34 / 66 (51.5)	7.4 [1.4; NE]	34 / 67 (50.7)	2.3 [1.0; NE]	0.7746 [0.4780; 1.2544] 0.2986	
Prior anthracycline use						0.9334
Yes	98 / 197 (49.7)	8.5 [2.2; NE]	42 / 198 (21.2)	NE [NE; NE]	2.5496 [1.7900; 3.6984] <.0001	
No	112 / 237 (47.3)	NE [3.7; NE]	45 / 219 (20.5)	NE [NE; NE]	2.5011 [1.7828; 3.5691] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.4508
Yes	145 / 294 (49.3)	7.7 [2.6; NE]	62 / 275 (22.5)	NE [NE; NE]	2.3639 [1.7655; 3.2056] <.0001	
No	65 / 140 (46.4)	NE [2.8; NE]	25 / 142 (17.6)	NE [NE; NE]	2.9057 [1.8566; 4.6939] <.0001	
ECOG						0.0019
0	122 / 251 (48.6)	11.7 [2.8; NE]	38 / 246 (15.4)	NE [NE; NE]	3.5678 [2.5042; 5.2026] <.0001	
>=1	85 / 178 (47.8)	9.7 [2.6; NE]	49 / 163 (30.1)	NE [NE; NE]	1.6018 [1.1321; 2.2916] 0.0081	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome						
Age at randomization						0.6504
<65 years of age	3 / 301 (1.0)	NE [NE; NE]	92 / 285 (32.3)	NE [NE; NE]	0.0209 [0.0051; 0.0558] <.0001	
>=65 years of age	1 / 133 (0.8)	NE [NE; NE]	54 / 132 (40.9)	9.5 [5.5; NE]	0.0118 [0.0007; 0.0541] <.0001	
Race						0.0528
Asian	0 / 153 (0.0)	NE [NE; NE]	53 / 147 (36.1)	NE [9.5; NE]	NE [NE; NE] NE	
White	2 / 231 (0.9)	NE [NE; NE]	79 / 223 (35.4)	NE [9.5; NE]	0.0161 [0.0026; 0.0513] <.0001	
Other	2 / 50 (4.0)	NE [NE; NE]	14 / 47 (29.8)	NE [6.9; NE]	0.0545 [0.0078; 0.2211] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0404
Asia	0 / 148 (0.0)	NE [NE; NE]	52 / 144 (36.1)	NE [9.5; NE]	NE [NE; NE] NE	
Europe	4 / 227 (1.8)	NE [NE; NE]	62 / 206 (30.1)	NE [12.5; NE]	0.0369 [0.0111; 0.0902] <.0001	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	32 / 67 (47.8)	5.2 [2.1; NE]	NE [NE; NE] NE	
HER2 IHC expression						0.6124
IHC 1+	2 / 239 (0.8)	NE [NE; NE]	79 / 226 (35.0)	NE [12.5; NE]	0.0164 [0.0027; 0.0523] <.0001	
IHC 2+/ISH-	1 / 116 (0.9)	NE [NE; NE]	43 / 115 (37.4)	NE [4.8; NE]	0.0145 [0.0008; 0.0673] <.0001	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	23 / 74 (31.1)	NE [6.3; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4828
Yes	4 / 393 (1.0)	NE [NE; NE]	135 / 377 (35.8)	NE [12.5; NE]	0.0184 [0.0056; 0.0437] <.0001	
No	0 / 41 (0.0)	NE [NE; NE]	11 / 40 (27.5)	NE [9.5; NE]	NE [NE; NE] NE	
Prior Taxane Use In The Non-Metastatic Setting						0.6947
Yes	1 / 177 (0.6)	NE [NE; NE]	52 / 172 (30.2)	NE [NE; NE]	0.0145 [0.0008; 0.0659] <.0001	
No	3 / 257 (1.2)	NE [NE; NE]	94 / 245 (38.4)	NE [6.3; NE]	0.0187 [0.0046; 0.0500] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4631
1	1 / 65 (1.5)	NE [NE; NE]	29 / 79 (36.7)	NE [5.6; NE]	0.0278 [0.0016; 0.1320] <.0001	
2	3 / 293 (1.0)	NE [NE; NE]	97 / 281 (34.5)	NE [9.5; NE]	0.0190 [0.0047; 0.0508] <.0001	
>=3	0 / 75 (0.0)	NE [NE; NE]	20 / 56 (35.7)	NE [3.5; NE]	NE [NE; NE] NE	
ER/PR status I						0.1344
ER+, PR+	1 / 252 (0.4)	NE [NE; NE]	84 / 234 (35.9)	NE [7.4; NE]	0.0070 [0.0004; 0.0318] <.0001	
ER+, PR-	3 / 166 (1.8)	NE [NE; NE]	59 / 171 (34.5)	NE [12.5; NE]	0.0358 [0.0087; 0.0975] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4548
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	2 / 14 (14.3)	NE [2.1; NE]	NE [NE; NE] NE	
ER >10%	2 / 362 (0.6)	NE [NE; NE]	112 / 343 (32.7)	NE [NE; NE]	0.0116 [0.0019; 0.0364] <.0001	
Positive	2 / 51 (3.9)	NE [NE; NE]	32 / 60 (53.3)	2.8 [1.4; NE]	0.0377 [0.0060; 0.1283] <.0001	
Endocrine Resistance						0.1300
Primary	0 / 127 (0.0)	NE [NE; NE]	44 / 137 (32.1)	NE [12.5; NE]	NE [NE; NE] NE	
Secondary	4 / 307 (1.3)	NE [NE; NE]	102 / 279 (36.6)	NE [8.3; NE]	0.0227 [0.0069; 0.0545] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.1045
Capecitabine	3 / 265 (1.1)	NE [NE; NE]	143 / 249 (57.4)	2.8 [2.1; 3.9]	0.0098 [0.0024; 0.0259] <.0001	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	1 / 101 (1.0)	NE [NE; NE]	NE [NE; NE] NE	
Paclitaxel	1 / 66 (1.5)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	0.1570 [0.0054; 2.3854] 0.1889	
Prior anthracycline use						0.5829
Yes	2 / 197 (1.0)	NE [NE; NE]	59 / 198 (29.8)	NE [NE; NE]	0.0238 [0.0039; 0.0766] <.0001	
No	2 / 237 (0.8)	NE [NE; NE]	87 / 219 (39.7)	12.5 [5.5; NE]	0.0133 [0.0022; 0.0423] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.3702
Yes	2 / 294 (0.7)	NE [NE; NE]	99 / 275 (36.0)	NE [9.5; NE]	0.0118 [0.0019; 0.0375] <.0001	
No	2 / 140 (1.4)	NE [NE; NE]	47 / 142 (33.1)	NE [9.5; NE]	0.0310 [0.0050; 0.1003] <.0001	
ECOG						0.9462
0	3 / 251 (1.2)	NE [NE; NE]	104 / 246 (42.3)	9.5 [5.5; NE]	0.0173 [0.0042; 0.0461] <.0001	
>=1	1 / 178 (0.6)	NE [NE; NE]	40 / 163 (24.5)	NE [NE; NE]	0.0174 [0.0010; 0.0801] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: All (any PT)						
Age at randomization						0.4047
<65 years of age	135 / 301 (44.9)	16.3 [10.6; NE]	65 / 285 (22.8)	NE [NE; NE]	1.8557 [1.3838; 2.5141] <.0001	
>=65 years of age	62 / 133 (46.6)	14.0 [5.3; NE]	42 / 132 (31.8)	NE [20.8; NE]	1.5171 [1.0286; 2.2596] 0.0365	
Race						0.0797
Asian	86 / 153 (56.2)	5.3 [3.1; 14.6]	38 / 147 (25.9)	NE [NE; NE]	2.4087 [1.6568; 3.5704] <.0001	
White	92 / 231 (39.8)	20.3 [13.7; NE]	56 / 223 (25.1)	NE [20.8; NE]	1.4610 [1.0502; 2.0505] 0.0249	
Other	19 / 50 (38.0)	NE [9.6; NE]	13 / 47 (27.7)	NE [NE; NE]	1.1733 [0.5716; 2.4699] 0.6683	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0161
Asia	84 / 148 (56.8)	5.6 [4.0; 14.6]	37 / 144 (25.7)	NE [NE; NE]	2.3775 [1.6277; 3.5428] <.0001	
Europe	80 / 227 (35.2)	NE [20.3; NE]	53 / 206 (25.7)	NE [NE; NE]	1.2126 [0.8573; 1.7288] 0.2786	
Rest of the World	33 / 59 (55.9)	5.7 [1.4; NE]	17 / 67 (25.4)	20.8 [20.8; NE]	2.4511 [1.3810; 4.5116] 0.0020	
HER2 IHC expression						0.0331
IHC 1+	103 / 239 (43.1)	19.1 [12.1; NE]	54 / 226 (23.9)	NE [NE; NE]	1.7690 [1.2766; 2.4789] 0.0006	
IHC 2+/ISH-	61 / 116 (52.6)	9.0 [4.4; NE]	25 / 115 (21.7)	NE [NE; NE]	2.4474 [1.5532; 3.9739] 0.0001	
IHC >0 <1+	32 / 76 (42.1)	18.9 [6.2; NE]	28 / 74 (37.8)	20.8 [4.1; NE]	1.0169 [0.6115; 1.7009] 0.9451	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3701
Yes	171 / 393 (43.5)	16.3 [12.1; NE]	94 / 377 (24.9)	NE [NE; NE]	1.6733 [1.3028; 2.1623] 0.0001	
No	26 / 41 (63.4)	4.4 [1.3; 19.1]	13 / 40 (32.5)	20.8 [9.7; NE]	2.3261 [1.2148; 4.6800] 0.0111	
Prior Taxane Use In The Non-Metastatic Setting						0.6213
Yes	79 / 177 (44.6)	14.6 [9.8; NE]	40 / 172 (23.3)	NE [NE; NE]	1.8574 [1.2759; 2.7468] 0.0013	
No	118 / 257 (45.9)	14.8 [9.7; NE]	67 / 245 (27.3)	NE [20.8; NE]	1.6391 [1.2170; 2.2257] 0.0012	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3150
1	24 / 65 (36.9)	14.2 [10.0; NE]	24 / 79 (30.4)	NE [9.7; NE]	1.1103 [0.6244; 1.9723] 0.7206	
2	138 / 293 (47.1)	14.8 [8.7; NE]	69 / 281 (24.6)	NE [20.8; NE]	1.8679 [1.4031; 2.5101] <.0001	
>=3	35 / 75 (46.7)	12.1 [4.4; NE]	14 / 56 (25.0)	NE [NE; NE]	1.9807 [1.0896; 3.8054] 0.0274	
ER/PR status I						0.4808
ER+, PR+	110 / 252 (43.7)	20.3 [12.1; NE]	54 / 234 (23.1)	NE [NE; NE]	1.9113 [1.3859; 2.6681] 0.0001	
ER+, PR-	80 / 166 (48.2)	12.0 [7.9; NE]	49 / 171 (28.7)	NE [NE; NE]	1.5510 [1.0886; 2.2316] 0.0154	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6048
ER <=10%	9 / 21 (42.9)	NE [4.2; NE]	2 / 14 (14.3)	NE [NE; NE]	2.3758 [0.6009; 15.7105] 0.2581	
ER >10%	165 / 362 (45.6)	14.8 [11.1; NE]	84 / 343 (24.5)	NE [NE; NE]	1.8220 [1.4042; 2.3820] <.0001	
Positive	23 / 51 (45.1)	13.7 [4.4; NE]	21 / 60 (35.0)	NE [4.4; NE]	1.3308 [0.7336; 2.4273] 0.3470	
Endocrine Resistance						0.0174
Primary	51 / 127 (40.2)	14.6 [11.1; NE]	44 / 137 (32.1)	NE [9.8; NE]	1.1070 [0.7375; 1.6684] 0.6221	
Secondary	146 / 307 (47.6)	14.0 [7.9; NE]	63 / 279 (22.6)	NE [NE; NE]	2.1385 [1.5989; 2.8955] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.7839
Capecitabine	122 / 265 (46.0)	14.6 [9.8; NE]	68 / 249 (27.3)	NE [20.8; NE]	1.6348 [1.2183; 2.2120] 0.0011	
Nab-Paclitaxel	46 / 103 (44.7)	14.8 [7.9; NE]	23 / 101 (22.8)	NE [NE; NE]	1.9878 [1.2171; 3.3388] 0.0061	
Paclitaxel	29 / 66 (43.9)	NE [4.4; NE]	16 / 67 (23.9)	NE [NE; NE]	1.7762 [0.9692; 3.3677] 0.0661	
Prior anthracycline use						0.7210
Yes	86 / 197 (43.7)	18.9 [10.4; NE]	50 / 198 (25.3)	NE [NE; NE]	1.6633 [1.1766; 2.3762] 0.0040	
No	111 / 237 (46.8)	14.6 [8.7; NE]	57 / 219 (26.0)	NE [20.8; NE]	1.7747 [1.2943; 2.4604] 0.0004	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0498
Yes	127 / 294 (43.2)	18.9 [13.1; NE]	76 / 275 (27.6)	NE [NE; NE]	1.4631 [1.1021; 1.9553] 0.0088	
No	70 / 140 (50.0)	10.0 [5.6; NE]	31 / 142 (21.8)	NE [20.8; NE]	2.3942 [1.5833; 3.7070] <.0001	
ECOG						0.0562
0	99 / 251 (39.4)	20.3 [14.6; NE]	44 / 246 (17.9)	NE [NE; NE]	2.1102 [1.4883; 3.0422] <.0001	
>=1	95 / 178 (53.4)	7.9 [3.1; 14.6]	61 / 163 (37.4)	NE [NE; NE]	1.3895 [1.0085; 1.9285] 0.0456	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Age at randomization						0.2350
<65 years of age	75 / 301 (24.9)	NE [NE; NE]	26 / 285 (9.1)	NE [NE; NE]	2.7175 [1.7619; 4.3280] <.0001	
>=65 years of age	39 / 133 (29.3)	NE [NE; NE]	22 / 132 (16.7)	NE [NE; NE]	1.7760 [1.0631; 3.0439] 0.0290	
Race						0.0239
Asian	50 / 153 (32.7)	NE [NE; NE]	12 / 147 (8.2)	NE [NE; NE]	4.3076 [2.3742; 8.4810] <.0001	
White	54 / 231 (23.4)	NE [NE; NE]	29 / 223 (13.0)	NE [NE; NE]	1.7301 [1.1098; 2.7530] 0.0161	
Other	10 / 50 (20.0)	NE [NE; NE]	7 / 47 (14.9)	NE [NE; NE]	1.2134 [0.4566; 3.3873] 0.7017	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0009
Asia	46 / 148 (31.1)	NE [NE; NE]	11 / 144 (7.6)	NE [NE; NE]	4.3148 [2.3198; 8.7752] <.0001	
Europe	47 / 227 (20.7)	NE [NE; NE]	32 / 206 (15.5)	NE [NE; NE]	1.2558 [0.8033; 1.9879] 0.3212	
Rest of the World	21 / 59 (35.6)	NE [10.3; NE]	5 / 67 (7.5)	NE [NE; NE]	5.0305 [2.0464; 15.0863] 0.0003	
HER2 IHC expression						0.4702
IHC 1+	56 / 239 (23.4)	NE [NE; NE]	24 / 226 (10.6)	NE [NE; NE]	2.1654 [1.3583; 3.5615] 0.0012	
IHC 2+/ISH-	39 / 116 (33.6)	NE [NE; NE]	13 / 115 (11.3)	NE [NE; NE]	3.0101 [1.6487; 5.8696] 0.0003	
IHC >0 <1+	19 / 76 (25.0)	NE [NE; NE]	11 / 74 (14.9)	NE [NE; NE]	1.6995 [0.8217; 3.6944] 0.1575	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1188
Yes	102 / 393 (26.0)	NE [NE; NE]	46 / 377 (12.2)	NE [NE; NE]	2.0998 [1.4914; 3.0033] <.0001	
No	12 / 41 (29.3)	NE [19.1; NE]	2 / 40 (5.0)	NE [NE; NE]	6.2772 [1.7090; 40.3897] 0.0059	
Prior Taxane Use In The Non-Metastatic Setting						0.9870
Yes	43 / 177 (24.3)	NE [NE; NE]	18 / 172 (10.5)	NE [NE; NE]	2.2200 [1.3010; 3.9517] 0.0036	
No	71 / 257 (27.6)	NE [NE; NE]	30 / 245 (12.2)	NE [NE; NE]	2.2984 [1.5150; 3.5769] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5373
1	12 / 65 (18.5)	NE [NE; NE]	10 / 79 (12.7)	NE [NE; NE]	1.3807 [0.5932; 3.2825] 0.4523	
2	82 / 293 (28.0)	NE [NE; NE]	32 / 281 (11.4)	NE [NE; NE]	2.4377 [1.6358; 3.7221] <.0001	
>=3	20 / 75 (26.7)	NE [NE; NE]	6 / 56 (10.7)	NE [NE; NE]	2.6741 [1.1388; 7.3130] 0.0277	
ER/PR status I						0.2440
ER+, PR+	66 / 252 (26.2)	NE [NE; NE]	22 / 234 (9.4)	NE [NE; NE]	2.8450 [1.7847; 4.7149] <.0001	
ER+, PR-	43 / 166 (25.9)	NE [NE; NE]	23 / 171 (13.5)	NE [NE; NE]	1.8138 [1.1013; 3.0648] 0.0200	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1150
ER <=10%	2 / 21 (9.5)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER >10%	95 / 362 (26.2)	NE [NE; NE]	32 / 343 (9.3)	NE [NE; NE]	2.8024 [1.8978; 4.2490] <.0001	
Positive	17 / 51 (33.3)	NE [9.0; NE]	16 / 60 (26.7)	NE [NE; NE]	1.3207 [0.6640; 2.6392] 0.4266	
Endocrine Resistance						0.0930
Primary	23 / 127 (18.1)	NE [NE; NE]	17 / 137 (12.4)	NE [NE; NE]	1.3939 [0.7465; 2.6541] 0.2999	
Secondary	91 / 307 (29.6)	NE [NE; NE]	31 / 279 (11.1)	NE [NE; NE]	2.7034 [1.8188; 4.1289] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.1062
Capecitabine	71 / 265 (26.8)	NE [NE; NE]	36 / 249 (14.5)	NE [NE; NE]	1.8324 [1.2353; 2.7668] 0.0027	
Nab-Paclitaxel	22 / 103 (21.4)	NE [NE; NE]	4 / 101 (4.0)	NE [NE; NE]	5.4692 [2.0900; 18.7220] 0.0004	
Paclitaxel	21 / 66 (31.8)	NE [NE; NE]	8 / 67 (11.9)	NE [NE; NE]	2.6914 [1.2317; 6.4921] 0.0140	
Prior anthracycline use						0.8382
Yes	48 / 197 (24.4)	NE [NE; NE]	20 / 198 (10.1)	NE [NE; NE]	2.3485 [1.4148; 4.0509] 0.0010	
No	66 / 237 (27.8)	NE [NE; NE]	28 / 219 (12.8)	NE [NE; NE]	2.2013 [1.4299; 3.4822] 0.0003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0006
Yes	64 / 294 (21.8)	NE [NE; NE]	38 / 275 (13.8)	NE [NE; NE]	1.5024 [1.0096; 2.2663] 0.0465	
No	50 / 140 (35.7)	NE [NE; NE]	10 / 142 (7.0)	NE [NE; NE]	5.5005 [2.9143; 11.5160] <.0001	
ECOG						0.9617
0	63 / 251 (25.1)	NE [NE; NE]	27 / 246 (11.0)	NE [NE; NE]	2.2303 [1.4362; 3.5612] 0.0004	
>=1	50 / 178 (28.1)	NE [NE; NE]	20 / 163 (12.3)	NE [NE; NE]	2.3324 [1.4102; 4.0092] 0.0010	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: Hypokalaemia						
Age at randomization						0.8809
<65 years of age	31 / 301 (10.3)	NE [NE; NE]	7 / 285 (2.5)	NE [NE; NE]	2.8176 [1.3010; 7.0213] 0.0108	
>=65 years of age	25 / 133 (18.8)	NE [NE; NE]	8 / 132 (6.1)	NE [NE; NE]	2.9941 [1.4102; 7.0991] 0.0046	
Race						0.2468
Asian	30 / 153 (19.6)	NE [NE; NE]	5 / 147 (3.4)	NE [NE; NE]	4.9804 [2.1026; 14.6569] 0.0002	
White	20 / 231 (8.7)	NE [NE; NE]	8 / 223 (3.6)	NE [NE; NE]	1.8743 [0.8504; 4.5497] 0.1300	
Other	6 / 50 (12.0)	NE [NE; NE]	2 / 47 (4.3)	NE [NE; NE]	1.7690 [0.3819; 12.4631] 0.4894	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0933
Asia	33 / 148 (22.3)	NE [25.8; NE]	5 / 144 (3.5)	NE [NE; NE]	5.5520 [2.3650; 16.2500] 0.0001	
Europe	17 / 227 (7.5)	NE [NE; NE]	8 / 206 (3.9)	NE [NE; NE]	1.5121 [0.6665; 3.7311] 0.3351	
Rest of the World	6 / 59 (10.2)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	2.5890 [0.5839; 17.8622] 0.2321	
HER2 IHC expression						0.9771
IHC 1+	31 / 239 (13.0)	NE [NE; NE]	9 / 226 (4.0)	NE [NE; NE]	2.5114 [1.2376; 5.6336] 0.0126	
IHC 2+/ISH-	13 / 116 (11.2)	NE [NE; NE]	3 / 115 (2.6)	NE [NE; NE]	3.2055 [1.0215; 14.0652] 0.0567	
IHC >0 <1+	11 / 76 (14.5)	NE [18.9; NE]	3 / 74 (4.1)	NE [NE; NE]	3.3338 [1.0398; 14.7479] 0.0501	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2302
Yes	47 / 393 (12.0)	NE [NE; NE]	14 / 377 (3.7)	NE [NE; NE]	2.5442 [1.4333; 4.8134] 0.0016	
No	9 / 41 (22.0)	NE [25.8; NE]	1 / 40 (2.5)	NE [NE; NE]	7.1657 [1.3070; 133.1515] 0.0305	
Prior Taxane Use In The Non-Metastatic Setting						0.9629
Yes	30 / 177 (16.9)	NE [NE; NE]	8 / 172 (4.7)	NE [NE; NE]	2.8872 [1.3755; 6.8060] 0.0059	
No	26 / 257 (10.1)	NE [NE; NE]	7 / 245 (2.9)	NE [NE; NE]	2.7696 [1.2640; 6.9427] 0.0130	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6506
1	7 / 65 (10.8)	NE [NE; NE]	3 / 79 (3.8)	NE [NE; NE]	2.2573 [0.6175; 10.5912] 0.2309	
2	39 / 293 (13.3)	NE [NE; NE]	11 / 281 (3.9)	NE [NE; NE]	2.7042 [1.4280; 5.5657] 0.0026	
>=3	10 / 75 (13.3)	NE [18.6; NE]	1 / 56 (1.8)	NE [NE; NE]	5.9898 [1.1386; 110.1379] 0.0529	
ER/PR status I						0.3436
ER+, PR+	34 / 252 (13.5)	NE [NE; NE]	6 / 234 (2.6)	NE [NE; NE]	4.3072 [1.9384; 11.4336] 0.0003	
ER+, PR-	20 / 166 (12.0)	NE [NE; NE]	7 / 171 (4.1)	NE [NE; NE]	2.1432 [0.9363; 5.5134] 0.0798	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5803
ER <=10%	3 / 21 (14.3)	NE [10.6; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER >10%	47 / 362 (13.0)	NE [NE; NE]	12 / 343 (3.5)	NE [NE; NE]	2.9492 [1.6100; 5.8451] 0.0005	
Positive	6 / 51 (11.8)	NE [NE; NE]	3 / 60 (5.0)	NE [NE; NE]	1.9010 [0.4998; 9.0323] 0.3546	
Endocrine Resistance						0.4752
Primary	15 / 127 (11.8)	NE [NE; NE]	6 / 137 (4.4)	NE [NE; NE]	2.0147 [0.8093; 5.7030] 0.1438	
Secondary	41 / 307 (13.4)	NE [NE; NE]	9 / 279 (3.2)	NE [NE; NE]	3.3681 [1.7097; 7.4168] 0.0005	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.1357
Capecitabine	34 / 265 (12.8)	NE [NE; NE]	10 / 249 (4.0)	NE [NE; NE]	2.6328 [1.3474; 5.6335] 0.0053	
Nab-Paclitaxel	20 / 103 (19.4)	NE [25.8; NE]	3 / 101 (3.0)	NE [NE; NE]	5.5471 [1.8770; 23.7145] 0.0021	
Paclitaxel	2 / 66 (3.0)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	0.2401 [0.0106; 2.7018] 0.2294	
Prior anthracycline use						0.7508
Yes	30 / 197 (15.2)	NE [NE; NE]	9 / 198 (4.5)	NE [NE; NE]	2.6099 [1.2798; 5.8734] 0.0096	
No	26 / 237 (11.0)	NE [NE; NE]	6 / 219 (2.7)	NE [NE; NE]	3.2079 [1.4062; 8.6390] 0.0068	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5706
Yes	36 / 294 (12.2)	NE [NE; NE]	8 / 275 (2.9)	NE [NE; NE]	3.3247 [1.6196; 7.7305] 0.0012	
No	20 / 140 (14.3)	NE [NE; NE]	7 / 142 (4.9)	NE [NE; NE]	2.3248 [1.0215; 5.9577] 0.0499	
ECOG						0.2331
0	26 / 251 (10.4)	NE [NE; NE]	5 / 246 (2.0)	NE [NE; NE]	4.0102 [1.6689; 11.8882] 0.0022	
>=1	28 / 178 (15.7)	NE [NE; NE]	10 / 163 (6.1)	NE [NE; NE]	2.0313 [1.0105; 4.4276] 0.0526	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: All (any PT)						
Age at randomization						0.5260
<65 years of age	122 / 301 (40.5)	NE [13.4; NE]	126 / 285 (44.2)	9.1 [5.3; 14.7]	0.7559 [0.5869; 0.9732] 0.0283	
>=65 years of age	47 / 133 (35.3)	NE [13.9; NE]	62 / 132 (47.0)	7.7 [4.0; 18.1]	0.6312 [0.4294; 0.9219] 0.0168	
Race						0.9530
Asian	49 / 153 (32.0)	NE [NE; NE]	61 / 147 (41.5)	9.2 [6.6; NE]	0.6870 [0.4688; 1.0015] 0.0499	
White	97 / 231 (42.0)	20.0 [10.5; NE]	105 / 223 (47.1)	8.3 [3.7; 14.7]	0.7122 [0.5381; 0.9416] 0.0161	
Other	23 / 50 (46.0)	13.1 [5.9; NE]	22 / 47 (46.8)	7.4 [2.0; NE]	0.7342 [0.3987; 1.3494] 0.3118	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0379
Asia	45 / 148 (30.4)	NE [NE; NE]	57 / 144 (39.6)	11.8 [7.7; NE]	0.6684 [0.4489; 0.9893] 0.0433	
Europe	88 / 227 (38.8)	22.0 [13.9; NE]	100 / 206 (48.5)	7.4 [3.4; 12.5]	0.6108 [0.4559; 0.8168] 0.0008	
Rest of the World	36 / 59 (61.0)	5.3 [2.0; 9.3]	31 / 67 (46.3)	7.2 [2.3; NE]	1.2617 [0.7776; 2.0573] 0.3506	
HER2 IHC expression						0.5886
IHC 1+	91 / 239 (38.1)	NE [14.2; NE]	105 / 226 (46.5)	8.9 [5.3; 12.5]	0.6795 [0.5109; 0.9020] 0.0072	
IHC 2+/ISH-	49 / 116 (42.2)	NE [6.5; NE]	49 / 115 (42.6)	7.4 [3.6; NE]	0.8751 [0.5861; 1.3071] 0.5058	
IHC >0 <1+	27 / 76 (35.5)	NE [10.1; NE]	34 / 74 (45.9)	8.5 [2.8; 20.9]	0.5843 [0.3474; 0.9730] 0.0369	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0707
Yes	152 / 393 (38.7)	NE [14.9; NE]	176 / 377 (46.7)	8.0 [4.9; 10.9]	0.6666 [0.5345; 0.8303] 0.0003	
No	17 / 41 (41.5)	NE [5.2; NE]	12 / 40 (30.0)	NE [5.9; NE]	1.3991 [0.6725; 3.0047] 0.3735	
Prior Taxane Use In The Non-Metastatic Setting						0.9263
Yes	68 / 177 (38.4)	NE [14.2; NE]	76 / 172 (44.2)	8.9 [5.3; 18.1]	0.7000 [0.5003; 0.9771] 0.0347	
No	101 / 257 (39.3)	NE [13.4; NE]	112 / 245 (45.7)	8.5 [3.7; 14.7]	0.7150 [0.5447; 0.9372] 0.0145	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0125
1	30 / 65 (46.2)	11.3 [3.7; NE]	33 / 79 (41.8)	8.0 [4.9; NE]	0.9975 [0.6008; 1.6481] 0.9848	
2	118 / 293 (40.3)	NE [14.5; NE]	122 / 281 (43.4)	9.5 [5.8; 20.9]	0.7932 [0.6142; 1.0240] 0.0726	
>=3	21 / 75 (28.0)	NE [14.9; NE]	32 / 56 (57.1)	4.1 [2.2; 10.9]	0.3009 [0.1680; 0.5268] <.0001	
ER/PR status I						0.9415
ER+, PR+	93 / 252 (36.9)	NE [14.9; NE]	100 / 234 (42.7)	9.5 [7.2; 20.9]	0.7136 [0.5363; 0.9486] 0.0196	
ER+, PR-	67 / 166 (40.4)	22.0 [13.1; NE]	82 / 171 (48.0)	7.6 [3.7; 14.3]	0.6794 [0.4873; 0.9433] 0.0195	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3123
ER <=10%	5 / 21 (23.8)	NE [5.5; NE]	6 / 14 (42.9)	3.7 [1.2; NE]	0.4188 [0.1174; 1.4237] 0.1476	
ER >10%	141 / 362 (39.0)	NE [14.5; NE]	155 / 343 (45.2)	9.1 [5.3; 14.3]	0.7080 [0.5617; 0.8916] 0.0031	
Positive	23 / 51 (45.1)	8.4 [3.2; NE]	27 / 60 (45.0)	8.0 [2.5; NE]	0.9231 [0.5239; 1.6128] 0.7743	
Endocrine Resistance						0.7218
Primary	47 / 127 (37.0)	NE [13.2; NE]	61 / 137 (44.5)	5.9 [3.7; NE]	0.7039 [0.4759; 1.0343] 0.0722	
Secondary	122 / 307 (39.7)	NE [13.9; NE]	127 / 279 (45.5)	9.1 [6.6; 14.3]	0.7216 [0.5613; 0.9271] 0.0101	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						<.0001
Capecitabine	125 / 265 (47.2)	13.4 [6.5; NE]	87 / 249 (34.9)	18.1 [10.9; NE]	1.2718 [0.9678; 1.6788] 0.0886	
Nab-Paclitaxel	22 / 103 (21.4)	NE [NE; NE]	51 / 101 (50.5)	6.6 [4.6; 11.9]	0.2997 [0.1763; 0.4926] <.0001	
Paclitaxel	22 / 66 (33.3)	NE [13.1; NE]	50 / 67 (74.6)	1.4 [1.0; 2.1]	0.2045 [0.1148; 0.3499] <.0001	
Prior anthracycline use						0.5691
Yes	73 / 197 (37.1)	NE [14.9; NE]	88 / 198 (44.4)	9.5 [5.3; 12.5]	0.6625 [0.4817; 0.9081] 0.0101	
No	96 / 237 (40.5)	NE [11.3; NE]	100 / 219 (45.7)	8.3 [4.6; 14.7]	0.7535 [0.5680; 0.9991] 0.0473	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.1644
Yes	112 / 294 (38.1)	NE [13.9; NE]	128 / 275 (46.5)	7.7 [4.0; 12.5]	0.6346 [0.4902; 0.8203] 0.0005	
No	57 / 140 (40.7)	NE [13.2; NE]	60 / 142 (42.3)	11.8 [7.2; NE]	0.8902 [0.6167; 1.2835] 0.5252	
ECOG						0.0020
0	107 / 251 (42.6)	22.0 [11.3; NE]	100 / 246 (40.7)	14.3 [7.7; NE]	0.9529 [0.7242; 1.2550] 0.7179	
>=1	61 / 178 (34.3)	NE [14.2; NE]	85 / 163 (52.1)	4.0 [2.8; 9.1]	0.4664 [0.3319; 0.6512] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Headache						
Age at randomization						0.5489
<65 years of age	58 / 301 (19.3)	NE [28.1; NE]	30 / 285 (10.5)	NE [NE; NE]	1.6270 [1.0508; 2.5698] 0.0310	
>=65 years of age	16 / 133 (12.0)	NE [NE; NE]	12 / 132 (9.1)	NE [NE; NE]	1.2773 [0.6069; 2.7621] 0.5219	
Race						0.4682
Asian	21 / 153 (13.7)	NE [NE; NE]	8 / 147 (5.4)	NE [NE; NE]	2.3680 [1.0854; 5.7057] 0.0333	
White	40 / 231 (17.3)	NE [NE; NE]	27 / 223 (12.1)	NE [NE; NE]	1.2914 [0.7948; 2.1304] 0.3083	
Other	13 / 50 (26.0)	28.1 [22.0; NE]	7 / 47 (14.9)	NE [NE; NE]	1.4558 [0.5760; 3.9551] 0.4382	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0990
Asia	19 / 148 (12.8)	NE [NE; NE]	5 / 144 (3.5)	NE [NE; NE]	3.4587 [1.3859; 10.4552] 0.0088	
Europe	32 / 227 (14.1)	NE [NE; NE]	23 / 206 (11.2)	NE [NE; NE]	1.1061 [0.6476; 1.9184] 0.7173	
Rest of the World	23 / 59 (39.0)	28.1 [8.1; NE]	14 / 67 (20.9)	NE [NE; NE]	1.8753 [0.9678; 3.7568] 0.0639	
HER2 IHC expression						0.2759
IHC 1+	35 / 239 (14.6)	NE [NE; NE]	19 / 226 (8.4)	NE [NE; NE]	1.5842 [0.9137; 2.8315] 0.1061	
IHC 2+/ISH-	27 / 116 (23.3)	NE [NE; NE]	12 / 115 (10.4)	NE [NE; NE]	2.1082 [1.0889; 4.3322] 0.0289	
IHC >0 <1+	11 / 76 (14.5)	NE [28.1; NE]	11 / 74 (14.9)	NE [NE; NE]	0.8039 [0.3340; 1.9120] 0.6167	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4498
Yes	67 / 393 (17.0)	NE [NE; NE]	36 / 377 (9.5)	NE [NE; NE]	1.6351 [1.0955; 2.4807] 0.0171	
No	7 / 41 (17.1)	NE [25.9; NE]	6 / 40 (15.0)	NE [NE; NE]	0.9481 [0.2961; 3.0356] 0.9266	
Prior Taxane Use In The Non-Metastatic Setting						0.2001
Yes	31 / 177 (17.5)	NE [NE; NE]	13 / 172 (7.6)	NE [NE; NE]	2.0693 [1.1019; 4.1151] 0.0260	
No	43 / 257 (16.7)	NE [28.1; NE]	29 / 245 (11.8)	NE [NE; NE]	1.2843 [0.8036; 2.0814] 0.3003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5278
1	12 / 65 (18.5)	28.1 [28.1; NE]	9 / 79 (11.4)	NE [NE; NE]	1.4548 [0.6001; 3.6190] 0.4058	
2	54 / 293 (18.4)	NE [NE; NE]	27 / 281 (9.6)	NE [NE; NE]	1.7715 [1.1249; 2.8568] 0.0145	
>=3	8 / 75 (10.7)	NE [NE; NE]	6 / 56 (10.7)	NE [NE; NE]	0.8928 [0.3100; 2.7159] 0.8357	
ER/PR status I						0.8325
ER+, PR+	41 / 252 (16.3)	NE [NE; NE]	23 / 234 (9.8)	NE [NE; NE]	1.5220 [0.9206; 2.5784] 0.1056	
ER+, PR-	29 / 166 (17.5)	NE [25.9; NE]	17 / 171 (9.9)	NE [NE; NE]	1.5253 [0.8384; 2.8566] 0.1739	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1356
ER <=10%	3 / 21 (14.3)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER >10%	60 / 362 (16.6)	NE [NE; NE]	38 / 343 (11.1)	NE [NE; NE]	1.3357 [0.8906; 2.0272] 0.1665	
Positive	11 / 51 (21.6)	NE [NE; NE]	4 / 60 (6.7)	NE [NE; NE]	3.1654 [1.0814; 11.4284] 0.0373	
Endocrine Resistance						0.9180
Primary	21 / 127 (16.5)	NE [NE; NE]	13 / 137 (9.5)	NE [NE; NE]	1.6454 [0.8304; 3.3838] 0.1582	
Secondary	53 / 307 (17.3)	NE [28.1; NE]	29 / 279 (10.4)	NE [NE; NE]	1.5019 [0.9603; 2.3960] 0.0784	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0168
Capecitabine	56 / 265 (21.1)	NE [28.1; NE]	23 / 249 (9.2)	NE [NE; NE]	2.1809 [1.3596; 3.6186] 0.0013	
Nab-Paclitaxel	11 / 103 (10.7)	NE [25.9; NE]	8 / 101 (7.9)	NE [NE; NE]	1.1382 [0.4461; 2.9966] 0.7871	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	11 / 67 (16.4)	NE [NE; NE]	0.5067 [0.1855; 1.2940] 0.1546	
Prior anthracycline use						0.3786
Yes	33 / 197 (16.8)	NE [NE; NE]	16 / 198 (8.1)	NE [NE; NE]	1.8583 [1.0347; 3.4769] 0.0405	
No	41 / 237 (17.3)	NE [28.1; NE]	26 / 219 (11.9)	NE [NE; NE]	1.3337 [0.8188; 2.2109] 0.2538	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.3686
Yes	55 / 294 (18.7)	NE [28.1; NE]	27 / 275 (9.8)	NE [NE; NE]	1.7078 [1.0839; 2.7552] 0.0225	
No	19 / 140 (13.6)	NE [NE; NE]	15 / 142 (10.6)	NE [NE; NE]	1.1900 [0.6042; 2.3856] 0.6191	
ECOG						0.1147
0	51 / 251 (20.3)	NE [28.1; NE]	24 / 246 (9.8)	NE [NE; NE]	1.9658 [1.2215; 3.2544] 0.0057	
>=1	23 / 178 (12.9)	NE [NE; NE]	18 / 163 (11.0)	NE [NE; NE]	1.0028 [0.5395; 1.8916] 0.9944	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Dysgeusia						
Age at randomization						0.9472
<65 years of age	36 / 301 (12.0)	NE [NE; NE]	16 / 285 (5.6)	NE [NE; NE]	1.8378 [1.0348; 3.4127] 0.0408	
>=65 years of age	15 / 133 (11.3)	NE [NE; NE]	8 / 132 (6.1)	NE [NE; NE]	1.7270 [0.7497; 4.2923] 0.2069	
Race						0.0711
Asian	17 / 153 (11.1)	NE [NE; NE]	5 / 147 (3.4)	NE [NE; NE]	3.1043 [1.2262; 9.4518] 0.0191	
White	31 / 231 (13.4)	NE [NE; NE]	14 / 223 (6.3)	NE [NE; NE]	1.8239 [0.9868; 3.5457] 0.0592	
Other	3 / 50 (6.0)	NE [NE; NE]	5 / 47 (10.6)	NE [NE; NE]	0.4423 [0.0877; 1.8550] 0.2638	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0172
Asia	15 / 148 (10.1)	NE [NE; NE]	4 / 144 (2.8)	NE [NE; NE]	3.4084 [1.2350; 11.9687] 0.0207	
Europe	27 / 227 (11.9)	NE [NE; NE]	19 / 206 (9.2)	NE [NE; NE]	1.0595 [0.5898; 1.9418] 0.8473	
Rest of the World	9 / 59 (15.3)	NE [NE; NE]	1 / 67 (1.5)	NE [NE; NE]	9.5313 [1.7840; 175.9174] 0.0090	
HER2 IHC expression						0.3162
IHC 1+	29 / 239 (12.1)	NE [NE; NE]	11 / 226 (4.9)	NE [NE; NE]	2.2007 [1.1287; 4.6132] 0.0228	
IHC 2+/ISH-	16 / 116 (13.8)	NE [NE; NE]	7 / 115 (6.1)	NE [NE; NE]	2.0597 [0.8765; 5.3735] 0.1046	
IHC >0 <1+	6 / 76 (7.9)	NE [NE; NE]	6 / 74 (8.1)	NE [NE; NE]	0.8062 [0.2511; 2.5877] 0.7097	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1914
Yes	49 / 393 (12.5)	NE [NE; NE]	24 / 377 (6.4)	NE [NE; NE]	1.7057 [1.0562; 2.8306] 0.0308	
No	2 / 41 (4.9)	NE [NE; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
Prior Taxane Use In The Non-Metastatic Setting						0.5934
Yes	18 / 177 (10.2)	NE [NE; NE]	10 / 172 (5.8)	NE [NE; NE]	1.4720 [0.6884; 3.3307] 0.3270	
No	33 / 257 (12.8)	NE [NE; NE]	14 / 245 (5.7)	NE [NE; NE]	2.0218 [1.1039; 3.9072] 0.0245	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6748
1	8 / 65 (12.3)	NE [NE; NE]	6 / 79 (7.6)	NE [NE; NE]	1.4901 [0.5150; 4.5473] 0.4610	
2	38 / 293 (13.0)	NE [NE; NE]	15 / 281 (5.3)	NE [NE; NE]	2.1124 [1.1840; 3.9683] 0.0125	
>=3	5 / 75 (6.7)	NE [NE; NE]	3 / 56 (5.4)	NE [NE; NE]	1.0479 [0.2539; 5.1521] 0.9460	
ER/PR status I						0.5124
ER+, PR+	30 / 252 (11.9)	NE [NE; NE]	16 / 234 (6.8)	NE [NE; NE]	1.4840 [0.8183; 2.7936] 0.2010	
ER+, PR-	18 / 166 (10.8)	NE [NE; NE]	8 / 171 (4.7)	NE [NE; NE]	2.0647 [0.9219; 5.0557] 0.0834	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6539
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER >10%	41 / 362 (11.3)	NE [NE; NE]	20 / 343 (5.8)	NE [NE; NE]	1.6898 [1.0006; 2.9486] 0.0529	
Positive	9 / 51 (17.6)	NE [NE; NE]	4 / 60 (6.7)	NE [NE; NE]	2.5347 [0.8245; 9.3661] 0.1088	
Endocrine Resistance						0.8598
Primary	12 / 127 (9.4)	NE [NE; NE]	6 / 137 (4.4)	NE [NE; NE]	1.9042 [0.7336; 5.5012] 0.1934	
Secondary	39 / 307 (12.7)	NE [NE; NE]	18 / 279 (6.5)	NE [NE; NE]	1.7307 [1.0039; 3.1012] 0.0520	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0067
Capecitabine	40 / 265 (15.1)	NE [NE; NE]	11 / 249 (4.4)	NE [NE; NE]	3.0479 [1.6183; 6.2490] 0.0006	
Nab-Paclitaxel	4 / 103 (3.9)	NE [NE; NE]	3 / 101 (3.0)	NE [NE; NE]	1.1650 [0.2544; 5.9541] 0.8423	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	10 / 67 (14.9)	NE [NE; NE]	0.5482 [0.1958; 1.4471] 0.2240	
Prior anthracycline use						0.3459
Yes	19 / 197 (9.6)	NE [NE; NE]	12 / 198 (6.1)	NE [NE; NE]	1.3957 [0.6827; 2.9671] 0.3661	
No	32 / 237 (13.5)	NE [NE; NE]	12 / 219 (5.5)	NE [NE; NE]	2.1793 [1.1511; 4.4119] 0.0187	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0981
Yes	28 / 294 (9.5)	NE [NE; NE]	17 / 275 (6.2)	NE [NE; NE]	1.2934 [0.7127; 2.4171] 0.4042	
No	23 / 140 (16.4)	NE [NE; NE]	7 / 142 (4.9)	NE [NE; NE]	3.1484 [1.4183; 7.9494] 0.0052	
ECOG						0.4892
0	32 / 251 (12.7)	NE [NE; NE]	14 / 246 (5.7)	NE [NE; NE]	1.9937 [1.0837; 3.8638] 0.0287	
>=1	18 / 178 (10.1)	NE [NE; NE]	10 / 163 (6.1)	NE [NE; NE]	1.4596 [0.6854; 3.2920] 0.3358	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Age at randomization						0.6135
<65 years of age	7 / 301 (2.3)	NE [NE; NE]	31 / 285 (10.9)	NE [NE; NE]	0.1711 [0.0689; 0.3683] <.0001	
>=65 years of age	5 / 133 (3.8)	NE [NE; NE]	18 / 132 (13.6)	NE [NE; NE]	0.2419 [0.0798; 0.6069] 0.0023	
Race						0.8904
Asian	5 / 153 (3.3)	NE [NE; NE]	20 / 147 (13.6)	NE [NE; NE]	0.1977 [0.0656; 0.4896] 0.0003	
White	6 / 231 (2.6)	NE [NE; NE]	23 / 223 (10.3)	NE [NE; NE]	0.2115 [0.0779; 0.4890] 0.0002	
Other	1 / 50 (2.0)	NE [NE; NE]	6 / 47 (12.8)	NE [NE; NE]	0.1409 [0.0075; 0.8266] 0.0344	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1894
Asia	5 / 148 (3.4)	NE [NE; NE]	20 / 144 (13.9)	NE [NE; NE]	0.1994 [0.0662; 0.4938] 0.0004	
Europe	7 / 227 (3.1)	NE [NE; NE]	21 / 206 (10.2)	NE [NE; NE]	0.2493 [0.0978; 0.5620] 0.0006	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	8 / 67 (11.9)	NE [NE; NE]	NE [NE; NE] NE	
HER2 IHC expression						0.0658
IHC 1+	9 / 239 (3.8)	NE [NE; NE]	24 / 226 (10.6)	NE [NE; NE]	0.3100 [0.1361; 0.6452] 0.0016	
IHC 2+/ISH-	3 / 116 (2.6)	NE [NE; NE]	16 / 115 (13.9)	NE [NE; NE]	0.1355 [0.0312; 0.4126] 0.0003	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	9 / 74 (12.2)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4776
Yes	10 / 393 (2.5)	NE [NE; NE]	44 / 377 (11.7)	NE [NE; NE]	0.1820 [0.0863; 0.3474] <.0001	
No	2 / 41 (4.9)	NE [NE; NE]	5 / 40 (12.5)	NE [NE; NE]	0.3348 [0.0478; 1.5609] 0.1711	
Prior Taxane Use In The Non-Metastatic Setting						0.9029
Yes	5 / 177 (2.8)	NE [NE; NE]	20 / 172 (11.6)	NE [NE; NE]	0.2114 [0.0703; 0.5228] 0.0006	
No	7 / 257 (2.7)	NE [NE; NE]	29 / 245 (11.8)	NE [NE; NE]	0.1861 [0.0747; 0.4027] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.7897
1	1 / 65 (1.5)	NE [NE; NE]	10 / 79 (12.7)	NE [NE; NE]	0.1135 [0.0062; 0.5932] 0.0122	
2	7 / 293 (2.4)	NE [NE; NE]	28 / 281 (10.0)	NE [NE; NE]	0.1997 [0.0801; 0.4334] <.0001	
>=3	4 / 75 (5.3)	NE [NE; NE]	11 / 56 (19.6)	NE [NE; NE]	0.2041 [0.0559; 0.6055] 0.0031	
ER/PR status I						0.4847
ER+, PR+	7 / 252 (2.8)	NE [NE; NE]	23 / 234 (9.8)	NE [NE; NE]	0.2342 [0.0926; 0.5207] 0.0003	
ER+, PR-	4 / 166 (2.4)	NE [NE; NE]	24 / 171 (14.0)	NE [NE; NE]	0.1419 [0.0415; 0.3698] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3358
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	3 / 14 (21.4)	NE [3.7; NE]	NE [NE; NE] NE	
ER >10%	10 / 362 (2.8)	NE [NE; NE]	38 / 343 (11.1)	NE [NE; NE]	0.2055 [0.0966; 0.3976] <.0001	
Positive	2 / 51 (3.9)	NE [NE; NE]	8 / 60 (13.3)	NE [NE; NE]	0.2586 [0.0390; 1.0351] 0.0658	
Endocrine Resistance						0.9458
Primary	4 / 127 (3.1)	NE [NE; NE]	19 / 137 (13.9)	NE [NE; NE]	0.1982 [0.0573; 0.5287] 0.0011	
Secondary	8 / 307 (2.6)	NE [NE; NE]	30 / 279 (10.8)	NE [NE; NE]	0.1952 [0.0832; 0.4071] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0057
Capecitabine	8 / 265 (3.0)	NE [NE; NE]	13 / 249 (5.2)	NE [NE; NE]	0.5122 [0.2023; 1.2181] 0.1305	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	11 / 101 (10.9)	NE [NE; NE]	NE [NE; NE] NE	
Paclitaxel	4 / 66 (6.1)	NE [NE; NE]	25 / 67 (37.3)	NE [2.7; NE]	0.0831 [0.0238; 0.2222] <.0001	
Prior anthracycline use						0.1626
Yes	7 / 197 (3.6)	NE [NE; NE]	19 / 198 (9.6)	NE [NE; NE]	0.3265 [0.1274; 0.7439] 0.0078	
No	5 / 237 (2.1)	NE [NE; NE]	30 / 219 (13.7)	NE [NE; NE]	0.1231 [0.0418; 0.2915] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.8495
Yes	9 / 294 (3.1)	NE [NE; NE]	34 / 275 (12.4)	NE [NE; NE]	0.2042 [0.0918; 0.4088] <.0001	
No	3 / 140 (2.1)	NE [NE; NE]	15 / 142 (10.6)	NE [NE; NE]	0.1687 [0.0390; 0.5134] 0.0015	
ECOG						0.3987
0	6 / 251 (2.4)	NE [NE; NE]	19 / 246 (7.7)	NE [NE; NE]	0.2601 [0.0945; 0.6171] 0.0020	
>=1	6 / 178 (3.4)	NE [NE; NE]	29 / 163 (17.8)	NE [NE; NE]	0.1525 [0.0570; 0.3441] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)						
Age at randomization						0.3641
<65 years of age	148 / 301 (49.2)	12.2 [8.8; 15.4]	67 / 285 (23.5)	NE [20.4; NE]	1.6781 [1.2611; 2.2567] 0.0004	
>=65 years of age	61 / 133 (45.9)	13.1 [8.3; NE]	39 / 132 (29.5)	NE [16.1; NE]	1.3374 [0.8982; 2.0151] 0.1555	
Race						0.2066
Asian	69 / 153 (45.1)	15.0 [9.9; 26.8]	28 / 147 (19.0)	NE [16.3; NE]	2.0878 [1.3605; 3.2921] 0.0008	
White	116 / 231 (50.2)	10.4 [7.4; 15.4]	66 / 223 (29.6)	NE [21.3; NE]	1.4177 [1.0500; 1.9300] 0.0235	
Other	24 / 50 (48.0)	14.0 [8.2; NE]	12 / 47 (25.5)	NE [5.6; NE]	1.0298 [0.5100; 2.1806] 0.9298	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1058
Asia	65 / 148 (43.9)	15.3 [11.4; 26.8]	25 / 144 (17.4)	NE [16.3; NE]	2.2442 [1.4333; 3.6266] 0.0004	
Europe	107 / 227 (47.1)	12.2 [8.6; 21.2]	59 / 206 (28.6)	21.3 [21.3; NE]	1.2785 [0.9317; 1.7711] 0.1318	
Rest of the World	37 / 59 (62.7)	7.6 [3.8; 12.1]	22 / 67 (32.8)	NE [5.5; NE]	1.6134 [0.9534; 2.7916] 0.0769	
HER2 IHC expression						0.0537
IHC 1+	114 / 239 (47.7)	12.9 [8.7; 19.0]	54 / 226 (23.9)	NE [21.3; NE]	1.6826 [1.2225; 2.3453] 0.0015	
IHC 2+/ISH-	57 / 116 (49.1)	12.2 [8.3; 23.5]	39 / 115 (33.9)	20.4 [8.1; NE]	1.0436 [0.6926; 1.5876] 0.8397	
IHC >0 <1+	37 / 76 (48.7)	11.8 [7.4; 19.2]	13 / 74 (17.6)	NE [16.3; NE]	2.5401 [1.3846; 4.9690] 0.0028	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3715
Yes	193 / 393 (49.1)	12.1 [8.9; 15.2]	100 / 377 (26.5)	NE [20.4; NE]	1.5069 [1.1855; 1.9272] 0.0008	
No	16 / 41 (39.0)	NE [8.1; NE]	6 / 40 (15.0)	NE [15.5; NE]	2.3205 [0.9532; 6.4719] 0.0711	
Prior Taxane Use In The Non-Metastatic Setting						0.2431
Yes	81 / 177 (45.8)	15.3 [8.9; 21.4]	46 / 172 (26.7)	NE [21.3; NE]	1.3583 [0.9477; 1.9698] 0.0984	
No	128 / 257 (49.8)	11.0 [8.3; 14.9]	60 / 245 (24.5)	NE [16.3; NE]	1.7303 [1.2787; 2.3685] 0.0004	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6926
1	37 / 65 (56.9)	5.2 [3.8; 15.3]	23 / 79 (29.1)	NE [13.7; NE]	2.0645 [1.2346; 3.5255] 0.0054	
2	134 / 293 (45.7)	14.9 [11.8; 19.2]	66 / 281 (23.5)	NE [21.3; NE]	1.5173 [1.1331; 2.0519] 0.0055	
>=3	38 / 75 (50.7)	9.7 [7.2; 23.5]	16 / 56 (28.6)	20.4 [20.4; NE]	1.5499 [0.8791; 2.8625] 0.1391	
ER/PR status I						0.3741
ER+, PR+	114 / 252 (45.2)	13.2 [9.9; 21.4]	52 / 234 (22.2)	NE [NE; NE]	1.6828 [1.2182; 2.3564] 0.0017	
ER+, PR-	82 / 166 (49.4)	12.4 [8.3; 18.2]	52 / 171 (30.4)	20.4 [16.1; NE]	1.2902 [0.9110; 1.8427] 0.1538	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.0618
ER <=10%	9 / 21 (42.9)	19.0 [4.2; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER >10%	171 / 362 (47.2)	13.2 [10.0; 15.9]	90 / 343 (26.2)	NE [21.3; NE]	1.4616 [1.1340; 1.8965] 0.0036	
Positive	29 / 51 (56.9)	7.2 [5.4; 14.9]	16 / 60 (26.7)	20.4 [16.3; NE]	2.1141 [1.1608; 3.9920] 0.0143	
Endocrine Resistance						0.5036
Primary	65 / 127 (51.2)	8.9 [5.4; 18.2]	35 / 137 (25.5)	NE [NE; NE]	1.8424 [1.2286; 2.8100] 0.0032	
Secondary	144 / 307 (46.9)	14.0 [10.6; 15.9]	71 / 279 (25.4)	NE [20.4; NE]	1.4583 [1.1007; 1.9497] 0.0091	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0013
Capecitabine	138 / 265 (52.1)	11.8 [8.2; 14.9]	65 / 249 (26.1)	NE [20.4; NE]	1.7127 [1.2805; 2.3152] 0.0003	
Nab-Paclitaxel	46 / 103 (44.7)	15.4 [8.1; 23.5]	17 / 101 (16.8)	NE [NE; NE]	2.3245 [1.3537; 4.1824] 0.0024	
Paclitaxel	25 / 66 (37.9)	NE [10.5; NE]	24 / 67 (35.8)	NE [3.9; NE]	0.6564 [0.3670; 1.1730] 0.1511	
Prior anthracycline use						0.3273
Yes	96 / 197 (48.7)	14.0 [8.1; 18.2]	55 / 198 (27.8)	NE [21.3; NE]	1.4045 [1.0103; 1.9718] 0.0448	
No	113 / 237 (47.7)	11.9 [8.8; 19.2]	51 / 219 (23.3)	NE [16.3; NE]	1.7179 [1.2403; 2.4128] 0.0012	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.8642
Yes	134 / 294 (45.6)	12.2 [9.7; 18.2]	67 / 275 (24.4)	NE [20.4; NE]	1.5380 [1.1501; 2.0765] 0.0039	
No	75 / 140 (53.6)	12.9 [8.1; 15.4]	39 / 142 (27.5)	NE [15.5; NE]	1.5919 [1.0868; 2.3690] 0.0179	
ECOG						0.5857
0	120 / 251 (47.8)	13.1 [8.7; 21.2]	66 / 246 (26.8)	NE [21.3; NE]	1.4968 [1.1113; 2.0335] 0.0083	
>=1	85 / 178 (47.8)	12.2 [8.9; 15.3]	37 / 163 (22.7)	20.4 [15.5; NE]	1.6884 [1.1542; 2.5186] 0.0076	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Age at randomization						0.7921
<65 years of age	33 / 301 (11.0)	NE [NE; NE]	11 / 285 (3.9)	NE [NE; NE]	1.9098 [0.9875; 3.9865] 0.0621	
>=65 years of age	11 / 133 (8.3)	NE [26.8; NE]	4 / 132 (3.0)	NE [NE; NE]	2.3251 [0.7886; 8.4302] 0.1393	
Race						0.8227
Asian	8 / 153 (5.2)	NE [NE; NE]	2 / 147 (1.4)	NE [NE; NE]	2.3874 [0.5878; 15.9656] 0.2612	
White	31 / 231 (13.4)	NE [NE; NE]	12 / 223 (5.4)	NE [NE; NE]	1.9767 [1.0386; 4.0162] 0.0422	
Other	5 / 50 (10.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	2.1147 [0.3213; 41.5472] 0.4949	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.6501
Asia	8 / 148 (5.4)	NE [NE; NE]	2 / 144 (1.4)	NE [NE; NE]	2.5049 [0.6197; 16.7114] 0.2329	
Europe	26 / 227 (11.5)	NE [NE; NE]	10 / 206 (4.9)	NE [NE; NE]	1.6986 [0.8396; 3.7185] 0.1533	
Rest of the World	10 / 59 (16.9)	NE [NE; NE]	3 / 67 (4.5)	NE [NE; NE]	3.0939 [0.9383; 13.8681] 0.0727	
HER2 IHC expression						0.4598
IHC 1+	24 / 239 (10.0)	NE [NE; NE]	6 / 226 (2.7)	NE [NE; NE]	2.9021 [1.2568; 7.8697] 0.0153	
IHC 2+/ISH-	14 / 116 (12.1)	NE [NE; NE]	5 / 115 (4.3)	NE [NE; NE]	1.8795 [0.7104; 5.8660] 0.2235	
IHC >0 <1+	6 / 76 (7.9)	NE [NE; NE]	4 / 74 (5.4)	NE [NE; NE]	1.1116 [0.3155; 4.3706] 0.8704	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2540
Yes	42 / 393 (10.7)	NE [NE; NE]	15 / 377 (4.0)	NE [NE; NE]	1.9769 [1.1160; 3.6973] 0.0221	
No	2 / 41 (4.9)	NE [NE; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
Prior Taxane Use In The Non-Metastatic Setting						0.7460
Yes	14 / 177 (7.9)	NE [NE; NE]	4 / 172 (2.3)	NE [NE; NE]	2.5166 [0.8923; 8.9423] 0.0952	
No	30 / 257 (11.7)	NE [NE; NE]	11 / 245 (4.5)	NE [NE; NE]	1.9590 [1.0070; 4.1020] 0.0534	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0371
1	4 / 65 (6.2)	NE [NE; NE]	4 / 79 (5.1)	NE [NE; NE]	1.1023 [0.2602; 4.6687] 0.8907	
2	36 / 293 (12.3)	NE [NE; NE]	7 / 281 (2.5)	NE [NE; NE]	3.5439 [1.6697; 8.7240] 0.0012	
>=3	4 / 75 (5.3)	NE [26.8; NE]	4 / 56 (7.1)	NE [NE; NE]	0.5605 [0.1281; 2.4263] 0.4173	
ER/PR status I						0.6746
ER+, PR+	26 / 252 (10.3)	NE [NE; NE]	10 / 234 (4.3)	NE [NE; NE]	1.7818 [0.8825; 3.8953] 0.1177	
ER+, PR-	15 / 166 (9.0)	NE [NE; NE]	5 / 171 (2.9)	NE [NE; NE]	2.3211 [0.8848; 7.2093] 0.0982	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9558
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER >10%	36 / 362 (9.9)	NE [NE; NE]	12 / 343 (3.5)	NE [NE; NE]	2.0967 [1.1169; 4.2234] 0.0244	
Positive	8 / 51 (15.7)	NE [NE; NE]	3 / 60 (5.0)	NE [16.3; NE]	2.6257 [0.7574; 12.0087] 0.1398	
Endocrine Resistance						0.6869
Primary	11 / 127 (8.7)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	1.8078 [0.6513; 5.7792] 0.2695	
Secondary	33 / 307 (10.7)	NE [NE; NE]	10 / 279 (3.6)	NE [NE; NE]	2.2205 [1.1297; 4.7706] 0.0243	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.1598
Capecitabine	31 / 265 (11.7)	NE [NE; NE]	7 / 249 (2.8)	NE [NE; NE]	3.2716 [1.5225; 8.1097] 0.0028	
Nab-Paclitaxel	7 / 103 (6.8)	NE [NE; NE]	4 / 101 (4.0)	NE [NE; NE]	1.3249 [0.3920; 5.1273] 0.6572	
Paclitaxel	6 / 66 (9.1)	NE [NE; NE]	4 / 67 (6.0)	NE [NE; NE]	0.6972 [0.1887; 2.8471] 0.5900	
Prior anthracycline use						0.1134
Yes	21 / 197 (10.7)	NE [NE; NE]	4 / 198 (2.0)	NE [NE; NE]	4.0377 [1.5258; 13.9032] 0.0060	
No	23 / 237 (9.7)	NE [NE; NE]	11 / 219 (5.0)	NE [NE; NE]	1.4041 [0.6959; 3.0099] 0.3561	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.6916
Yes	30 / 294 (10.2)	NE [NE; NE]	9 / 275 (3.3)	NE [NE; NE]	2.3106 [1.1364; 5.1893] 0.0244	
No	14 / 140 (10.0)	NE [26.8; NE]	6 / 142 (4.2)	NE [NE; NE]	1.7478 [0.6948; 4.9698] 0.2508	
ECOG						0.8568
0	29 / 251 (11.6)	NE [NE; NE]	10 / 246 (4.1)	NE [NE; NE]	2.2484 [1.1296; 4.8677] 0.0240	
>=1	15 / 178 (8.4)	NE [NE; NE]	5 / 163 (3.1)	NE [NE; NE]	1.7600 [0.6702; 5.4757] 0.2748	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)						
Age at randomization						0.3832
<65 years of age	88 / 301 (29.2)	28.3 [19.3; NE]	89 / 285 (31.2)	26.5 [14.3; NE]	0.6598 [0.4884; 0.8910] 0.0063	
>=65 years of age	41 / 133 (30.8)	NE [16.6; NE]	44 / 132 (33.3)	14.3 [11.3; NE]	0.8040 [0.5224; 1.2348] 0.3148	
Race						0.7929
Asian	29 / 153 (19.0)	NE [28.3; NE]	28 / 147 (19.0)	27.9 [NE; NE]	0.7561 [0.4434; 1.2882] 0.3006	
White	80 / 231 (34.6)	19.3 [16.4; NE]	85 / 223 (38.1)	12.2 [9.5; NE]	0.6892 [0.5056; 0.9384] 0.0173	
Other	20 / 50 (40.0)	17.1 [9.5; NE]	20 / 47 (42.6)	10.3 [2.3; NE]	0.5541 [0.2873; 1.0644] 0.0716	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2986
Asia	28 / 148 (18.9)	NE [28.3; NE]	28 / 144 (19.4)	27.9 [26.5; NE]	0.7419 [0.4324; 1.2697] 0.2731	
Europe	73 / 227 (32.2)	NE [17.1; NE]	79 / 206 (38.3)	12.2 [9.1; 14.4]	0.5823 [0.4211; 0.8041] 0.0009	
Rest of the World	28 / 59 (47.5)	17.0 [5.5; 19.5]	26 / 67 (38.8)	11.3 [4.5; NE]	1.0376 [0.6029; 1.7900] 0.8970	
HER2 IHC expression						0.2665
IHC 1+	69 / 239 (28.9)	28.3 [19.1; NE]	68 / 226 (30.1)	NE [12.0; NE]	0.7531 [0.5355; 1.0587] 0.1009	
IHC 2+/ISH-	41 / 116 (35.3)	NE [14.6; NE]	38 / 115 (33.0)	14.4 [10.3; NE]	0.7333 [0.4673; 1.1527] 0.1753	
IHC >0 <1+	17 / 76 (22.4)	NE [19.5; NE]	27 / 74 (36.5)	26.5 [8.0; NE]	0.4514 [0.2404; 0.8242] 0.0089	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5768
Yes	121 / 393 (30.8)	NE [19.1; NE]	122 / 377 (32.4)	26.5 [12.5; NE]	0.7079 [0.5483; 0.9138] 0.0076	
No	8 / 41 (19.5)	NE [28.3; NE]	11 / 40 (27.5)	NE [9.6; NE]	0.5056 [0.1852; 1.2894] 0.1519	
Prior Taxane Use In The Non-Metastatic Setting						0.5273
Yes	45 / 177 (25.4)	NE [NE; NE]	53 / 172 (30.8)	NE [12.0; NE]	0.6687 [0.4456; 0.9989] 0.0486	
No	84 / 257 (32.7)	19.5 [17.1; NE]	80 / 245 (32.7)	26.5 [12.5; NE]	0.7136 [0.5229; 0.9744] 0.0325	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0810
1	16 / 65 (24.6)	NE [19.1; NE]	29 / 79 (36.7)	14.4 [7.3; NE]	0.5621 [0.2960; 1.0291] 0.0630	
2	90 / 293 (30.7)	28.3 [18.5; NE]	94 / 281 (33.5)	26.5 [11.9; NE]	0.6486 [0.4829; 0.8703] 0.0036	
>=3	23 / 75 (30.7)	NE [19.5; NE]	10 / 56 (17.9)	NE [14.3; NE]	1.4954 [0.7281; 3.3010] 0.2878	
ER/PR status I						0.1579
ER+, PR+	77 / 252 (30.6)	NE [17.1; NE]	69 / 234 (29.5)	26.5 [11.9; NE]	0.7763 [0.5591; 1.0800] 0.1296	
ER+, PR-	45 / 166 (27.1)	NE [19.5; NE]	60 / 171 (35.1)	27.9 [12.5; NE]	0.5755 [0.3854; 0.8522] 0.0056	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4863
ER <=10%	8 / 21 (38.1)	NE [4.8; NE]	3 / 14 (21.4)	NE [4.5; NE]	0.9477 [0.2475; 4.5242] 0.9416	
ER >10%	110 / 362 (30.4)	28.3 [19.3; NE]	109 / 343 (31.8)	26.5 [12.5; NE]	0.7102 [0.5422; 0.9300] 0.0123	
Positive	11 / 51 (21.6)	NE [NE; NE]	21 / 60 (35.0)	NE [6.5; NE]	0.4989 [0.2313; 1.0174] 0.0572	
Endocrine Resistance						0.9279
Primary	32 / 127 (25.2)	NE [19.1; NE]	37 / 137 (27.0)	NE [14.3; NE]	0.7296 [0.4496; 1.1772] 0.1951	
Secondary	97 / 307 (31.6)	28.3 [18.5; NE]	95 / 279 (34.1)	26.5 [11.9; NE]	0.6848 [0.5136; 0.9130] 0.0093	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0001
Capecitabine	100 / 265 (37.7)	19.3 [16.4; NE]	81 / 249 (32.5)	26.5 [11.9; NE]	0.9616 [0.7167; 1.2942] 0.7917	
Nab-Paclitaxel	13 / 103 (12.6)	NE [28.3; NE]	23 / 101 (22.8)	NE [14.4; NE]	0.4160 [0.1990; 0.8261] 0.0120	
Paclitaxel	16 / 66 (24.2)	NE [16.6; NE]	29 / 67 (43.3)	12.5 [2.1; NE]	0.1864 [0.0833; 0.3818] <.0001	
Prior anthracycline use						0.8017
Yes	57 / 197 (28.9)	NE [19.1; NE]	61 / 198 (30.8)	14.4 [12.0; NE]	0.7346 [0.5083; 1.0599] 0.0978	
No	72 / 237 (30.4)	28.3 [19.3; NE]	72 / 219 (32.9)	26.5 [12.2; NE]	0.6629 [0.4754; 0.9239] 0.0144	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.8985
Yes	86 / 294 (29.3)	28.3 [19.3; NE]	86 / 275 (31.3)	26.5 [12.2; NE]	0.6895 [0.5084; 0.9348] 0.0159	
No	43 / 140 (30.7)	NE [17.1; NE]	47 / 142 (33.1)	27.9 [9.6; NE]	0.7105 [0.4663; 1.0798] 0.1076	
ECOG						0.8974
0	72 / 251 (28.7)	28.3 [28.3; NE]	78 / 246 (31.7)	26.5 [14.3; NE]	0.6630 [0.4784; 0.9173] 0.0125	
>=1	55 / 178 (30.9)	NE [19.3; NE]	52 / 163 (31.9)	NE [10.3; NE]	0.7594 [0.5167; 1.1173] 0.1598	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia						
Age at randomization						0.6597
<65 years of age	21 / 301 (7.0)	NE [NE; NE]	29 / 285 (10.2)	NE [NE; NE]	0.4600 [0.2567; 0.8103] 0.0064	
>=65 years of age	11 / 133 (8.3)	NE [NE; NE]	16 / 132 (12.1)	NE [NE; NE]	0.5655 [0.2543; 1.2122] 0.1422	
Race						0.8604
Asian	4 / 153 (2.6)	NE [NE; NE]	6 / 147 (4.1)	NE [NE; NE]	0.4750 [0.1203; 1.6798] 0.2425	
White	23 / 231 (10.0)	NE [NE; NE]	35 / 223 (15.7)	NE [NE; NE]	0.4473 [0.2596; 0.7563] 0.0024	
Other	5 / 50 (10.0)	NE [NE; NE]	4 / 47 (8.5)	NE [NE; NE]	0.8566 [0.2181; 3.5500] 0.8219	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5742
Asia	4 / 148 (2.7)	NE [NE; NE]	6 / 144 (4.2)	NE [NE; NE]	0.4927 [0.1249; 1.7404] 0.2669	
Europe	17 / 227 (7.5)	NE [NE; NE]	26 / 206 (12.6)	NE [NE; NE]	0.3783 [0.1998; 0.6977] 0.0015	
Rest of the World	11 / 59 (18.6)	NE [19.1; NE]	13 / 67 (19.4)	NE [NE; NE]	0.8022 [0.3505; 1.8016] 0.5896	
HER2 IHC expression						0.6123
IHC 1+	14 / 239 (5.9)	NE [NE; NE]	25 / 226 (11.1)	NE [NE; NE]	0.3883 [0.1953; 0.7416] 0.0037	
IHC 2+/ISH-	10 / 116 (8.6)	NE [NE; NE]	13 / 115 (11.3)	NE [NE; NE]	0.5406 [0.2286; 1.2404] 0.1425	
IHC >0 <1+	7 / 76 (9.2)	NE [19.5; NE]	7 / 74 (9.5)	NE [NE; NE]	0.7496 [0.2545; 2.2069] 0.5916	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4794
Yes	28 / 393 (7.1)	NE [NE; NE]	41 / 377 (10.9)	NE [NE; NE]	0.4714 [0.2871; 0.7630] 0.0020	
No	4 / 41 (9.8)	NE [NE; NE]	4 / 40 (10.0)	NE [NE; NE]	0.7337 [0.1716; 3.1346] 0.6630	
Prior Taxane Use In The Non-Metastatic Setting						0.9480
Yes	9 / 177 (5.1)	NE [NE; NE]	13 / 172 (7.6)	NE [NE; NE]	0.5216 [0.2132; 1.2205] 0.1315	
No	23 / 257 (8.9)	NE [NE; NE]	32 / 245 (13.1)	NE [NE; NE]	0.4843 [0.2788; 0.8281] 0.0073	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.9133
1	3 / 65 (4.6)	NE [NE; NE]	7 / 79 (8.9)	NE [NE; NE]	0.3908 [0.0831; 1.4283] 0.1638	
2	25 / 293 (8.5)	NE [NE; NE]	34 / 281 (12.1)	NE [NE; NE]	0.4875 [0.2862; 0.8190] 0.0060	
>=3	4 / 75 (5.3)	NE [NE; NE]	4 / 56 (7.1)	NE [NE; NE]	0.6069 [0.1416; 2.5955] 0.4800	
ER/PR status I						0.3712
ER+, PR+	19 / 252 (7.5)	NE [NE; NE]	24 / 234 (10.3)	NE [NE; NE]	0.5262 [0.2830; 0.9646] 0.0356	
ER+, PR-	9 / 166 (5.4)	NE [NE; NE]	20 / 171 (11.7)	NE [NE; NE]	0.3399 [0.1454; 0.7344] 0.0057	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9134
ER <=10%	2 / 21 (9.5)	NE [9.5; NE]	1 / 14 (7.1)	NE [4.5; NE]	0.0000 [NE; 2.5488] 0.1306	
ER >10%	26 / 362 (7.2)	NE [NE; NE]	35 / 343 (10.2)	NE [NE; NE]	0.5050 [0.2992; 0.8414] 0.0080	
Positive	4 / 51 (7.8)	NE [NE; NE]	9 / 60 (15.0)	NE [NE; NE]	0.4236 [0.1143; 1.3064] 0.1421	
Endocrine Resistance						0.5309
Primary	8 / 127 (6.3)	NE [NE; NE]	10 / 137 (7.3)	NE [NE; NE]	0.6582 [0.2489; 1.6840] 0.3796	
Secondary	24 / 307 (7.8)	NE [NE; NE]	35 / 279 (12.5)	NE [NE; NE]	0.4439 [0.2596; 0.7463] 0.0019	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.5361
Capecitabine	25 / 265 (9.4)	NE [NE; NE]	32 / 249 (12.9)	NE [NE; NE]	0.5472 [0.3204; 0.9243] 0.0229	
Nab-Paclitaxel	2 / 103 (1.9)	NE [NE; NE]	4 / 101 (4.0)	NE [NE; NE]	0.4670 [0.0647; 2.3941] 0.3680	
Paclitaxel	5 / 66 (7.6)	NE [NE; NE]	9 / 67 (13.4)	NE [NE; NE]	0.2084 [0.0522; 0.6869] 0.0082	
Prior anthracycline use						0.2190
Yes	16 / 197 (8.1)	NE [NE; NE]	17 / 198 (8.6)	NE [NE; NE]	0.6390 [0.3158; 1.2860] 0.2037	
No	16 / 237 (6.8)	NE [NE; NE]	28 / 219 (12.8)	NE [NE; NE]	0.3940 [0.2075; 0.7227] 0.0023	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9857
Yes	23 / 294 (7.8)	NE [NE; NE]	31 / 275 (11.3)	NE [NE; NE]	0.4817 [0.2760; 0.8288] 0.0075	
No	9 / 140 (6.4)	NE [NE; NE]	14 / 142 (9.9)	NE [NE; NE]	0.4932 [0.2035; 1.1352] 0.0954	
ECOG						0.9426
0	18 / 251 (7.2)	NE [NE; NE]	28 / 246 (11.4)	NE [NE; NE]	0.4714 [0.2551; 0.8492] 0.0116	
>=1	12 / 178 (6.7)	NE [NE; NE]	17 / 163 (10.4)	NE [NE; NE]	0.4308 [0.1976; 0.9092] 0.0248	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Blood and lymphatic system disorders; PT: Anaemia						
Age at randomization						0.7746
<65 years of age	104 / 301 (34.6)	NE [21.5; NE]	64 / 285 (22.5)	NE [NE; NE]	1.3426 [0.9841; 1.8456] 0.0665	
>=65 years of age	55 / 133 (41.4)	NE [8.9; NE]	43 / 132 (32.6)	NE [14.3; NE]	1.2408 [0.8340; 1.8580] 0.2875	
Race						0.5801
Asian	68 / 153 (44.4)	16.1 [9.0; NE]	41 / 147 (27.9)	NE [NE; NE]	1.4201 [0.9673; 2.1106] 0.0763	
White	74 / 231 (32.0)	NE [21.5; NE]	57 / 223 (25.6)	NE [18.7; NE]	1.1418 [0.8087; 1.6203] 0.4576	
Other	17 / 50 (34.0)	NE [9.3; NE]	9 / 47 (19.1)	NE [NE; NE]	1.7013 [0.7673; 4.0243] 0.2004	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5267
Asia	67 / 148 (45.3)	16.1 [8.5; NE]	42 / 144 (29.2)	NE [NE; NE]	1.3676 [0.9327; 2.0281] 0.1122	
Europe	84 / 227 (37.0)	NE [21.5; NE]	55 / 206 (26.7)	NE [NE; NE]	1.2883 [0.9188; 1.8208] 0.1470	
Rest of the World	8 / 59 (13.6)	NE [NE; NE]	10 / 67 (14.9)	NE [18.7; NE]	0.7634 [0.2885; 1.9539] 0.5712	
HER2 IHC expression						0.4341
IHC 1+	90 / 239 (37.7)	25.9 [16.1; NE]	56 / 226 (24.8)	NE [NE; NE]	1.3781 [0.9890; 1.9368] 0.0597	
IHC 2+/ISH-	36 / 116 (31.0)	NE [21.5; NE]	30 / 115 (26.1)	NE [NE; NE]	1.0140 [0.6234; 1.6609] 0.9649	
IHC >0 <1+	32 / 76 (42.1)	NE [4.6; NE]	21 / 74 (28.4)	NE [18.7; NE]	1.4454 [0.8382; 2.5452] 0.1886	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8734
Yes	141 / 393 (35.9)	NE [21.5; NE]	93 / 377 (24.7)	NE [NE; NE]	1.3026 [1.0032; 1.6990] 0.0486	
No	18 / 41 (43.9)	NE [2.9; NE]	14 / 40 (35.0)	18.7 [6.6; NE]	1.2057 [0.5989; 2.4762] 0.6066	
Prior Taxane Use In The Non-Metastatic Setting						0.3541
Yes	67 / 177 (37.9)	25.9 [16.1; NE]	40 / 172 (23.3)	NE [NE; NE]	1.4961 [1.0145; 2.2347] 0.0445	
No	92 / 257 (35.8)	NE [18.8; NE]	67 / 245 (27.3)	NE [18.7; NE]	1.1620 [0.8485; 1.5995] 0.3524	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.8659
1	26 / 65 (40.0)	NE [6.2; NE]	21 / 79 (26.6)	NE [NE; NE]	1.4650 [0.8223; 2.6398] 0.2003	
2	106 / 293 (36.2)	25.9 [21.5; NE]	72 / 281 (25.6)	NE [NE; NE]	1.2366 [0.9175; 1.6760] 0.1646	
>=3	26 / 75 (34.7)	NE [11.7; NE]	14 / 56 (25.0)	NE [NE; NE]	1.3039 [0.6909; 2.5679] 0.4256	
ER/PR status I						0.8247
ER+, PR+	92 / 252 (36.5)	NE [18.8; NE]	58 / 234 (24.8)	NE [NE; NE]	1.3372 [0.9645; 1.8688] 0.0842	
ER+, PR-	63 / 166 (38.0)	NE [16.1; NE]	46 / 171 (26.9)	NE [NE; NE]	1.2621 [0.8627; 1.8598] 0.2342	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9445
ER <=10%	7 / 21 (33.3)	NE [2.1; NE]	3 / 14 (21.4)	NE [1.9; NE]	1.3491 [0.3727; 6.2858] 0.6617	
ER >10%	137 / 362 (37.8)	25.9 [18.8; NE]	90 / 343 (26.2)	NE [NE; NE]	1.3015 [0.9983; 1.7051] 0.0533	
Positive	15 / 51 (29.4)	NE [11.7; NE]	14 / 60 (23.3)	NE [NE; NE]	1.1335 [0.5427; 2.3812] 0.7388	
Endocrine Resistance						0.1468
Primary	46 / 127 (36.2)	25.9 [16.1; NE]	43 / 137 (31.4)	NE [11.2; NE]	0.9624 [0.6306; 1.4704] 0.8544	
Secondary	113 / 307 (36.8)	NE [21.5; NE]	64 / 279 (22.9)	NE [NE; NE]	1.4826 [1.0941; 2.0265] 0.0116	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0654
Capecitabine	90 / 265 (34.0)	NE [NE; NE]	48 / 249 (19.3)	NE [NE; NE]	1.6350 [1.1570; 2.3394] 0.0056	
Nab-Paclitaxel	47 / 103 (45.6)	16.1 [6.3; NE]	37 / 101 (36.6)	NE [14.3; NE]	1.1127 [0.7209; 1.7297] 0.6332	
Paclitaxel	22 / 66 (33.3)	NE [21.5; NE]	22 / 67 (32.8)	NE [NE; NE]	0.8545 [0.4630; 1.5706] 0.6045	
Prior anthracycline use						0.2536
Yes	64 / 197 (32.5)	NE [25.9; NE]	51 / 198 (25.8)	NE [NE; NE]	1.1288 [0.7810; 1.6395] 0.5232	
No	95 / 237 (40.1)	21.5 [11.7; NE]	56 / 219 (25.6)	NE [18.7; NE]	1.4372 [1.0358; 2.0130] 0.0311	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.4392
Yes	106 / 294 (36.1)	25.9 [21.5; NE]	73 / 275 (26.5)	NE [NE; NE]	1.2181 [0.9047; 1.6490] 0.1995	
No	53 / 140 (37.9)	NE [16.1; NE]	34 / 142 (23.9)	NE [18.7; NE]	1.4371 [0.9370; 2.2338] 0.0985	
ECOG						0.8706
0	79 / 251 (31.5)	NE [25.9; NE]	54 / 246 (22.0)	NE [NE; NE]	1.2729 [0.9016; 1.8106] 0.1750	
>=1	77 / 178 (43.3)	21.5 [7.3; NE]	51 / 163 (31.3)	NE [NE; NE]	1.2642 [0.8890; 1.8129] 0.1950	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Infections and infestations; PT: COVID-19						
Age at randomization						0.8150
<65 years of age	76 / 301 (25.2)	NE [18.6; NE]	33 / 285 (11.6)	NE [NE; NE]	1.4428 [0.9635; 2.2077] 0.0804	
>=65 years of age	30 / 133 (22.6)	NE [19.5; NE]	19 / 132 (14.4)	NE [NE; NE]	1.3241 [0.7500; 2.3959] 0.3385	
Race						0.7723
Asian	44 / 153 (28.8)	18.6 [16.1; NE]	26 / 147 (17.7)	NE [14.9; NE]	1.1857 [0.7331; 1.9561] 0.4944	
White	51 / 231 (22.1)	NE [NE; NE]	23 / 223 (10.3)	NE [NE; NE]	1.6451 [1.0157; 2.7473] 0.0465	
Other	11 / 50 (22.0)	NE [15.9; NE]	3 / 47 (6.4)	NE [NE; NE]	1.8160 [0.5377; 8.2773] 0.3696	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5252
Asia	43 / 148 (29.1)	18.6 [16.1; NE]	24 / 144 (16.7)	NE [14.9; NE]	1.2745 [0.7777; 2.1379] 0.3439	
Europe	46 / 227 (20.3)	NE [NE; NE]	21 / 206 (10.2)	NE [NE; NE]	1.3665 [0.8225; 2.3456] 0.2384	
Rest of the World	17 / 59 (28.8)	NE [12.6; NE]	7 / 67 (10.4)	NE [13.7; NE]	2.2873 [0.9812; 5.9402] 0.0598	
HER2 IHC expression						0.6101
IHC 1+	67 / 239 (28.0)	20.0 [16.4; NE]	31 / 226 (13.7)	NE [19.3; NE]	1.5416 [1.0134; 2.3972] 0.0463	
IHC 2+/ISH-	22 / 116 (19.0)	NE [NE; NE]	13 / 115 (11.3)	NE [NE; NE]	1.1037 [0.5590; 2.2668] 0.7803	
IHC >0 <1+	17 / 76 (22.4)	NE [NE; NE]	8 / 74 (10.8)	NE [NE; NE]	1.5004 [0.6620; 3.7001] 0.3448	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3545
Yes	96 / 393 (24.4)	NE [19.5; NE]	44 / 377 (11.7)	NE [NE; NE]	1.4859 [1.0439; 2.1484] 0.0300	
No	10 / 41 (24.4)	NE [20.0; NE]	8 / 40 (20.0)	19.3 [11.7; NE]	0.9092 [0.3550; 2.4022] 0.8425	
Prior Taxane Use In The Non-Metastatic Setting						0.4791
Yes	47 / 177 (26.6)	NE [16.1; NE]	20 / 172 (11.6)	NE [NE; NE]	1.5934 [0.9541; 2.7599] 0.0811	
No	59 / 257 (23.0)	NE [20.0; NE]	32 / 245 (13.1)	NE [NE; NE]	1.2878 [0.8405; 2.0087] 0.2527	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5289
1	17 / 65 (26.2)	19.5 [12.4; NE]	8 / 79 (10.1)	NE [19.3; NE]	2.0315 [0.8975; 5.0065] 0.0938	
2	73 / 293 (24.9)	NE [20.0; NE]	35 / 281 (12.5)	NE [NE; NE]	1.3864 [0.9308; 2.1043] 0.1137	
>=3	16 / 75 (21.3)	NE [15.6; NE]	9 / 56 (16.1)	NE [13.3; NE]	1.0790 [0.4833; 2.5631] 0.8588	
ER/PR status I						0.3526
ER+, PR+	56 / 252 (22.2)	NE [NE; NE]	31 / 234 (13.2)	NE [19.3; NE]	1.1729 [0.7589; 1.8459] 0.4793	
ER+, PR-	45 / 166 (27.1)	NE [18.6; NE]	21 / 171 (12.3)	NE [NE; NE]	1.6214 [0.9735; 2.7885] 0.0677	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9846
ER <=10%	4 / 21 (19.0)	NE [12.4; NE]	1 / 14 (7.1)	NE [NE; NE]	1.3863 [0.1847; 28.1437] 0.7766	
ER >10%	93 / 362 (25.7)	NE [19.5; NE]	45 / 343 (13.1)	NE [NE; NE]	1.4032 [0.9857; 2.0265] 0.0636	
Positive	9 / 51 (17.6)	NE [12.8; NE]	6 / 60 (10.0)	NE [NE; NE]	1.5209 [0.5470; 4.5469] 0.4241	
Endocrine Resistance						0.3377
Primary	28 / 127 (22.0)	NE [16.4; NE]	12 / 137 (8.8)	NE [19.3; NE]	1.8445 [0.9554; 3.7855] 0.0737	
Secondary	78 / 307 (25.4)	NE [20.0; NE]	40 / 279 (14.3)	NE [NE; NE]	1.2740 [0.8731; 1.8876] 0.2159	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.1015
Capecitabine	71 / 265 (26.8)	NE [16.4; NE]	29 / 249 (11.6)	NE [NE; NE]	1.7769 [1.1656; 2.7822] 0.0084	
Nab-Paclitaxel	24 / 103 (23.3)	20.0 [16.4; NE]	21 / 101 (20.8)	19.3 [19.3; NE]	0.8494 [0.4677; 1.5527] 0.5889	
Paclitaxel	11 / 66 (16.7)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	2.6570 [0.6565; 17.7835] 0.2047	
Prior anthracycline use						0.9072
Yes	49 / 197 (24.9)	NE [16.4; NE]	25 / 198 (12.6)	NE [NE; NE]	1.4052 [0.8726; 2.3193] 0.1687	
No	57 / 237 (24.1)	NE [20.0; NE]	27 / 219 (12.3)	NE [NE; NE]	1.4197 [0.9046; 2.2838] 0.1346	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.7197
Yes	69 / 294 (23.5)	NE [19.5; NE]	31 / 275 (11.3)	NE [NE; NE]	1.5097 [0.9947; 2.3435] 0.0568	
No	37 / 140 (26.4)	NE [20.0; NE]	21 / 142 (14.8)	NE [14.1; NE]	1.2687 [0.7458; 2.2145] 0.3874	
ECOG						0.8595
0	64 / 251 (25.5)	NE [19.5; NE]	33 / 246 (13.4)	NE [NE; NE]	1.3772 [0.9097; 2.1241] 0.1357	
>=1	39 / 178 (21.9)	NE [NE; NE]	17 / 163 (10.4)	NE [NE; NE]	1.5079 [0.8611; 2.7522] 0.1607	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: General disorders and administration site conditions; PT: Oedema peripheral						
Age at randomization						0.3919
<65 years of age	23 / 301 (7.6)	NE [NE; NE]	30 / 285 (10.5)	NE [NE; NE]	0.5336 [0.3045; 0.9229] 0.0234	
>=65 years of age	13 / 133 (9.8)	NE [NE; NE]	29 / 132 (22.0)	NE [NE; NE]	0.3646 [0.1829; 0.6879] 0.0017	
Race						0.3720
Asian	11 / 153 (7.2)	NE [NE; NE]	18 / 147 (12.2)	NE [NE; NE]	0.4479 [0.2039; 0.9404] 0.0327	
White	23 / 231 (10.0)	NE [NE; NE]	34 / 223 (15.2)	NE [NE; NE]	0.5135 [0.2978; 0.8695] 0.0125	
Other	2 / 50 (4.0)	NE [NE; NE]	7 / 47 (14.9)	NE [NE; NE]	0.1624 [0.0228; 0.7186] 0.0156	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4043
Asia	10 / 148 (6.8)	NE [NE; NE]	16 / 144 (11.1)	NE [NE; NE]	0.4672 [0.2038; 1.0203] 0.0549	
Europe	18 / 227 (7.9)	NE [NE; NE]	33 / 206 (16.0)	NE [NE; NE]	0.3751 [0.2057; 0.6622] 0.0006	
Rest of the World	8 / 59 (13.6)	NE [NE; NE]	10 / 67 (14.9)	NE [12.4; NE]	0.7057 [0.2669; 1.8050] 0.4648	
HER2 IHC expression						0.7912
IHC 1+	19 / 239 (7.9)	NE [NE; NE]	28 / 226 (12.4)	NE [NE; NE]	0.5028 [0.2754; 0.8981] 0.0194	
IHC 2+/ISH-	12 / 116 (10.3)	NE [NE; NE]	20 / 115 (17.4)	NE [NE; NE]	0.4369 [0.2054; 0.8901] 0.0216	
IHC >0 <1+	5 / 76 (6.6)	NE [NE; NE]	11 / 74 (14.9)	NE [NE; NE]	0.3235 [0.1011; 0.8983] 0.0293	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.7165
Yes	34 / 393 (8.7)	NE [NE; NE]	54 / 377 (14.3)	NE [NE; NE]	0.4617 [0.2970; 0.7080] 0.0003	
No	2 / 41 (4.9)	NE [NE; NE]	5 / 40 (12.5)	NE [17.4; NE]	0.2680 [0.0378; 1.2723] 0.0975	
Prior Taxane Use In The Non-Metastatic Setting						0.9761
Yes	17 / 177 (9.6)	NE [NE; NE]	28 / 172 (16.3)	NE [NE; NE]	0.4483 [0.2385; 0.8180] 0.0084	
No	19 / 257 (7.4)	NE [NE; NE]	31 / 245 (12.7)	NE [NE; NE]	0.4430 [0.2451; 0.7800] 0.0044	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 9:57; Program name: T.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: T.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0206
1	10 / 65 (15.4)	NE [NE; NE]	7 / 79 (8.9)	NE [17.4; NE]	1.5934 [0.6045; 4.4246] 0.3455	
2	20 / 293 (6.8)	NE [NE; NE]	42 / 281 (14.9)	NE [NE; NE]	0.3209 [0.1836; 0.5420] <.0001	
>=3	6 / 75 (8.0)	NE [NE; NE]	10 / 56 (17.9)	NE [NE; NE]	0.3882 [0.1318; 1.0482] 0.0581	
ER/PR status I						0.0337
ER+, PR+	23 / 252 (9.1)	NE [NE; NE]	25 / 234 (10.7)	NE [NE; NE]	0.6631 [0.3723; 1.1755] 0.1560	
ER+, PR-	10 / 166 (6.0)	NE [NE; NE]	31 / 171 (18.1)	NE [17.4; NE]	0.2478 [0.1144; 0.4920] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7501
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	2 / 14 (14.3)	NE [4.4; NE]	0.2336 [0.0108; 2.4756] 0.1999	
ER >10%	31 / 362 (8.6)	NE [NE; NE]	49 / 343 (14.3)	NE [NE; NE]	0.4524 [0.2845; 0.7087] 0.0005	
Positive	4 / 51 (7.8)	NE [NE; NE]	8 / 60 (13.3)	NE [NE; NE]	0.4851 [0.1288; 1.5497] 0.2296	
Endocrine Resistance						0.7004
Primary	11 / 127 (8.7)	NE [NE; NE]	18 / 137 (13.1)	NE [17.4; NE]	0.4578 [0.2064; 0.9697] 0.0406	
Secondary	25 / 307 (8.1)	NE [NE; NE]	41 / 279 (14.7)	NE [NE; NE]	0.4315 [0.2581; 0.7069] 0.0007	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.4795
Capecitabine	22 / 265 (8.3)	NE [NE; NE]	29 / 249 (11.6)	NE [NE; NE]	0.5712 [0.3236; 0.9940] 0.0462	
Nab-Paclitaxel	7 / 103 (6.8)	NE [NE; NE]	18 / 101 (17.8)	NE [17.4; NE]	0.3106 [0.1196; 0.7205] 0.0063	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	12 / 67 (17.9)	NE [NE; NE]	0.3018 [0.1059; 0.7867] 0.0125	
Prior anthracycline use						0.8092
Yes	19 / 197 (9.6)	NE [NE; NE]	33 / 198 (16.7)	NE [NE; NE]	0.4365 [0.2420; 0.7649] 0.0035	
No	17 / 237 (7.2)	NE [NE; NE]	26 / 219 (11.9)	NE [NE; NE]	0.4620 [0.2453; 0.8477] 0.0118	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5134
Yes	26 / 294 (8.8)	NE [NE; NE]	37 / 275 (13.5)	NE [NE; NE]	0.4884 [0.2910; 0.8075] 0.0048	
No	10 / 140 (7.1)	NE [NE; NE]	22 / 142 (15.5)	NE [NE; NE]	0.3624 [0.1635; 0.7488] 0.0058	
ECOG						0.1898
0	17 / 251 (6.8)	NE [NE; NE]	36 / 246 (14.6)	NE [NE; NE]	0.3478 [0.1900; 0.6118] 0.0002	
>=1	19 / 178 (10.7)	NE [NE; NE]	21 / 163 (12.9)	NE [17.4; NE]	0.6601 [0.3496; 1.2378] 0.1913	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Tabelle 2.28.3 Unerwünschte Ereignisse nach SOC und PT mit Inzidenz ≥10 % in mindestens einem Arm – Subgruppenanalyse – Interaktions-p-Wert <0,05 – SAF

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: All (any PT)						
Age at randomization						0.0174
<65 years of age	269 / 301 (89.4)	0.1 [0.1; 0.1]	174 / 285 (61.1)	2.1 [1.2; 3.3]	2.5850 [2.1324; 3.1424] <.0001	
>=65 years of age	107 / 133 (80.5)	0.2 [0.1; 0.4]	82 / 132 (62.1)	1.2 [0.7; 4.3]	1.7520 [1.3144; 2.3438] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Nausea						
Number of prior lines of endocrine therapy in the metastatic setting						0.0216
1	53 / 65 (81.5)	0.1 [0.1; 0.2]	22 / 79 (27.8)	NE [NE; NE]	5.6259 [3.4349; 9.5236] <.0001	
2	203 / 293 (69.3)	0.2 [0.1; 0.3]	82 / 281 (29.2)	NE [NE; NE]	3.4011 [2.6397; 4.4246] <.0001	
>=3	46 / 75 (61.3)	0.8 [0.2; 3.9]	22 / 56 (39.3)	14.0 [1.8; NE]	1.9980 [1.2160; 3.3853] 0.0067	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Constipation						
Prior Taxane Use In The Non-Metastatic Setting						0.0236
Yes	55 / 177 (31.1)	NE [NE; NE]	35 / 172 (20.3)	NE [NE; NE]	1.4729 [0.9662; 2.2746] 0.0741	
No	82 / 257 (31.9)	NE [23.5; NE]	27 / 245 (11.0)	NE [NE; NE]	2.8627 [1.8776; 4.5056] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior anthracycline use						0.0335
Yes	61 / 197 (31.0)	NE [NE; NE]	38 / 198 (19.2)	NE [NE; NE]	1.5628 [1.0452; 2.3661] 0.0306	
No	76 / 237 (32.1)	NE [23.5; NE]	24 / 219 (11.0)	NE [NE; NE]	2.9155 [1.8707; 4.7130] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Vomiting						
Region						0.0439
Asia	48 / 148 (32.4)	NE [NE; NE]	8 / 144 (5.6)	NE [23.6; NE]	6.4820 [3.2460; 14.8275] <.0001	
Europe	73 / 227 (32.2)	NE [NE; NE]	29 / 206 (14.1)	NE [NE; NE]	2.3914 [1.5725; 3.7349] <.0001	
Rest of the World	25 / 59 (42.4)	18.6 [6.2; NE]	12 / 67 (17.9)	NE [NE; NE]	2.3710 [1.2113; 4.9047] 0.0119	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Dyspepsia						
Race						0.0171
Asian	7 / 153 (4.6)	NE [NE; NE]	9 / 147 (6.1)	NE [NE; NE]	0.6639 [0.2366; 1.7865] 0.4144	
White	41 / 231 (17.7)	NE [NE; NE]	10 / 223 (4.5)	NE [NE; NE]	3.5711 [1.8604; 7.5562] 0.0001	
Other	2 / 50 (4.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	1.2054 [0.1036; 27.2290] 0.8832	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0240
Yes	50 / 393 (12.7)	NE [NE; NE]	18 / 377 (4.8)	NE [NE; NE]	2.3021 [1.3656; 4.0608] 0.0019	
No	0 / 41 (0.0)	NE [NE; NE]	2 / 40 (5.0)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: All (any PT)						
Region						0.0161
Asia	84 / 148 (56.8)	5.6 [4.0; 14.6]	37 / 144 (25.7)	NE [NE; NE]	2.3775 [1.6277; 3.5428] <.0001	
Europe	80 / 227 (35.2)	NE [20.3; NE]	53 / 206 (25.7)	NE [NE; NE]	1.2126 [0.8573; 1.7288] 0.2786	
Rest of the World	33 / 59 (55.9)	5.7 [1.4; NE]	17 / 67 (25.4)	20.8 [20.8; NE]	2.4511 [1.3810; 4.5116] 0.0020	
HER2 IHC expression						0.0331
IHC 1+	103 / 239 (43.1)	19.1 [12.1; NE]	54 / 226 (23.9)	NE [NE; NE]	1.7690 [1.2766; 2.4789] 0.0006	
IHC 2+/ISH-	61 / 116 (52.6)	9.0 [4.4; NE]	25 / 115 (21.7)	NE [NE; NE]	2.4474 [1.5532; 3.9739] 0.0001	
IHC >0 <1+	32 / 76 (42.1)	18.9 [6.2; NE]	28 / 74 (37.8)	20.8 [4.1; NE]	1.0169 [0.6115; 1.7009] 0.9451	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Endocrine Resistance						0.0174
Primary	51 / 127 (40.2)	14.6 [11.1; NE]	44 / 137 (32.1)	NE [9.8; NE]	1.1070 [0.7375; 1.6684] 0.6221	
Secondary	146 / 307 (47.6)	14.0 [7.9; NE]	63 / 279 (22.6)	NE [NE; NE]	2.1385 [1.5989; 2.8955] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0498
Yes	127 / 294 (43.2)	18.9 [13.1; NE]	76 / 275 (27.6)	NE [NE; NE]	1.4631 [1.1021; 1.9553] 0.0088	
No	70 / 140 (50.0)	10.0 [5.6; NE]	31 / 142 (21.8)	NE [20.8; NE]	2.3942 [1.5833; 3.7070] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Race						0.0239
Asian	50 / 153 (32.7)	NE [NE; NE]	12 / 147 (8.2)	NE [NE; NE]	4.3076 [2.3742; 8.4810] <.0001	
White	54 / 231 (23.4)	NE [NE; NE]	29 / 223 (13.0)	NE [NE; NE]	1.7301 [1.1098; 2.7530] 0.0161	
Other	10 / 50 (20.0)	NE [NE; NE]	7 / 47 (14.9)	NE [NE; NE]	1.2134 [0.4566; 3.3873] 0.7017	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0009
Asia	46 / 148 (31.1)	NE [NE; NE]	11 / 144 (7.6)	NE [NE; NE]	4.3148 [2.3198; 8.7752] <.0001	
Europe	47 / 227 (20.7)	NE [NE; NE]	32 / 206 (15.5)	NE [NE; NE]	1.2558 [0.8033; 1.9879] 0.3212	
Rest of the World	21 / 59 (35.6)	NE [10.3; NE]	5 / 67 (7.5)	NE [NE; NE]	5.0305 [2.0464; 15.0863] 0.0003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0006
Yes	64 / 294 (21.8)	NE [NE; NE]	38 / 275 (13.8)	NE [NE; NE]	1.5024 [1.0096; 2.2663] 0.0465	
No	50 / 140 (35.7)	NE [NE; NE]	10 / 142 (7.0)	NE [NE; NE]	5.5005 [2.9143; 11.5160] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia						
Region						0.0423
Asia	70 / 148 (47.3)	NE [2.3; NE]	33 / 144 (22.9)	NE [NE; NE]	2.1777 [1.4521; 3.3350] 0.0002	
Europe	109 / 227 (48.0)	9.7 [3.5; NE]	47 / 206 (22.8)	NE [NE; NE]	2.2457 [1.6065; 3.1908] <.0001	
Rest of the World	31 / 59 (52.5)	4.4 [1.0; NE]	7 / 67 (10.4)	NE [NE; NE]	6.1432 [2.8631; 15.2121] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						<.0001
Capecitabine	135 / 265 (50.9)	5.5 [2.2; NE]	7 / 249 (2.8)	NE [NE; NE]	23.1606 [11.6856; 54.7105] <.0001	
Nab-Paclitaxel	41 / 103 (39.8)	NE [5.4; NE]	46 / 101 (45.5)	NE [1.1; NE]	0.7691 [0.5031; 1.1717] 0.2220	
Paclitaxel	34 / 66 (51.5)	7.4 [1.4; NE]	34 / 67 (50.7)	2.3 [1.0; NE]	0.7746 [0.4780; 1.2544] 0.2986	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0019
0	122 / 251 (48.6)	11.7 [2.8; NE]	38 / 246 (15.4)	NE [NE; NE]	3.5678 [2.5042; 5.2026] <.0001	
>=1	85 / 178 (47.8)	9.7 [2.6; NE]	49 / 163 (30.1)	NE [NE; NE]	1.6018 [1.1321; 2.2916] 0.0081	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)						
Age at randomization						0.0156
<65 years of age	182 / 301 (60.5)	2.2 [1.4; 3.8]	183 / 285 (64.2)	2.1 [1.4; 2.8]	0.8241 [0.6701; 1.0133] 0.0625	
>=65 years of age	68 / 133 (51.1)	6.3 [3.3; NE]	95 / 132 (72.0)	1.4 [1.2; 2.1]	0.4920 [0.3573; 0.6737] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome						
Region						0.0404
Asia	0 / 148 (0.0)	NE [NE; NE]	52 / 144 (36.1)	NE [9.5; NE]	NE [NE; NE] NE	
Europe	4 / 227 (1.8)	NE [NE; NE]	62 / 206 (30.1)	NE [12.5; NE]	0.0369 [0.0111; 0.0902] <.0001	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	32 / 67 (47.8)	5.2 [2.1; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 13DEC2024 11:07; Program name: T.2.28.3_10PCTTEAE_SAF_SUB_SIG.sas; Output name: T.2.28.3_10PCTTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: All (any PT)						
Region						0.0379
Asia	45 / 148 (30.4)	NE [NE; NE]	57 / 144 (39.6)	11.8 [7.7; NE]	0.6684 [0.4489; 0.9893] 0.0433	
Europe	88 / 227 (38.8)	22.0 [13.9; NE]	100 / 206 (48.5)	7.4 [3.4; 12.5]	0.6108 [0.4559; 0.8168] 0.0008	
Rest of the World	36 / 59 (61.0)	5.3 [2.0; 9.3]	31 / 67 (46.3)	7.2 [2.3; NE]	1.2617 [0.7776; 2.0573] 0.3506	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0125
1	30 / 65 (46.2)	11.3 [3.7; NE]	33 / 79 (41.8)	8.0 [4.9; NE]	0.9975 [0.6008; 1.6481] 0.9848	
2	118 / 293 (40.3)	NE [14.5; NE]	122 / 281 (43.4)	9.5 [5.8; 20.9]	0.7932 [0.6142; 1.0240] 0.0726	
>=3	21 / 75 (28.0)	NE [14.9; NE]	32 / 56 (57.1)	4.1 [2.2; 10.9]	0.3009 [0.1680; 0.5268] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						<.0001
Capecitabine	125 / 265 (47.2)	13.4 [6.5; NE]	87 / 249 (34.9)	18.1 [10.9; NE]	1.2718 [0.9678; 1.6788] 0.0886	
Nab-Paclitaxel	22 / 103 (21.4)	NE [NE; NE]	51 / 101 (50.5)	6.6 [4.6; 11.9]	0.2997 [0.1763; 0.4926] <.0001	
Paclitaxel	22 / 66 (33.3)	NE [13.1; NE]	50 / 67 (74.6)	1.4 [1.0; 2.1]	0.2045 [0.1148; 0.3499] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0020
0	107 / 251 (42.6)	22.0 [11.3; NE]	100 / 246 (40.7)	14.3 [7.7; NE]	0.9529 [0.7242; 1.2550] 0.7179	
>=1	61 / 178 (34.3)	NE [14.2; NE]	85 / 163 (52.1)	4.0 [2.8; 9.1]	0.4664 [0.3319; 0.6512] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Dysgeusia						
Region						0.0172
Asia	15 / 148 (10.1)	NE [NE; NE]	4 / 144 (2.8)	NE [NE; NE]	3.4084 [1.2350; 11.9687] 0.0207	
Europe	27 / 227 (11.9)	NE [NE; NE]	19 / 206 (9.2)	NE [NE; NE]	1.0595 [0.5898; 1.9418] 0.8473	
Rest of the World	9 / 59 (15.3)	NE [NE; NE]	1 / 67 (1.5)	NE [NE; NE]	9.5313 [1.7840; 175.9174] 0.0090	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0067
Capecitabine	40 / 265 (15.1)	NE [NE; NE]	11 / 249 (4.4)	NE [NE; NE]	3.0479 [1.6183; 6.2490] 0.0006	
Nab-Paclitaxel	4 / 103 (3.9)	NE [NE; NE]	3 / 101 (3.0)	NE [NE; NE]	1.1650 [0.2544; 5.9541] 0.8423	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	10 / 67 (14.9)	NE [NE; NE]	0.5482 [0.1958; 1.4471] 0.2240	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Headache						
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0168
Capecitabine	56 / 265 (21.1)	NE [28.1; NE]	23 / 249 (9.2)	NE [NE; NE]	2.1809 [1.3596; 3.6186] 0.0013	
Nab-Paclitaxel	11 / 103 (10.7)	NE [25.9; NE]	8 / 101 (7.9)	NE [NE; NE]	1.1382 [0.4461; 2.9966] 0.7871	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	11 / 67 (16.4)	NE [NE; NE]	0.5067 [0.1855; 1.2940] 0.1546	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0057
Capecitabine	8 / 265 (3.0)	NE [NE; NE]	13 / 249 (5.2)	NE [NE; NE]	0.5122 [0.2023; 1.2181] 0.1305	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	11 / 101 (10.9)	NE [NE; NE]	NE [NE; NE] NE	
Paclitaxel	4 / 66 (6.1)	NE [NE; NE]	25 / 67 (37.3)	NE [2.7; NE]	0.0831 [0.0238; 0.2222] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: All (any PT)						
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0109
Capecitabine	174 / 265 (65.7)	4.2 [2.7; 5.5]	77 / 249 (30.9)	23.3 [14.0; 26.2]	2.4287 [1.8647; 3.1944] <.0001	
Nab-Paclitaxel	72 / 103 (69.9)	2.6 [0.6; 4.9]	50 / 101 (49.5)	7.7 [0.9; NE]	1.4526 [1.0144; 2.0962] 0.0412	
Paclitaxel	35 / 66 (53.0)	7.6 [5.1; NE]	24 / 67 (35.8)	NE [3.6; NE]	1.0801 [0.6347; 1.8639] 0.7751	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Race						0.0065
Asian	54 / 153 (35.3)	NE [NE; NE]	28 / 147 (19.0)	NE [NE; NE]	1.8618 [1.1897; 2.9791] 0.0068	
White	49 / 231 (21.2)	NE [22.6; NE]	16 / 223 (7.2)	NE [NE; NE]	2.5781 [1.4948; 4.6900] 0.0007	
Other	14 / 50 (28.0)	NE [19.8; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0108
Asia	52 / 148 (35.1)	NE [NE; NE]	27 / 144 (18.8)	NE [NE; NE]	1.8799 [1.1915; 3.0352] 0.0069	
Europe	60 / 227 (26.4)	27.7 [22.6; NE]	11 / 206 (5.3)	NE [NE; NE]	4.3955 [2.4010; 8.8517] <.0001	
Rest of the World	5 / 59 (8.5)	NE [20.5; NE]	6 / 67 (9.0)	NE [NE; NE]	0.8187 [0.2348; 2.7310] 0.7419	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 13DEC2024 11:07; Program name: T.2.28.3_10PCTTEAE_SAF_SUB_SIG.sas; Output name: T.2.28.3_10PCTTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Alanine aminotransferase increased						
Race						0.0077
Asian	50 / 153 (32.7)	NE [NE; NE]	34 / 147 (23.1)	NE [NE; NE]	1.3981 [0.9077; 2.1793] 0.1307	
White	33 / 231 (14.3)	NE [NE; NE]	14 / 223 (6.3)	NE [NE; NE]	2.0648 [1.1268; 3.9916] 0.0206	
Other	10 / 50 (20.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Endocrine Resistance						0.0236
Primary	26 / 127 (20.5)	NE [NE; NE]	24 / 137 (17.5)	NE [NE; NE]	1.0620 [0.6069; 1.8658] 0.8310	
Secondary	67 / 307 (21.8)	NE [NE; NE]	24 / 279 (8.6)	NE [NE; NE]	2.4660 [1.5692; 4.0106] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Blood alkaline phosphatase increased						
Endocrine Resistance						0.0156
Primary	14 / 127 (11.0)	NE [25.2; NE]	11 / 137 (8.0)	NE [NE; NE]	0.9850 [0.4363; 2.2627] 0.9700	
Secondary	34 / 307 (11.1)	NE [NE; NE]	6 / 279 (2.2)	NE [NE; NE]	4.0164 [1.8088; 10.6566] 0.0007	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior anthracycline use						0.0120
Yes	20 / 197 (10.2)	NE [NE; NE]	13 / 198 (6.6)	NE [NE; NE]	1.1883 [0.5917; 2.4668] 0.6326	
No	28 / 237 (11.8)	NE [NE; NE]	4 / 219 (1.8)	NE [NE; NE]	4.9691 [1.9413; 16.8222] 0.0009	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)						
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0013
Capecitabine	138 / 265 (52.1)	11.8 [8.2; 14.9]	65 / 249 (26.1)	NE [20.4; NE]	1.7127 [1.2805; 2.3152] 0.0003	
Nab-Paclitaxel	46 / 103 (44.7)	15.4 [8.1; 23.5]	17 / 101 (16.8)	NE [NE; NE]	2.3245 [1.3537; 4.1824] 0.0024	
Paclitaxel	25 / 66 (37.9)	NE [10.5; NE]	24 / 67 (35.8)	NE [3.9; NE]	0.6564 [0.3670; 1.1730] 0.1511	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Number of prior lines of endocrine therapy in the metastatic setting						0.0371
1	4 / 65 (6.2)	NE [NE; NE]	4 / 79 (5.1)	NE [NE; NE]	1.1023 [0.2602; 4.6687] 0.8907	
2	36 / 293 (12.3)	NE [NE; NE]	7 / 281 (2.5)	NE [NE; NE]	3.5439 [1.6697; 8.7240] 0.0012	
>=3	4 / 75 (5.3)	NE [26.8; NE]	4 / 56 (7.1)	NE [NE; NE]	0.5605 [0.1281; 2.4263] 0.4173	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)						
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0001
Capecitabine	100 / 265 (37.7)	19.3 [16.4; NE]	81 / 249 (32.5)	26.5 [11.9; NE]	0.9616 [0.7167; 1.2942] 0.7917	
Nab-Paclitaxel	13 / 103 (12.6)	NE [28.3; NE]	23 / 101 (22.8)	NE [14.4; NE]	0.4160 [0.1990; 0.8261] 0.0120	
Paclitaxel	16 / 66 (24.2)	NE [16.6; NE]	29 / 67 (43.3)	12.5 [2.1; NE]	0.1864 [0.0833; 0.3818] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.28.3 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: General disorders and administration site conditions; PT: Oedema peripheral						
Number of prior lines of endocrine therapy in the metastatic setting						0.0206
1	10 / 65 (15.4)	NE [NE; NE]	7 / 79 (8.9)	NE [17.4; NE]	1.5934 [0.6045; 4.4246] 0.3455	
2	20 / 293 (6.8)	NE [NE; NE]	42 / 281 (14.9)	NE [NE; NE]	0.3209 [0.1836; 0.5420] <.0001	
>=3	6 / 75 (8.0)	NE [NE; NE]	10 / 56 (17.9)	NE [NE; NE]	0.3882 [0.1318; 1.0482] 0.0581	
ER/PR status I						0.0337
ER+, PR+	23 / 252 (9.1)	NE [NE; NE]	25 / 234 (10.7)	NE [NE; NE]	0.6631 [0.3723; 1.1755] 0.1560	
ER+, PR-	10 / 166 (6.0)	NE [NE; NE]	31 / 171 (18.1)	NE [17.4; NE]	0.2478 [0.1144; 0.4920] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Abbildung 2.28.1 Unerwünschte Ereignisse nach SOC und PT mit Inzidenz ≥10 % in mindestens einem Arm – Kaplan-Meier-Plot – SAF

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Data Intelligence - Evidence Generation
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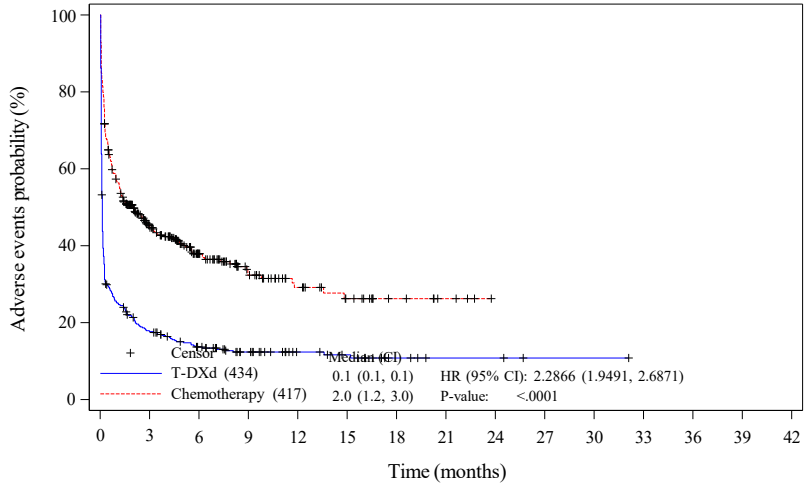
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: All (any PT)



Patients still at risk:

T-DXd(434)	434	72	48	31	18	14	6	3	3	1	1	0
Chemotherapy (417)	417	141	79	43	25	16	8	4	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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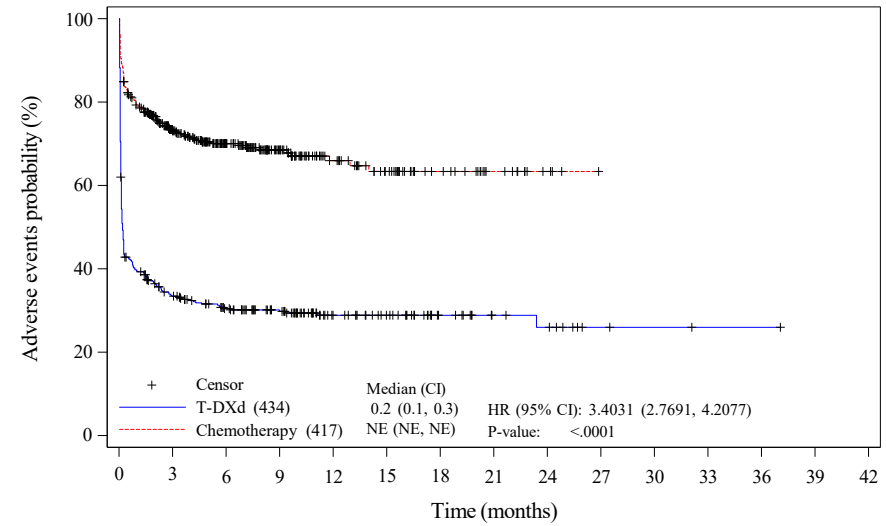
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Nausea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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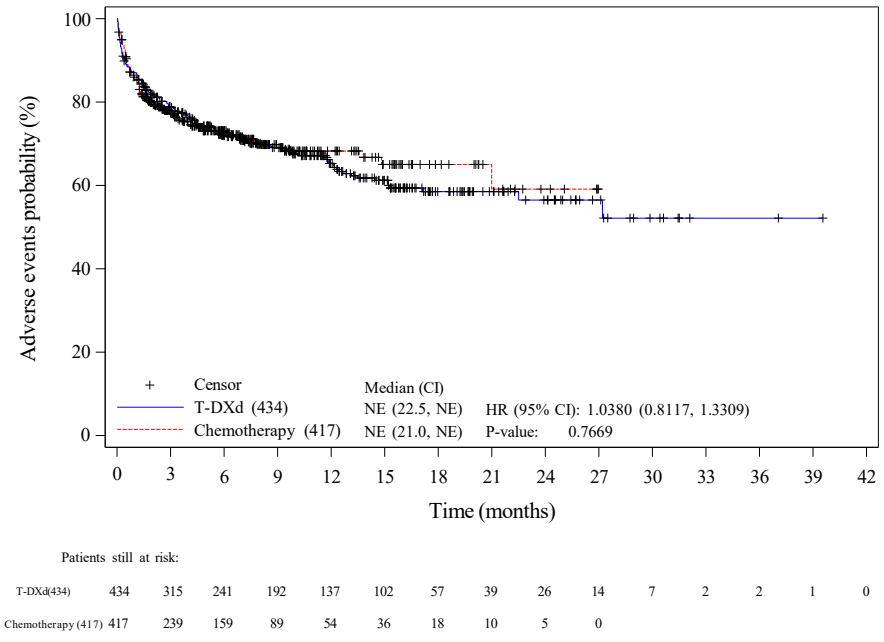
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Diarrhoea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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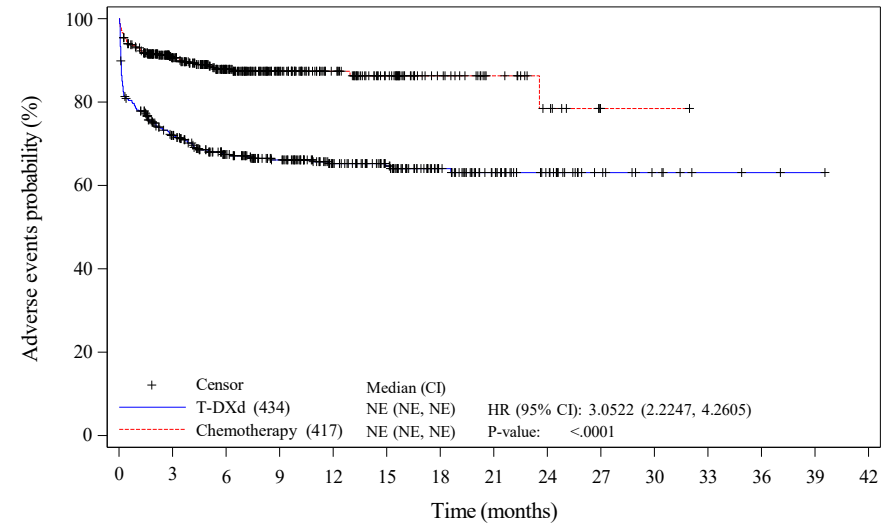
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Vomiting



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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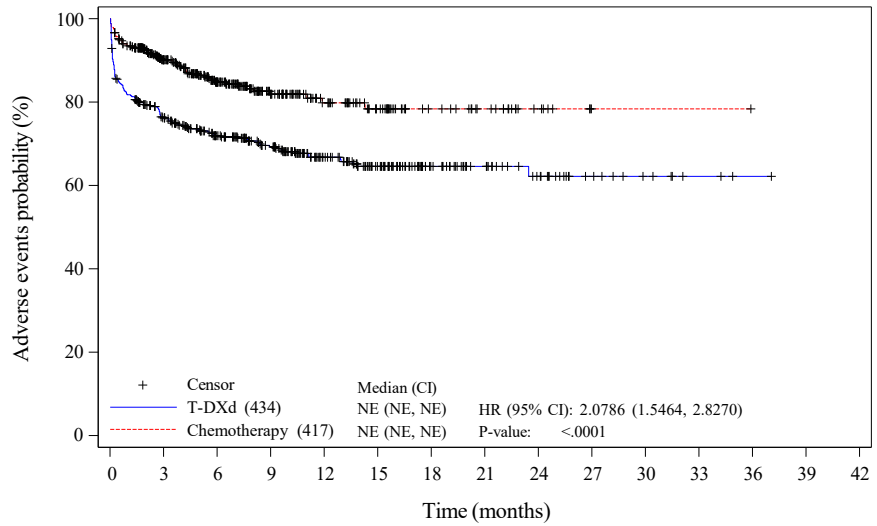
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Constipation



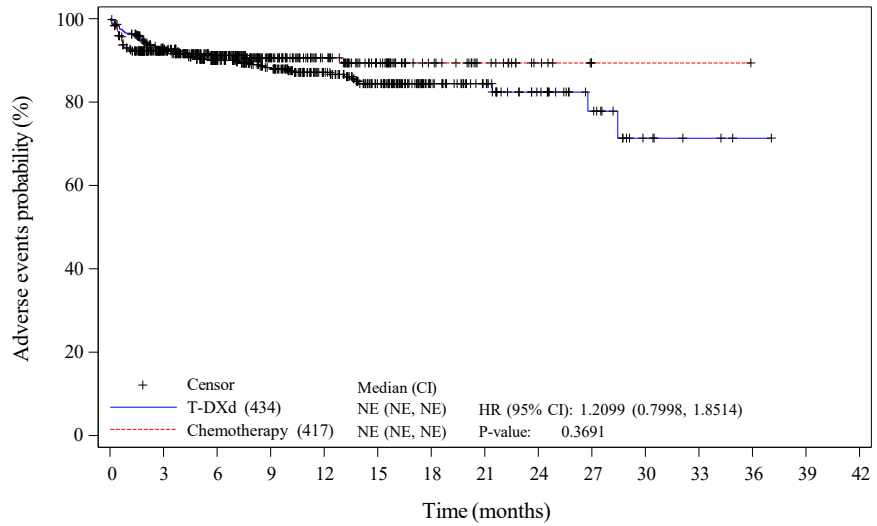
Patients still at risk:

T-DXd(434)	434	306	244	193	134	96	53	37	24	12	7	3	1	0
Chemotherapy (417)	417	290	192	116	72	48	27	19	8	1	1	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Stomatitis



Patients still at risk:

T-DXd(434)	434	368	299	245	180	129	68	47	29	17	6	3	1	0
Chemotherapy (417)	417	292	207	123	80	52	28	17	7	1	1	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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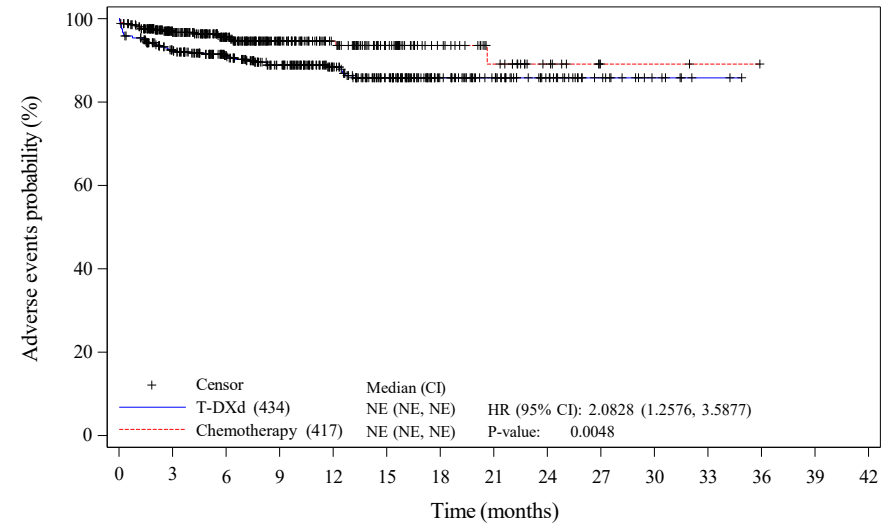
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia



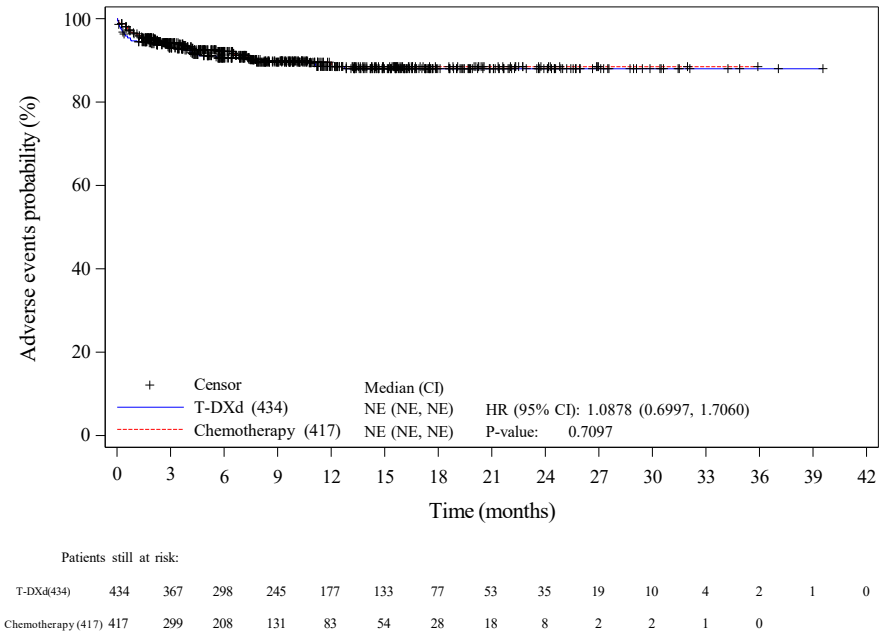
Patients still at risk:

T-DXd(434)	434	365	301	241	179	131	74	52	31	16	7	2	0
Chemotherapy (417)	417	309	217	135	90	58	33	20	9	2	2	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Abdominal pain



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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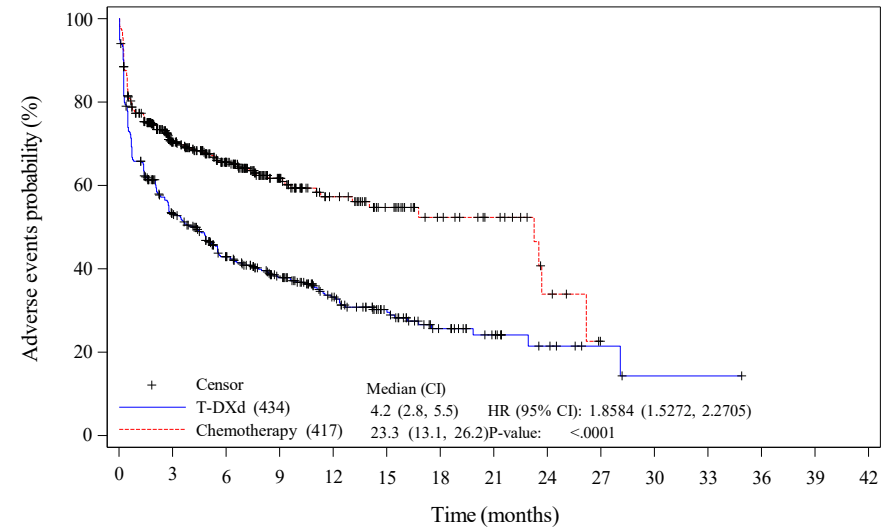
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Patients still at risk:

T-DXd(434)	434	213	150	108	71	46	25	14	7	3	1	1	0
Chemotherapy (417)	417	219	147	85	51	33	20	14	5	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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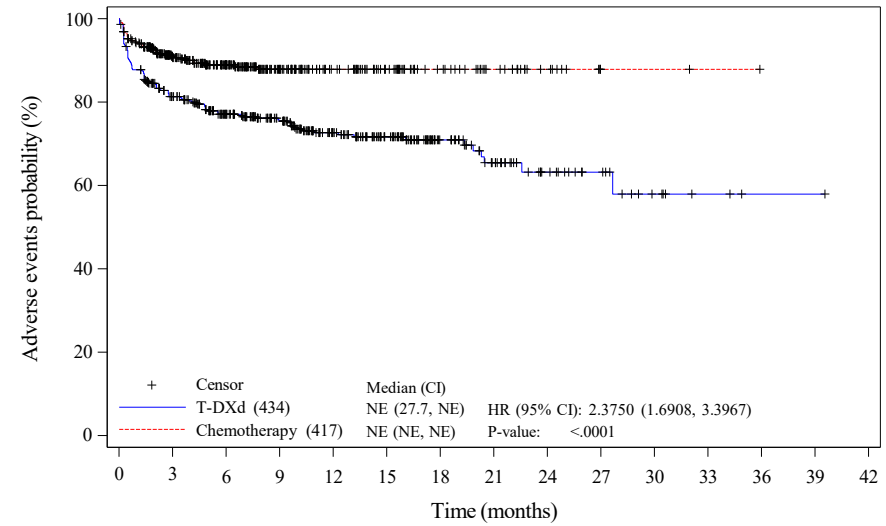
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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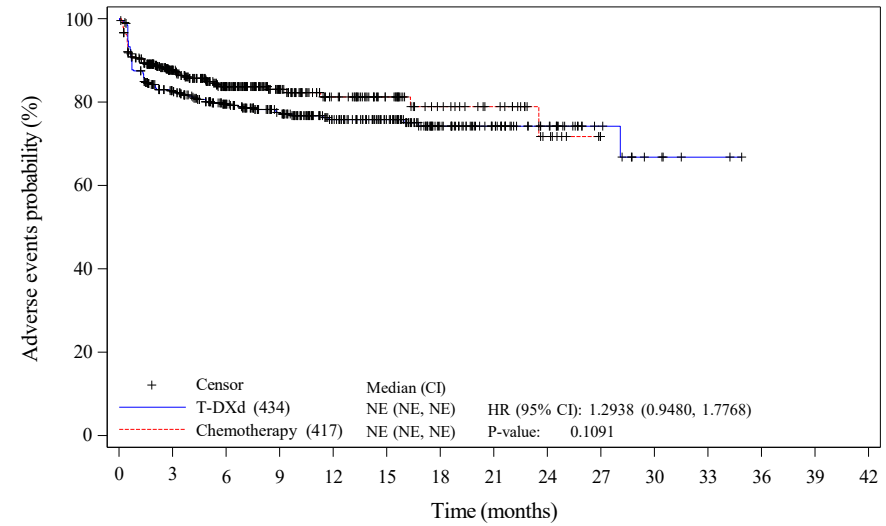
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Neutrophil count decreased



Patients still at risk:

T-DXd(434)	434	325	262	213	156	119	68	44	26	11	5	2	0
Chemotherapy (417)	417	276	187	114	72	47	28	20	8	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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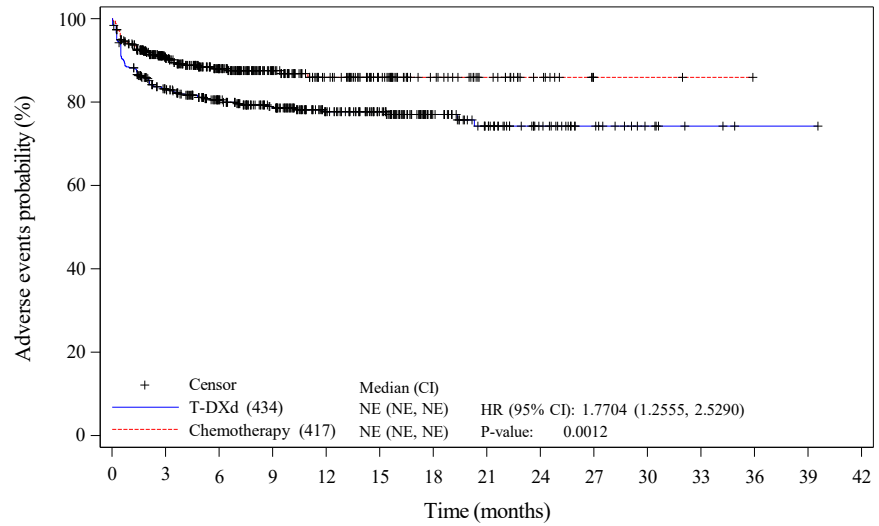
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Alanine aminotransferase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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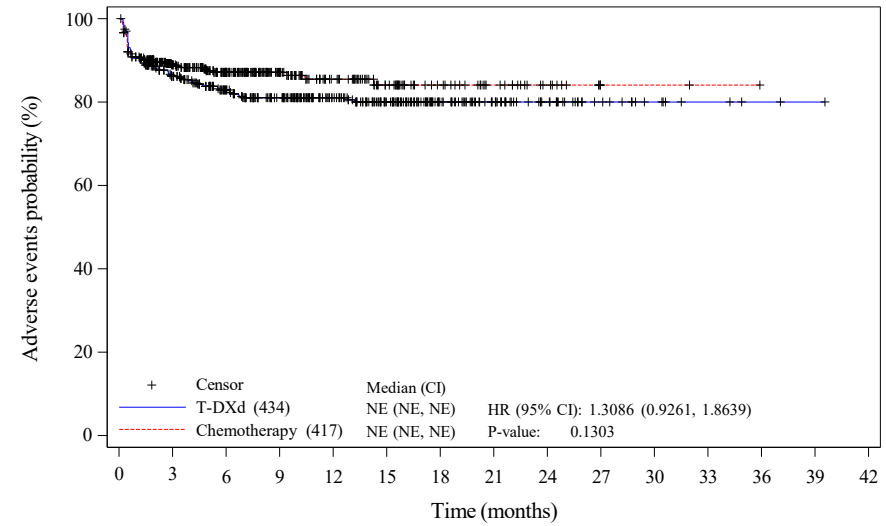
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: White blood cell count decreased



Patients still at risk:

T-DXd(434)	434	340	274	227	169	125	75	50	30	15	8	4	2	1	0
Chemotherapy (417)	417	280	195	122	80	53	33	21	11	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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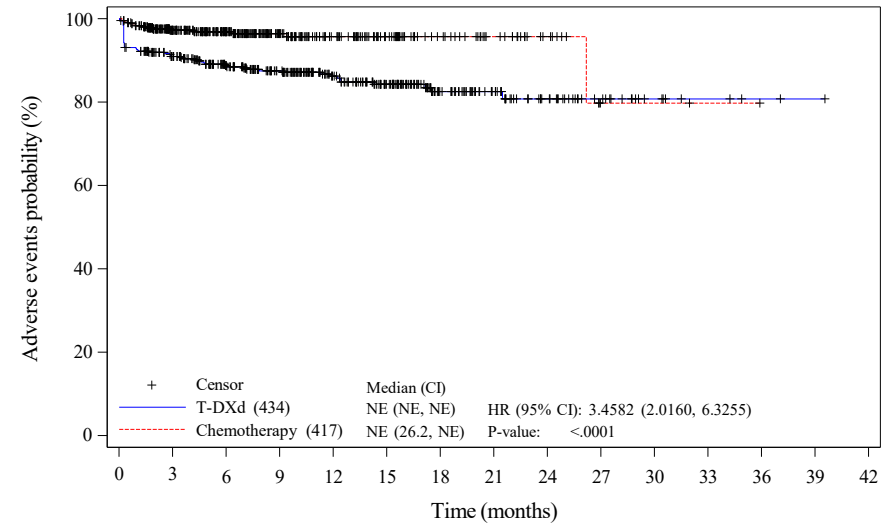
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Platelet count decreased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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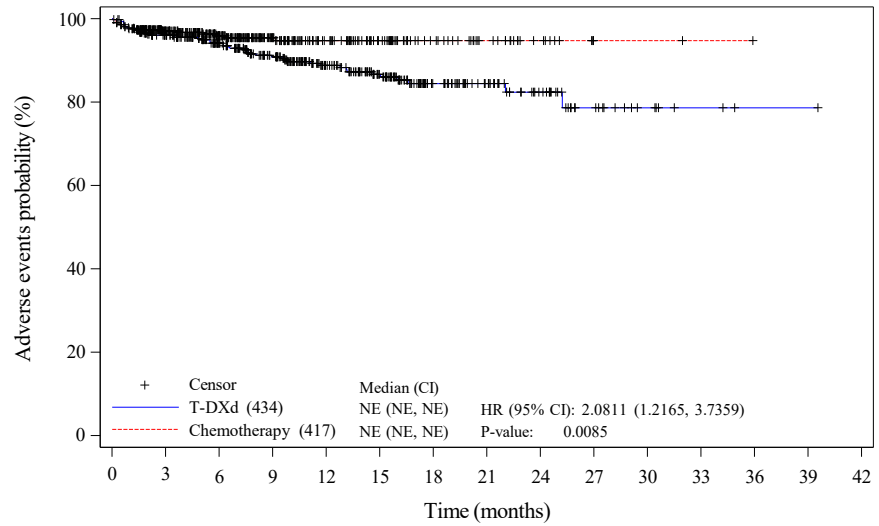
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Blood alkaline phosphatase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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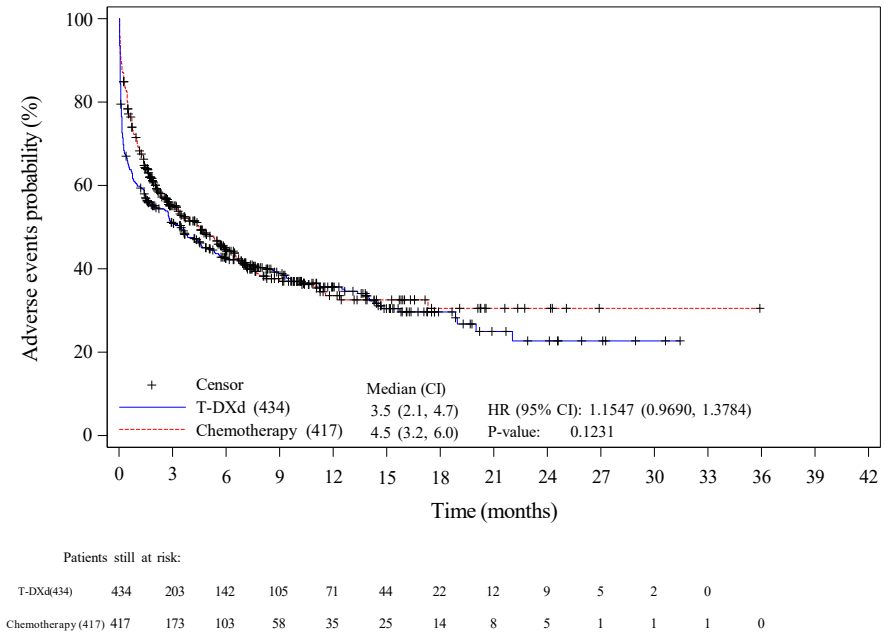
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: All (any PT)



Patients still at risk:

T-DXd(434)	434	203	142	105	71	44	22	12	9	5	2	0
Chemotherapy (417)	417	173	103	58	35	25	14	8	5	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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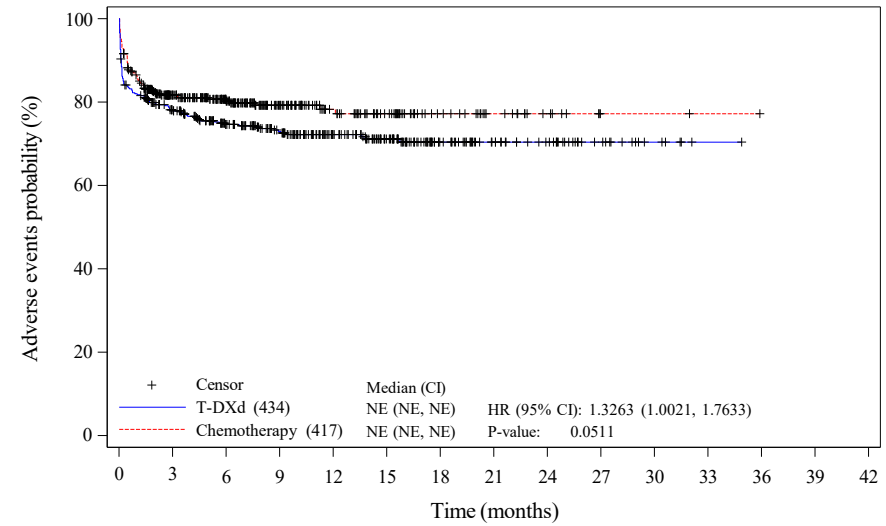
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Fatigue



Patients still at risk:

T-DXd(434)	434	308	248	203	150	110	62	41	30	15	6	1	0
Chemotherapy (417)	417	262	186	117	74	52	28	17	9	2	2	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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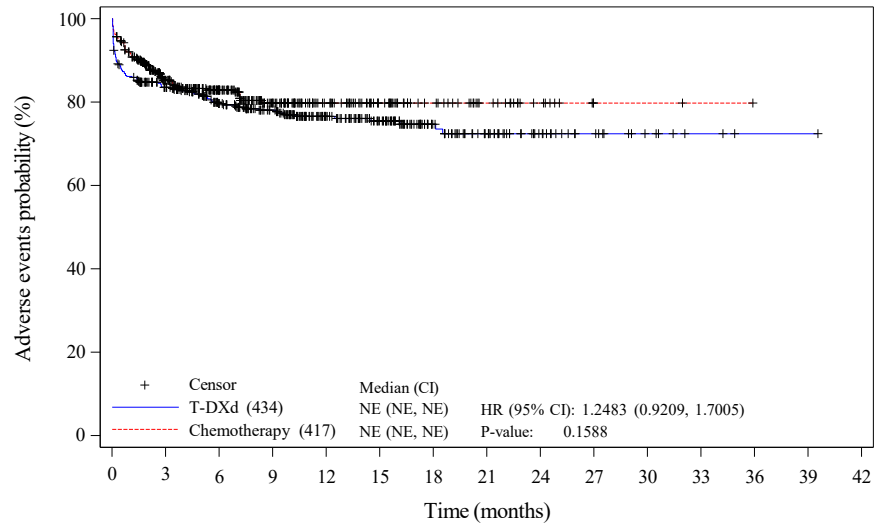
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Asthenia



Patients still at risk:

T-DXd(434)	434	331	268	220	154	117	67	45	24	14	7	3	1	1	0
Chemotherapy (417)	417	271	191	121	77	51	33	20	10	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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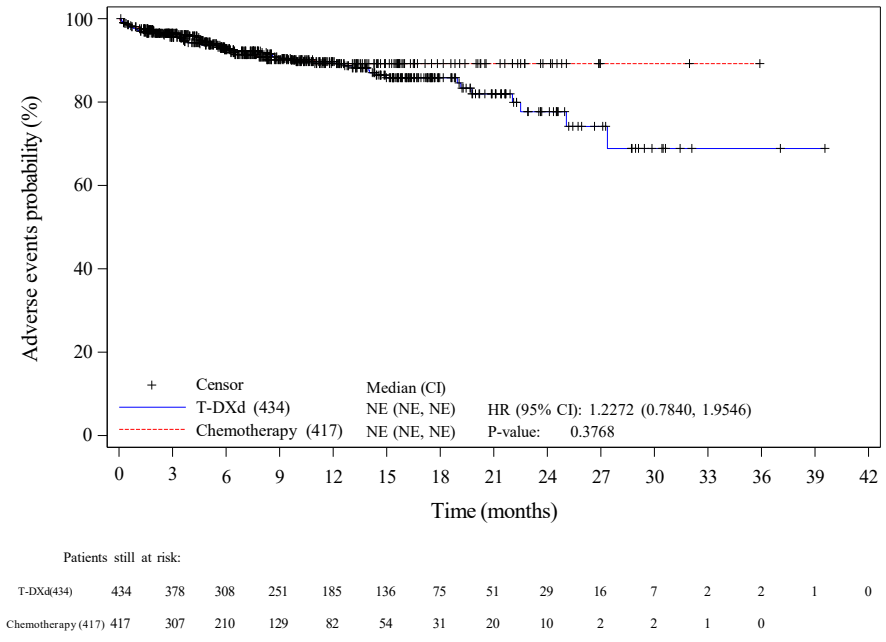
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Pyrexia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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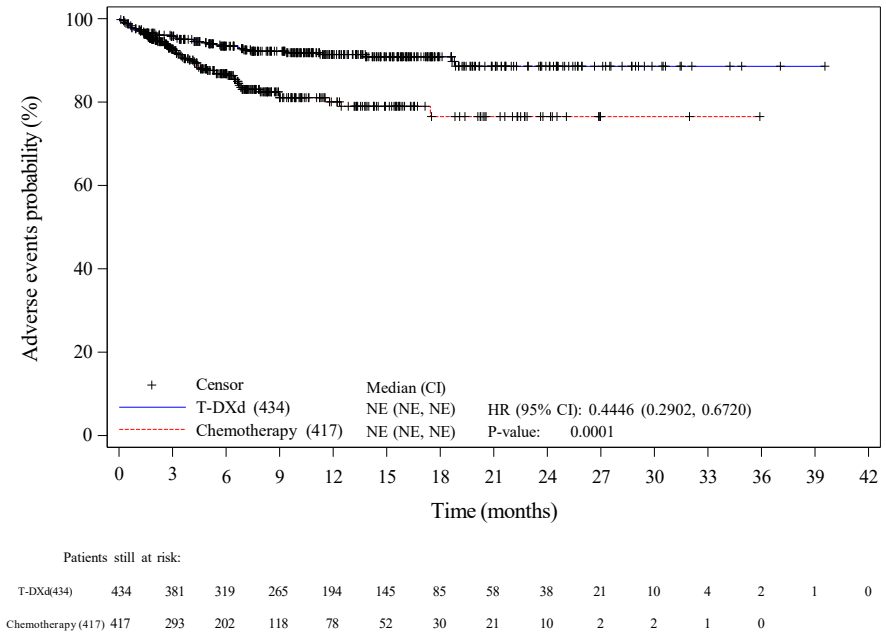
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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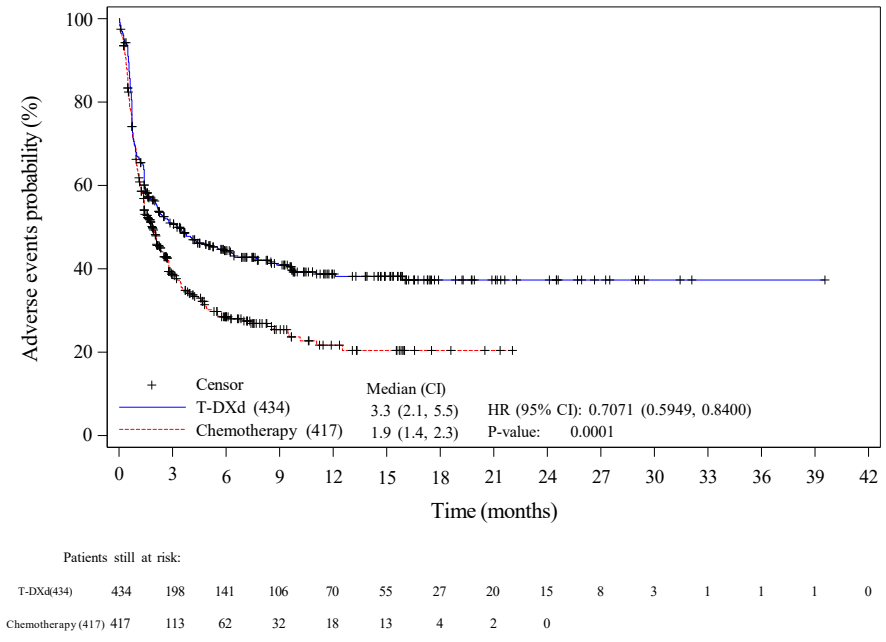
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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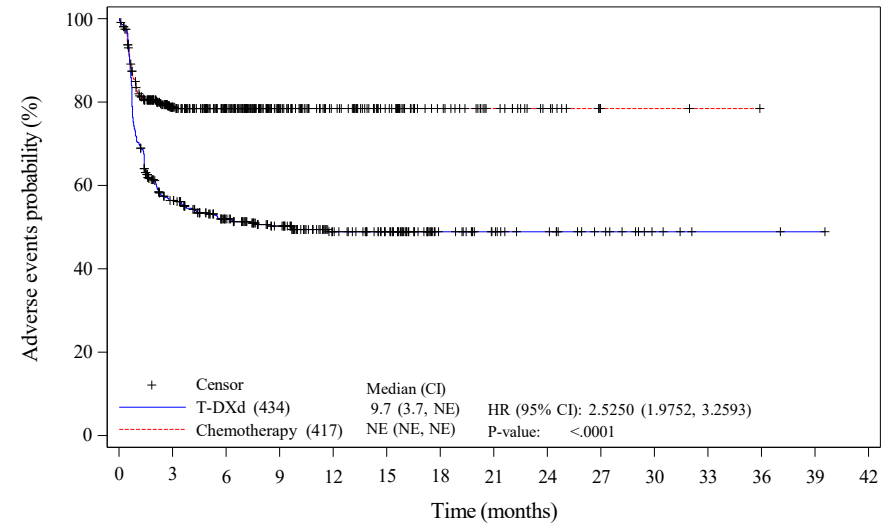
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Patients still at risk:

T-DXd(434)	434	220	167	132	89	70	34	24	19	12	5	2	2	1	0
Chemotherapy (417)	417	249	185	118	82	57	34	21	11	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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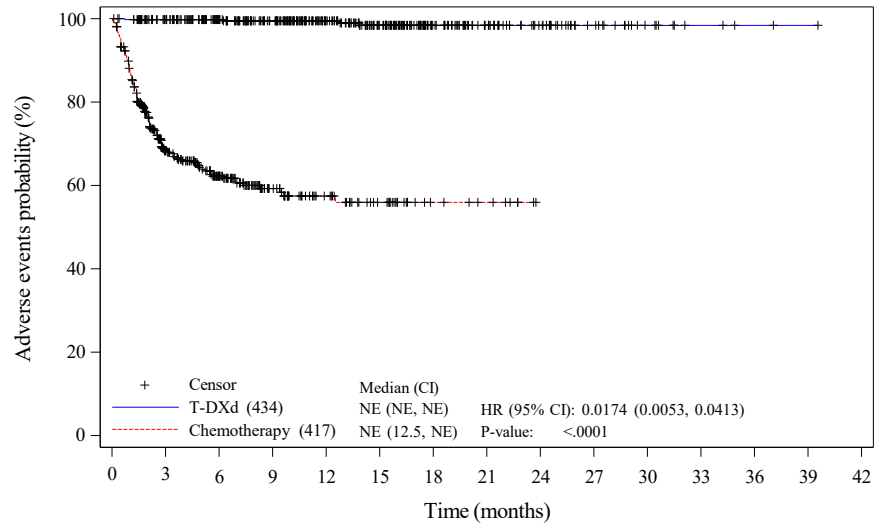
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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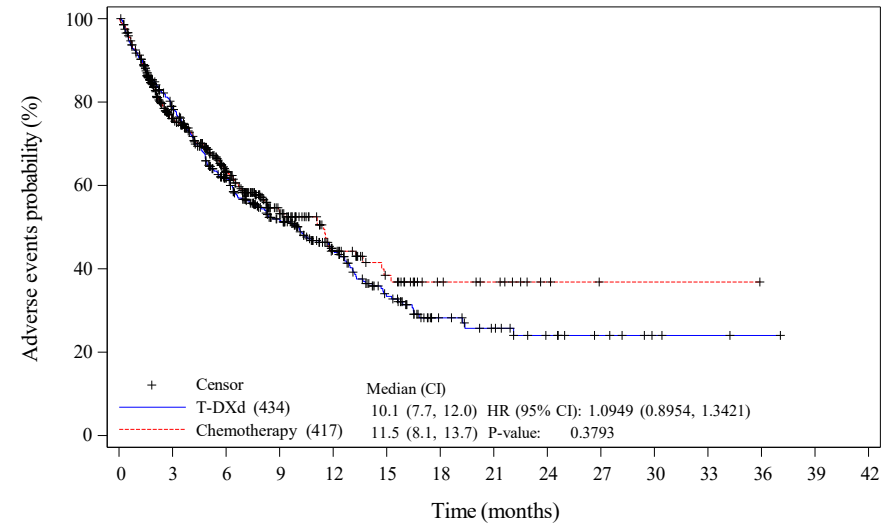
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: All (any PT)



Patients still at risk:

T-DXd(434)	434	311	210	144	89	53	25	18	11	7	3	2	1	0
Chemotherapy (417)	417	241	149	76	41	24	12	9	3	1	1	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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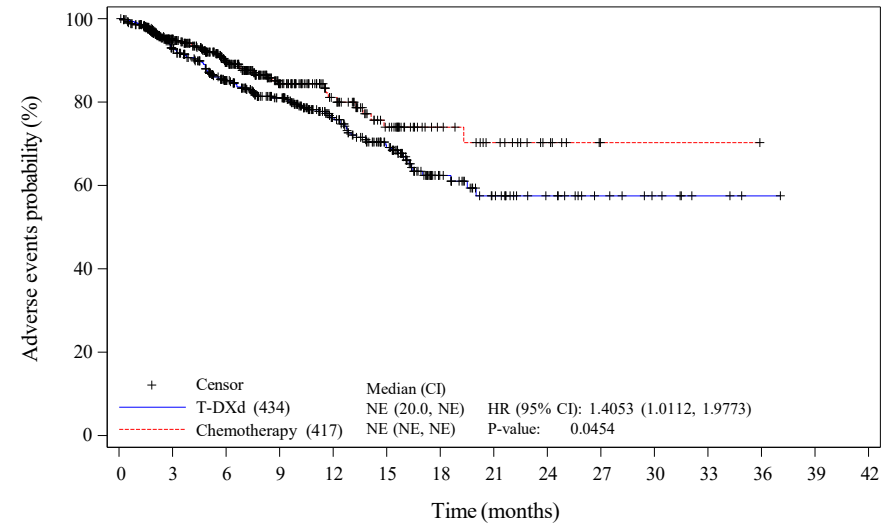
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: COVID-19



Patients still at risk:

T-DXd(434)	434	367	286	222	151	106	46	28	18	11	7	3	1	0
Chemotherapy (417)	417	302	204	117	71	43	22	15	7	1	1	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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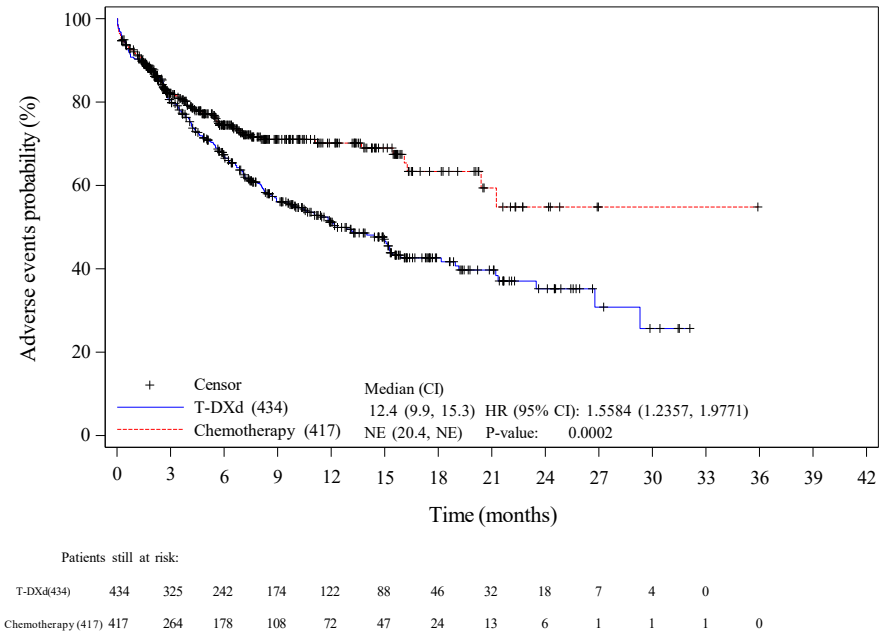
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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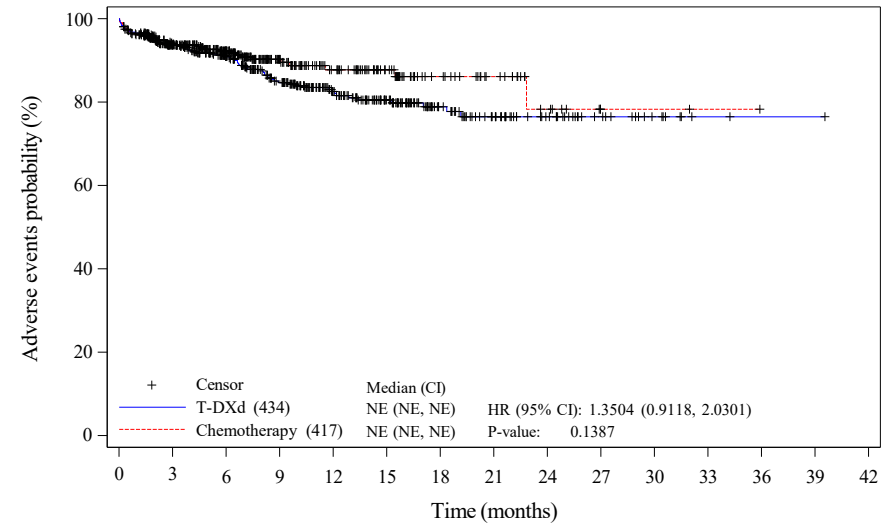
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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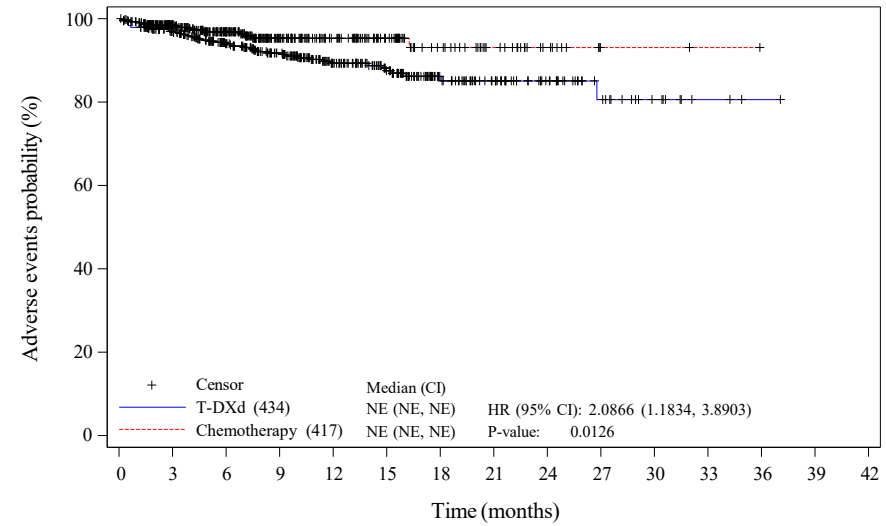
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis



Patients still at risk:

T-DXd(434)	434	385	315	257	186	140	80	56	34	18	9	3	1	0
Chemotherapy (417)	417	313	222	136	91	60	34	21	10	2	2	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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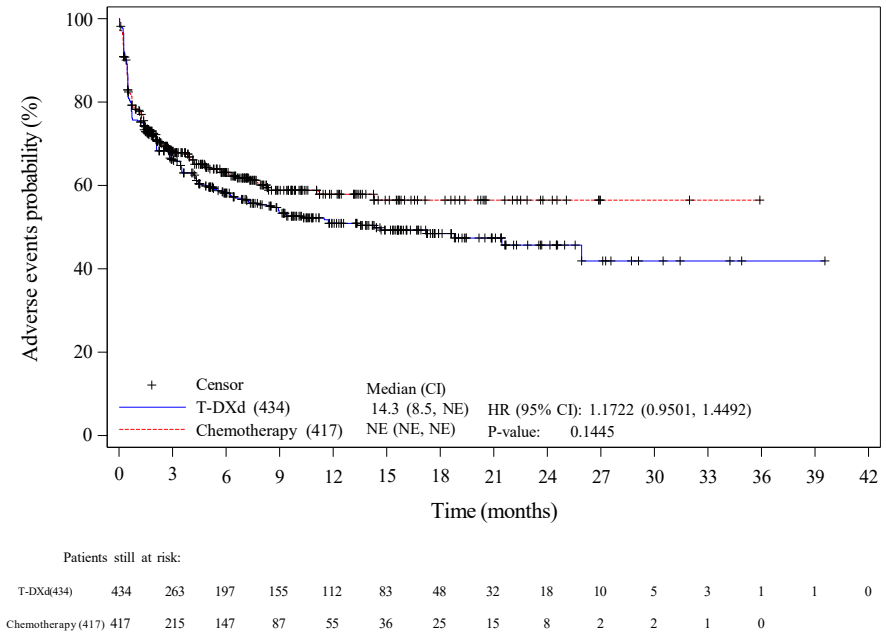
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: All (any PT)



Patients still at risk:

T-DXd(434)	434	263	197	155	112	83	48	32	18	10	5	3	1	1	0
Chemotherapy (417)	417	215	147	87	55	36	25	15	8	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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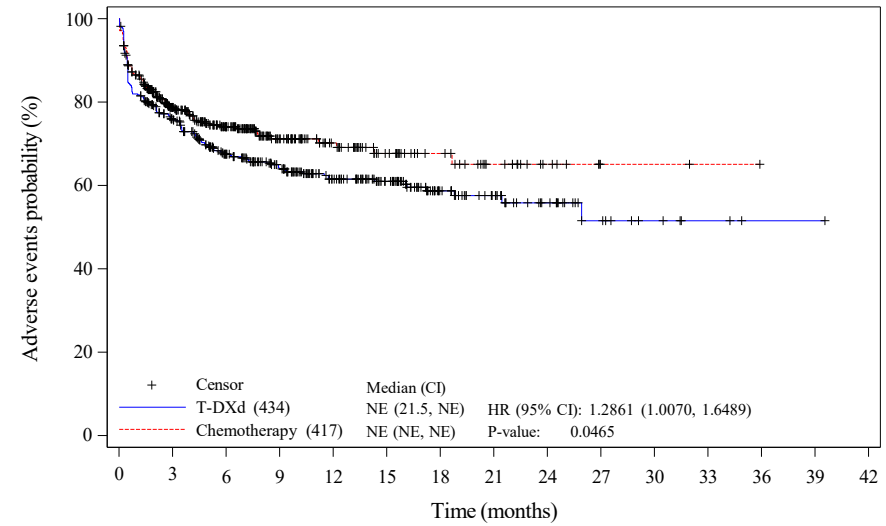
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Anaemia



Patients still at risk:

T-DXd(434)	434	303	230	184	136	103	56	39	23	11	6	3	1	1	0
Chemotherapy (417)	417	247	169	101	65	42	28	17	8	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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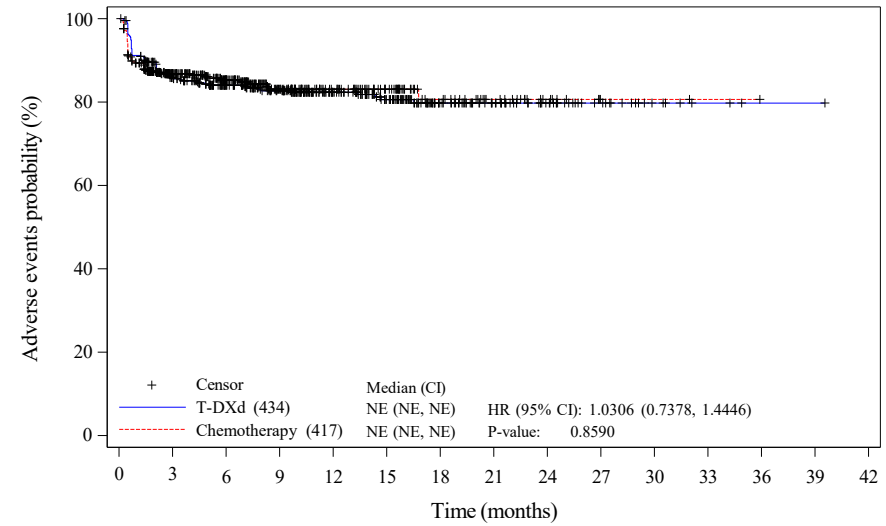
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Neutropenia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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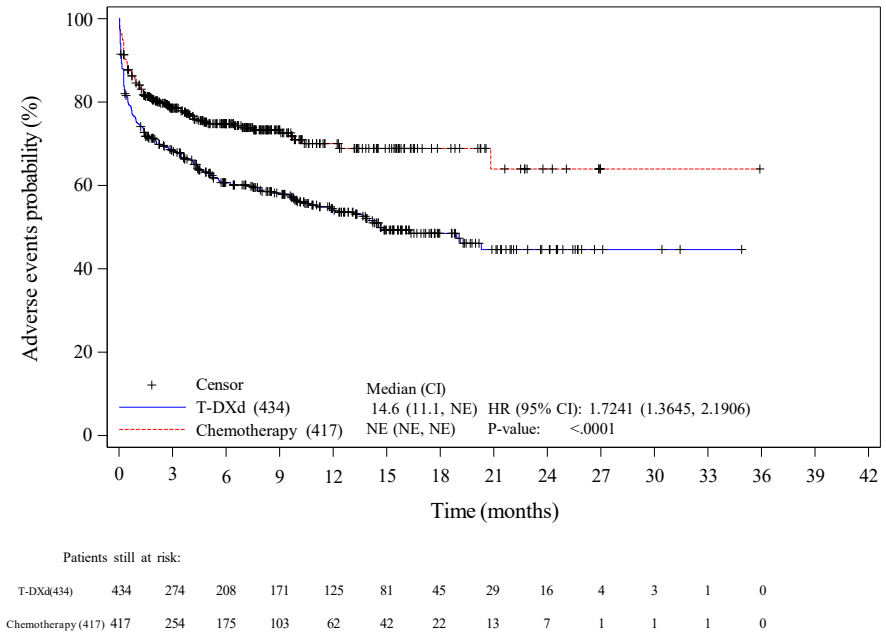
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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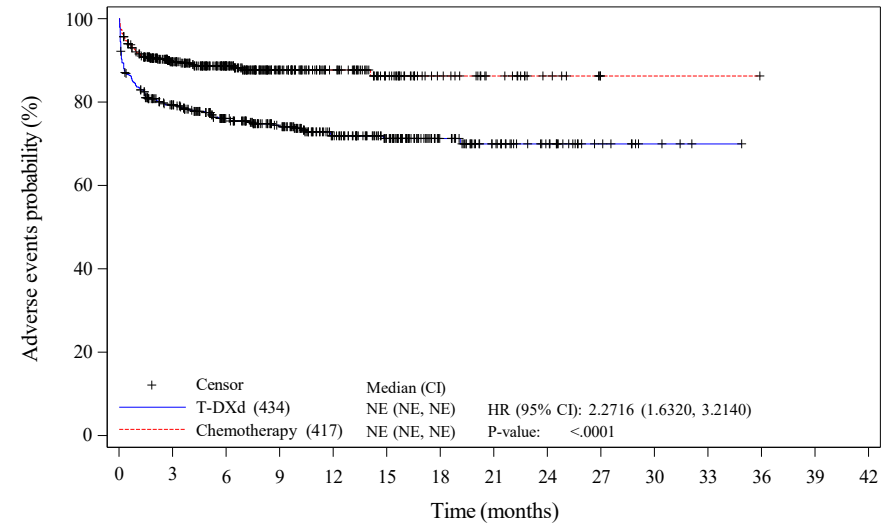
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



Patients still at risk:

T-DXd(434)	434	313	251	203	148	109	61	39	24	10	4	1	0
Chemotherapy (417)	417	288	205	124	81	50	27	17	8	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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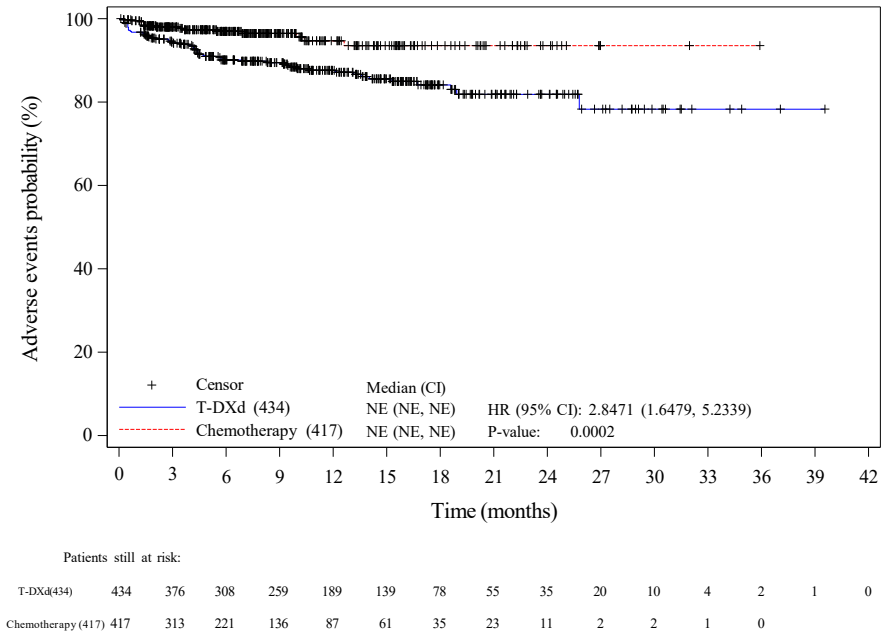
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hypokalaemia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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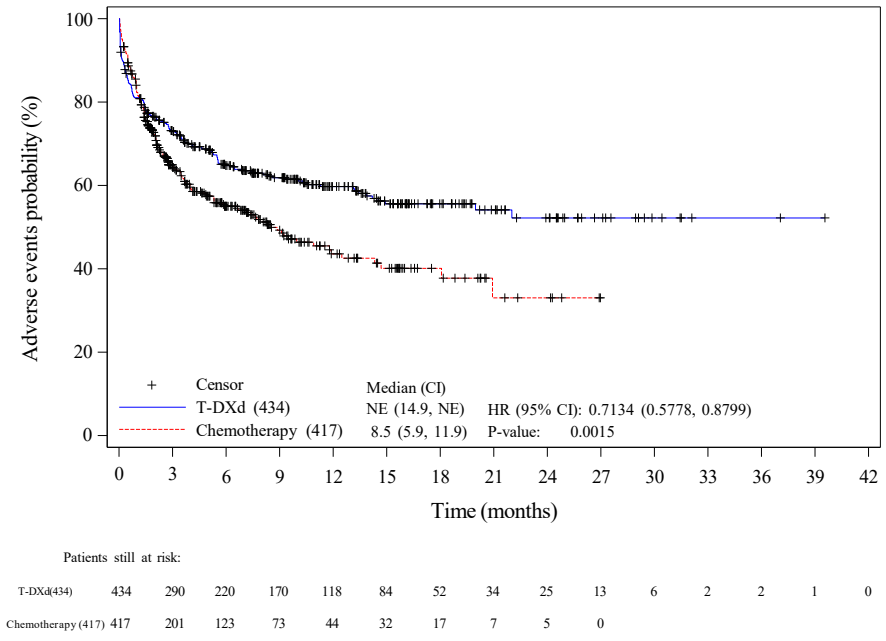
Run date: 10DEC2024 6:35; Program name: F.2.28.1_10PCTTEAE_SAF.sas; Output name: F.2.28.1_10PCTTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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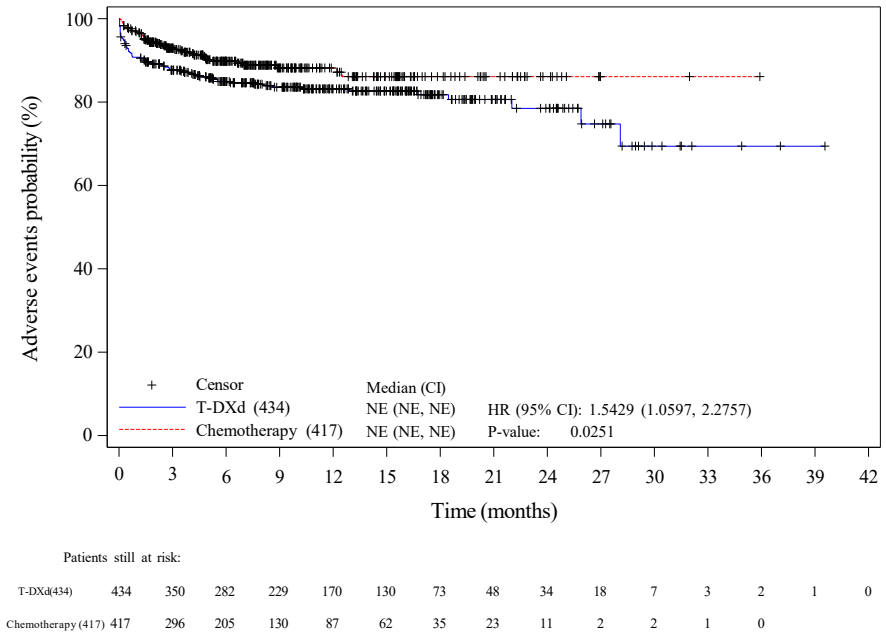
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: Headache



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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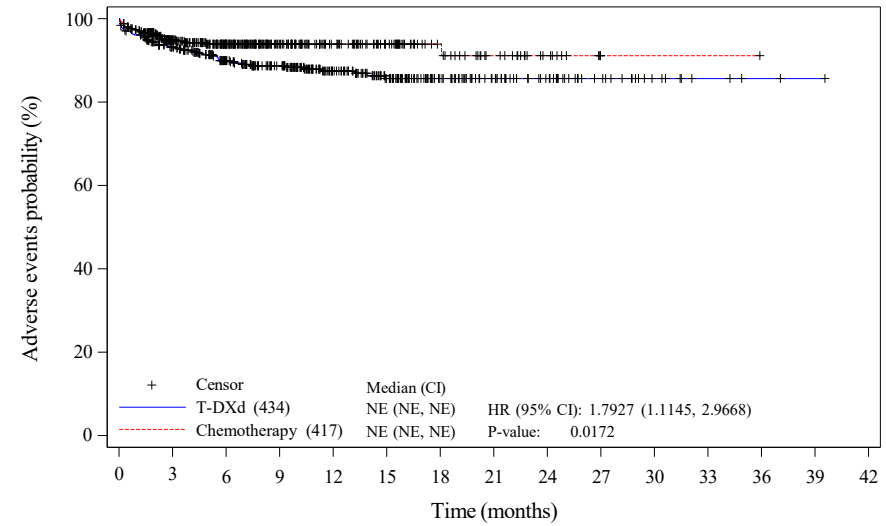
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: Dysgeusia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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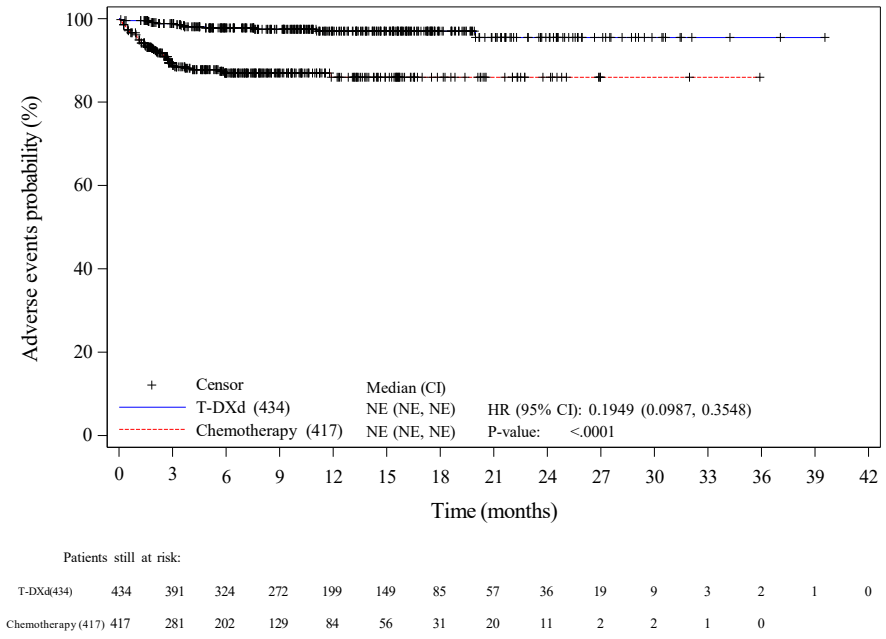
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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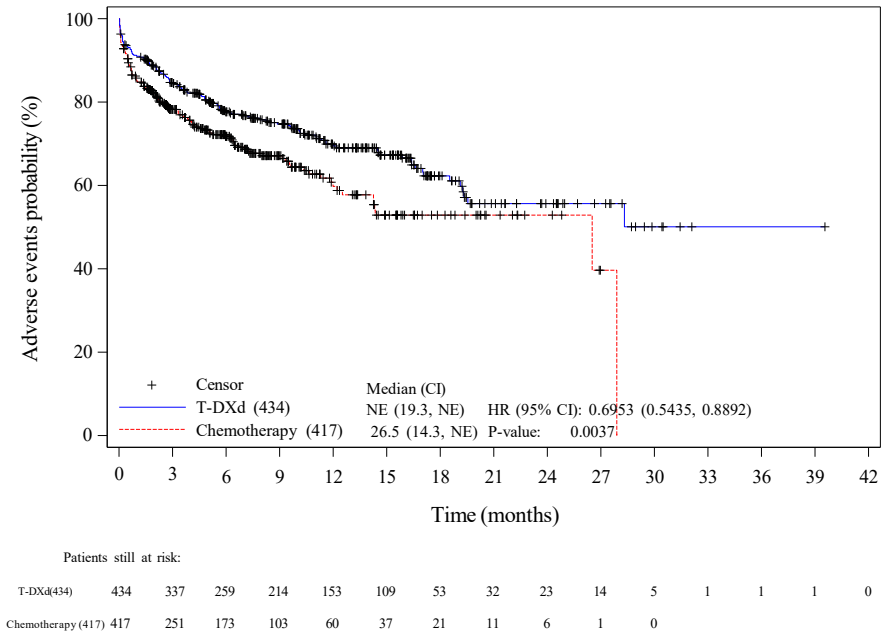
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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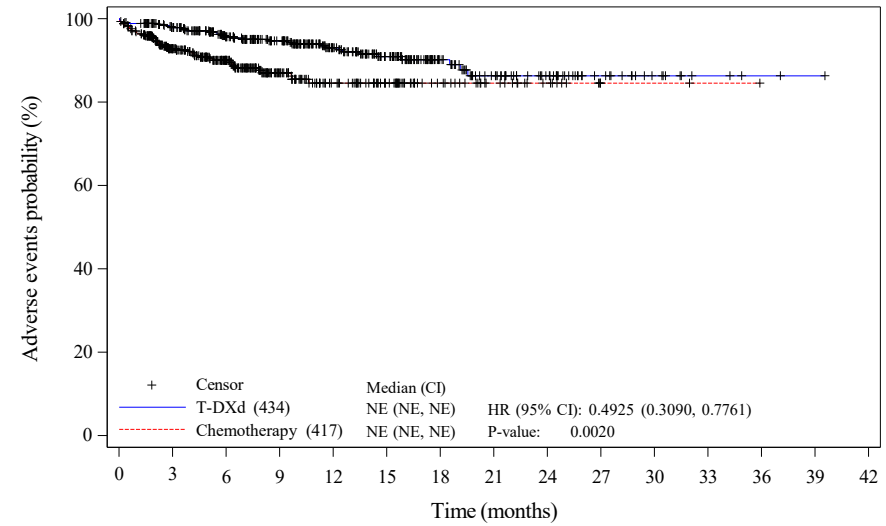
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia



Patients still at risk:

T-DXd(434)	434	388	318	264	194	142	78	54	36	19	10	4	2	1	0
Chemotherapy (417)	417	298	208	123	79	55	31	19	11	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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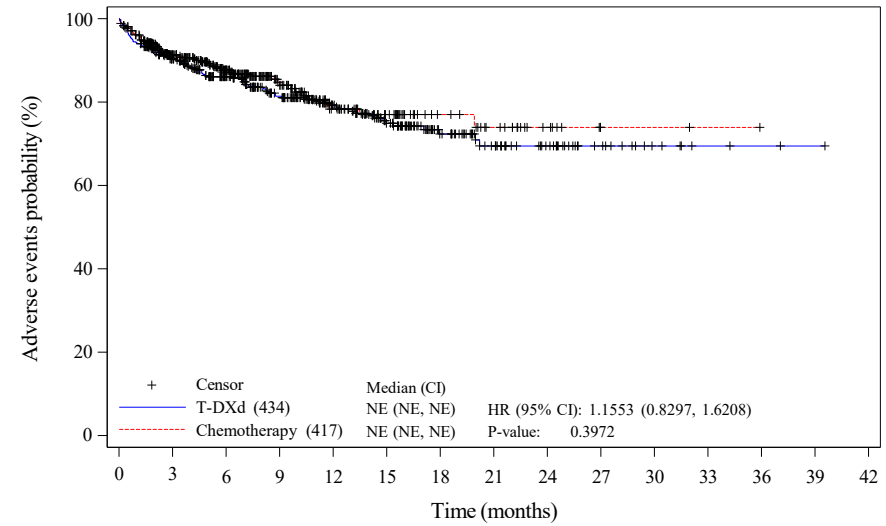
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Eye disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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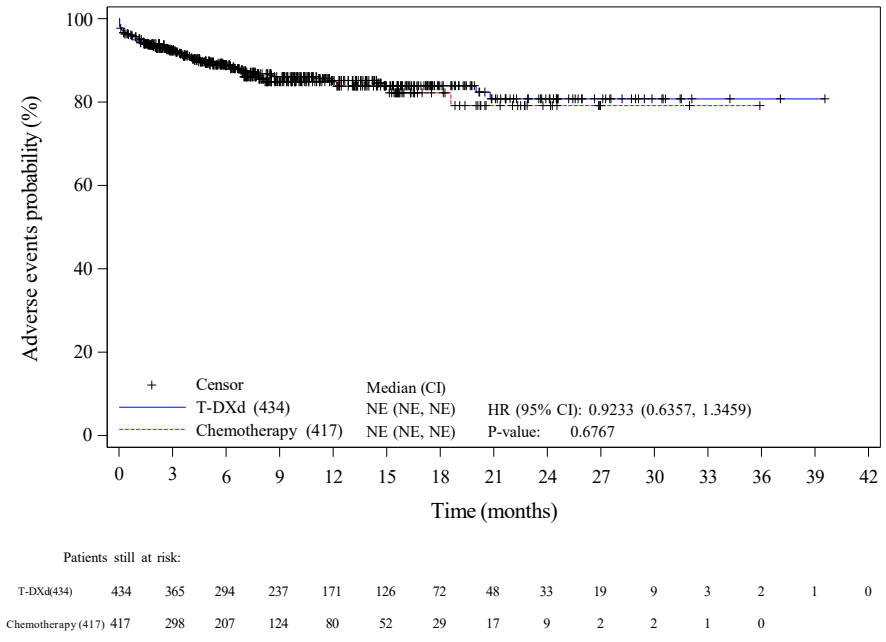
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Vascular disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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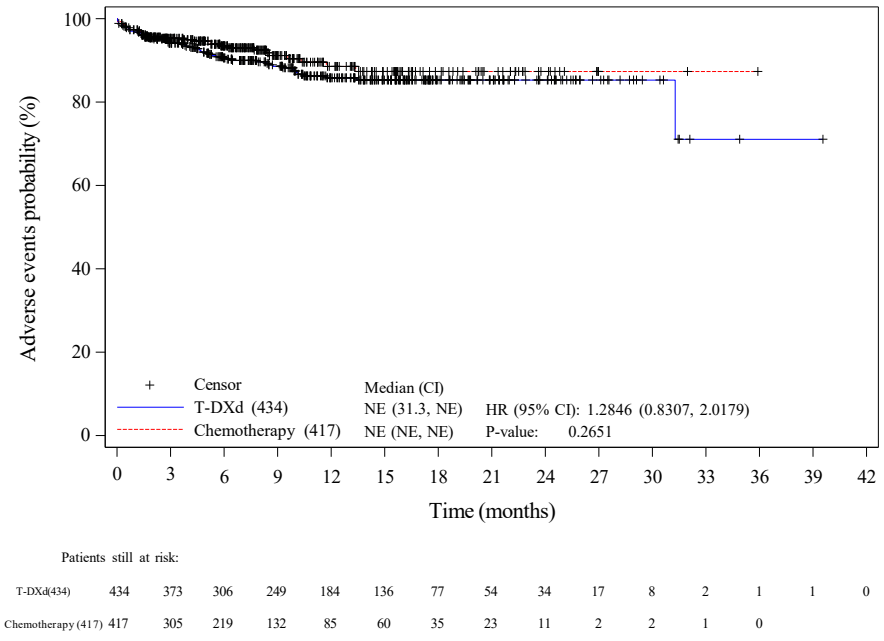
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Psychiatric disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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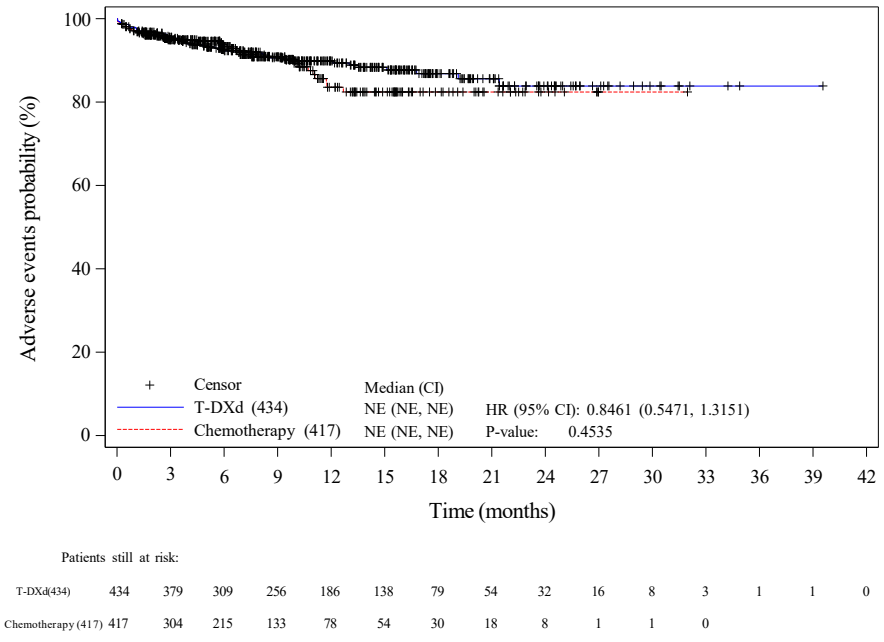
Figure 2.28.1 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Injury, poisoning and procedural complications; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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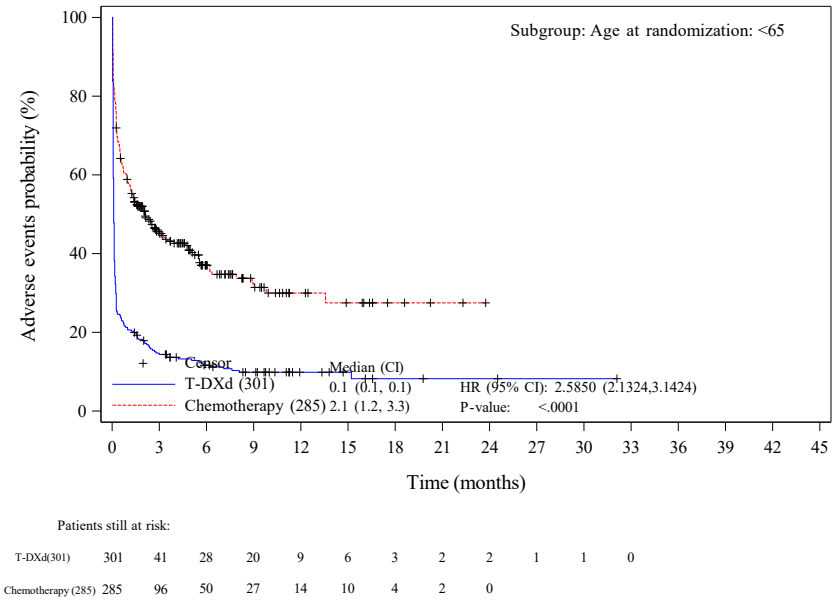
Abbildung 2.28.2 Unerwünschte Ereignisse nach SOC und PT mit Inzidenz ≥10 % in mindestens einem Arm – Kaplan-Meier-Plot – Analyse nach Subgruppe – SAF

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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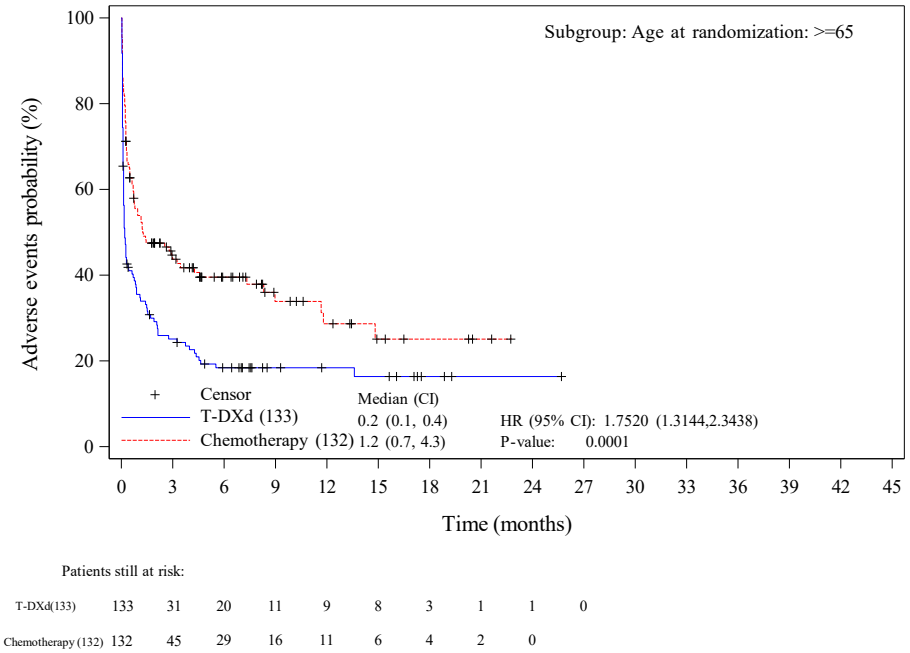
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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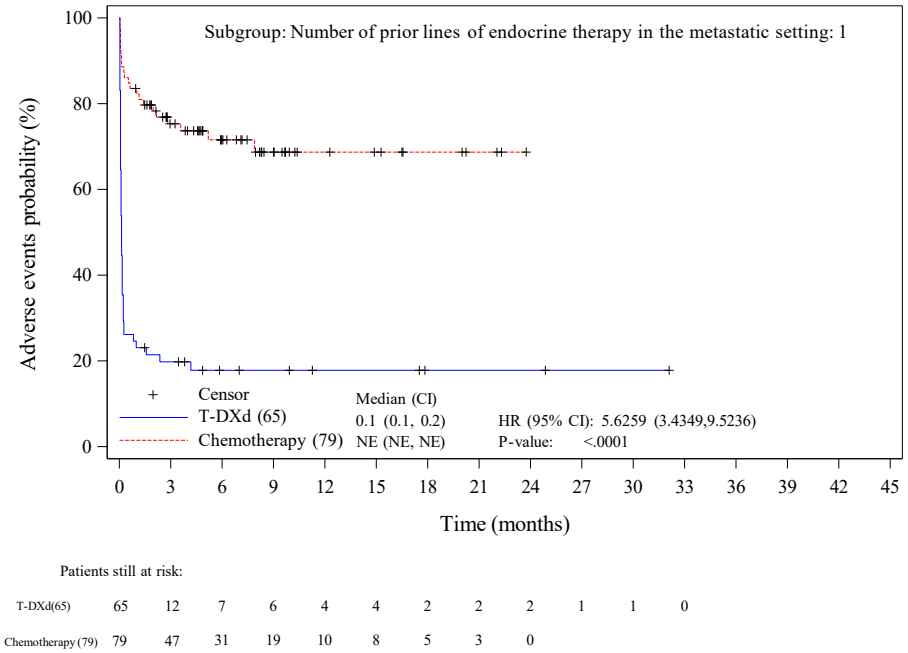
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Nausea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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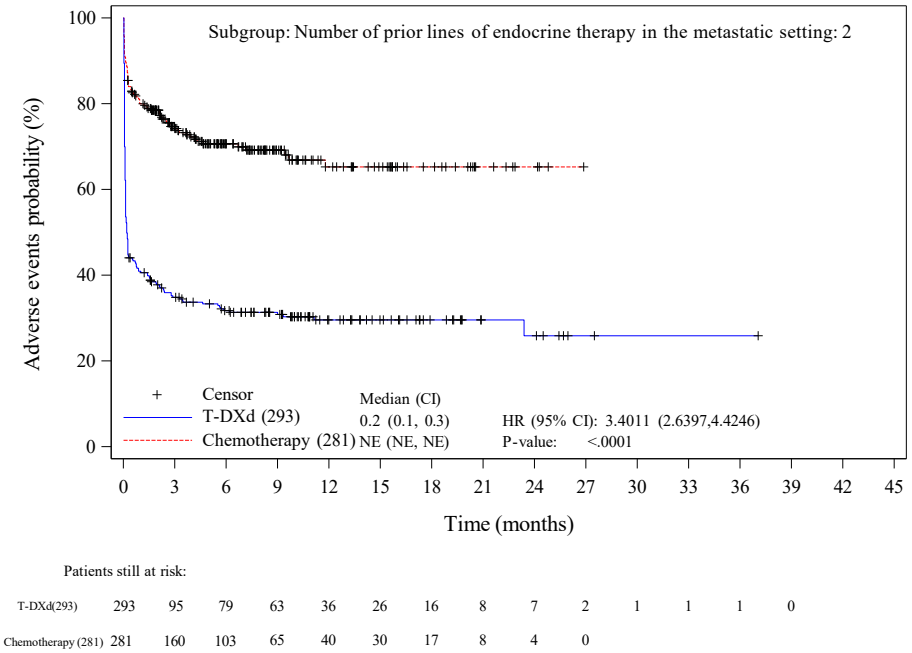
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Nausea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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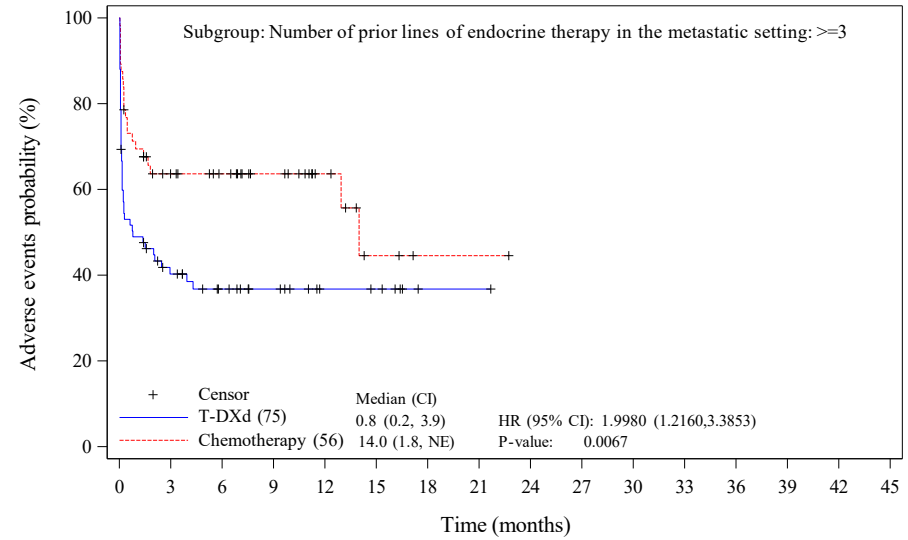
Run date: 13DEC2024 11:19; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Nausea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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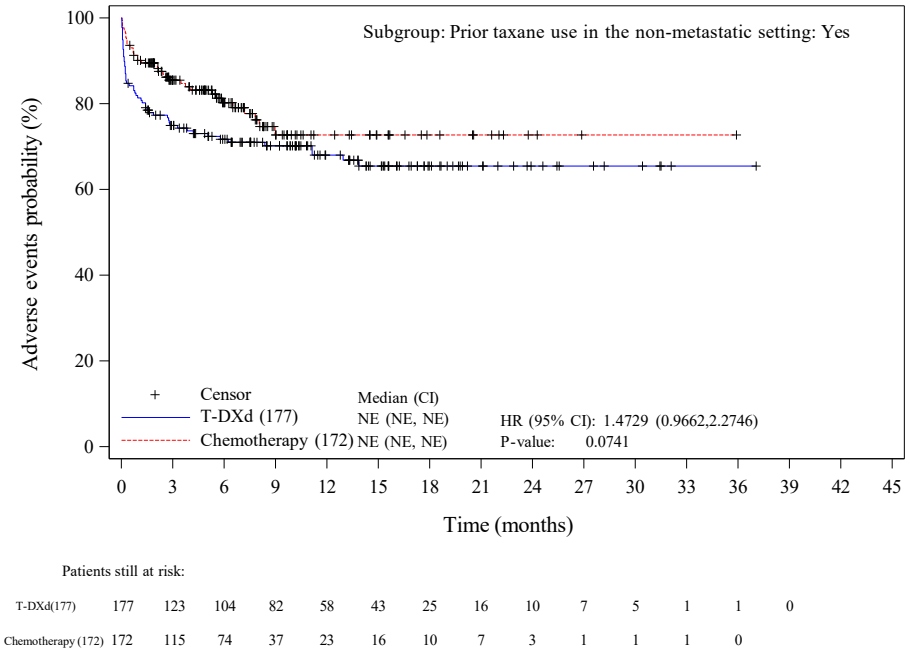
Run date: 13DEC2024 11:19; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Constipation



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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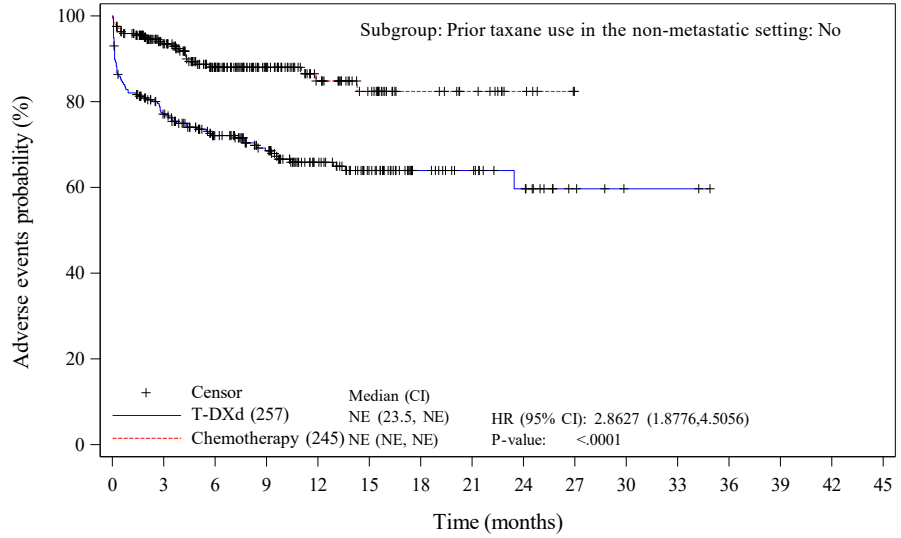
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Constipation



Patients still at risk:

T-DXd(257)	257	183	140	111	76	53	28	21	14	5	2	2	0
Chemotherapy (245)	245	175	118	79	49	32	17	12	5	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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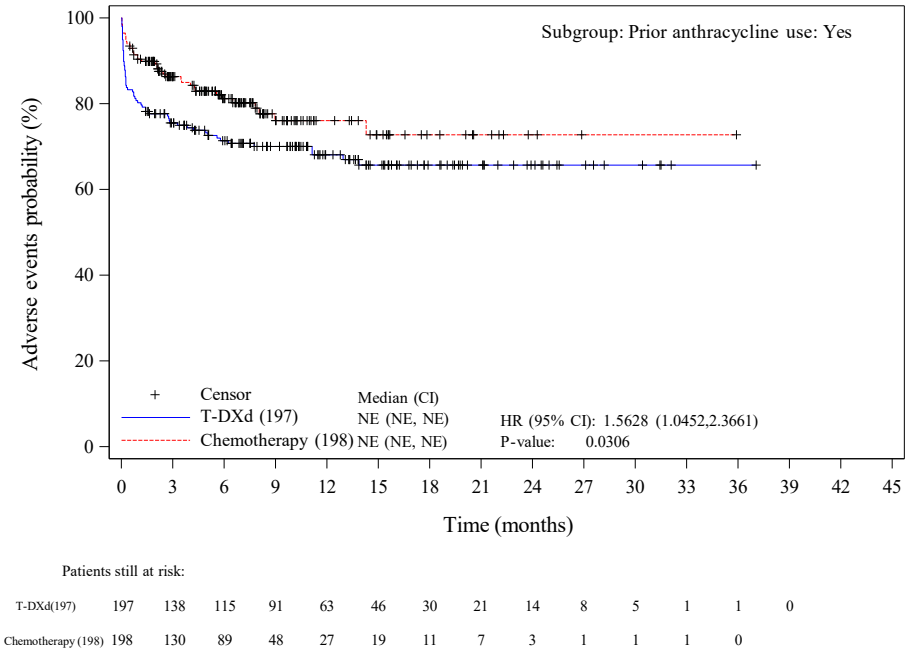
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Constipation



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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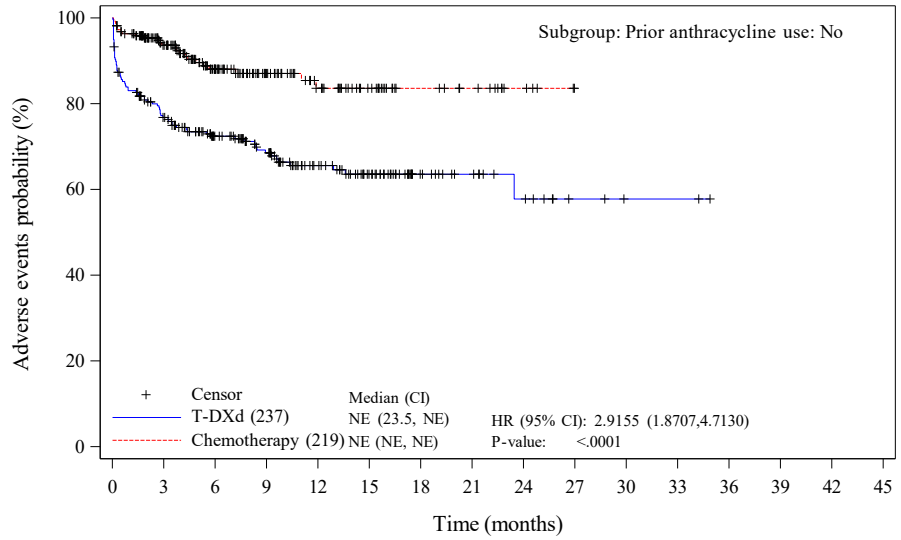
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Constipation



Patients still at risk:

T-DXd(237)	237	168	129	102	71	50	23	16	10	4	2	2	0
Chemotherapy (219)	219	160	103	68	45	29	16	12	5	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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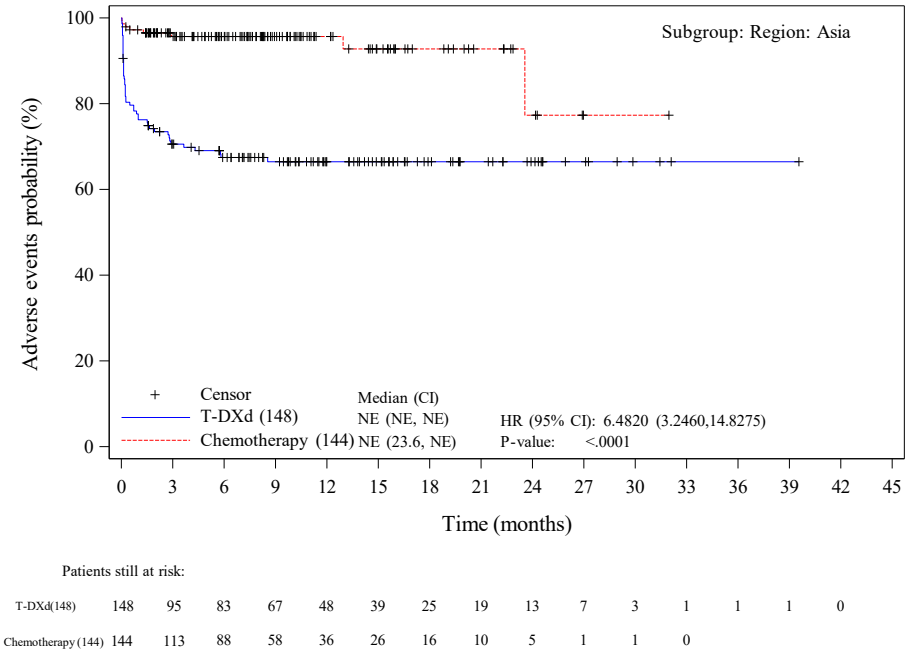
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Vomiting



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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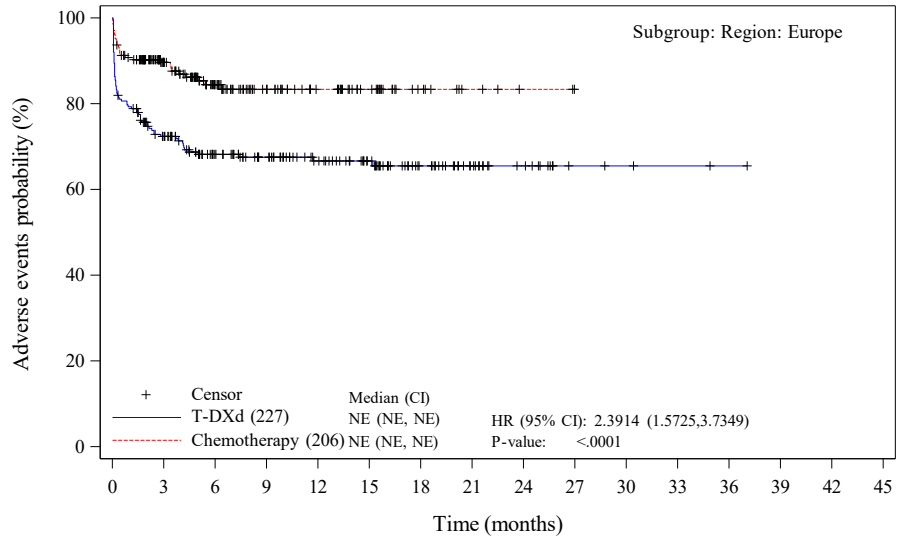
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Vomiting



Patients still at risk:

T-DXd(227)	227	150	113	94	75	59	36	22	13	4	3	2	1	0
Chemotherapy (206)	206	135	83	55	39	26	11	5	2	0				

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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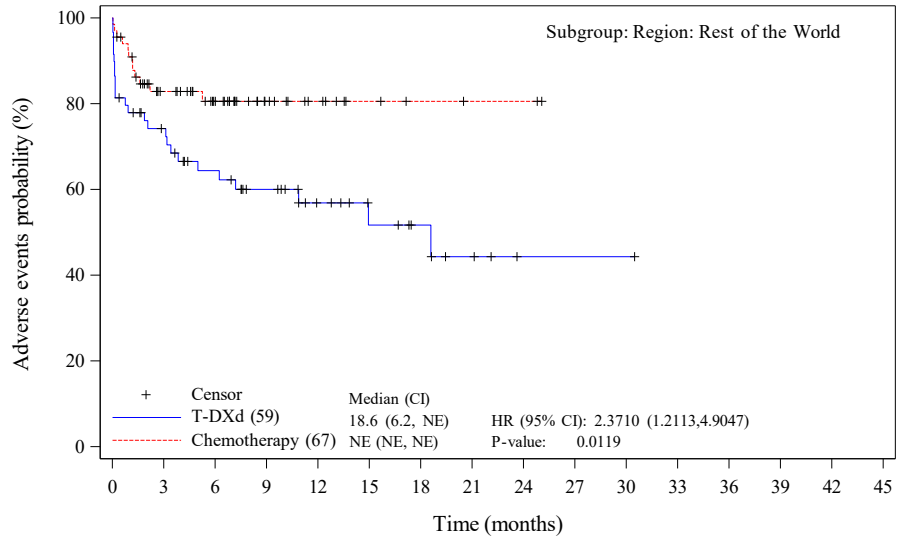
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Vomiting



Patients still at risk:

T-DXd(59)	59	39	30	23	15	10	7	4	1	1	1	0
Chemotherapy (67)	67	43	31	16	10	5	3	2	2	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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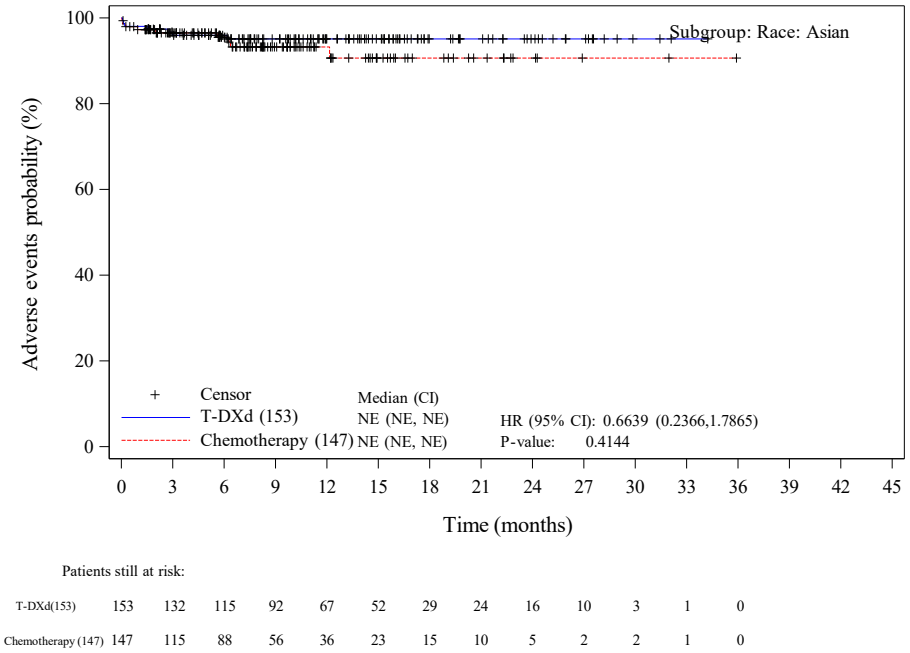
Run date: 13DEC2024 11:19; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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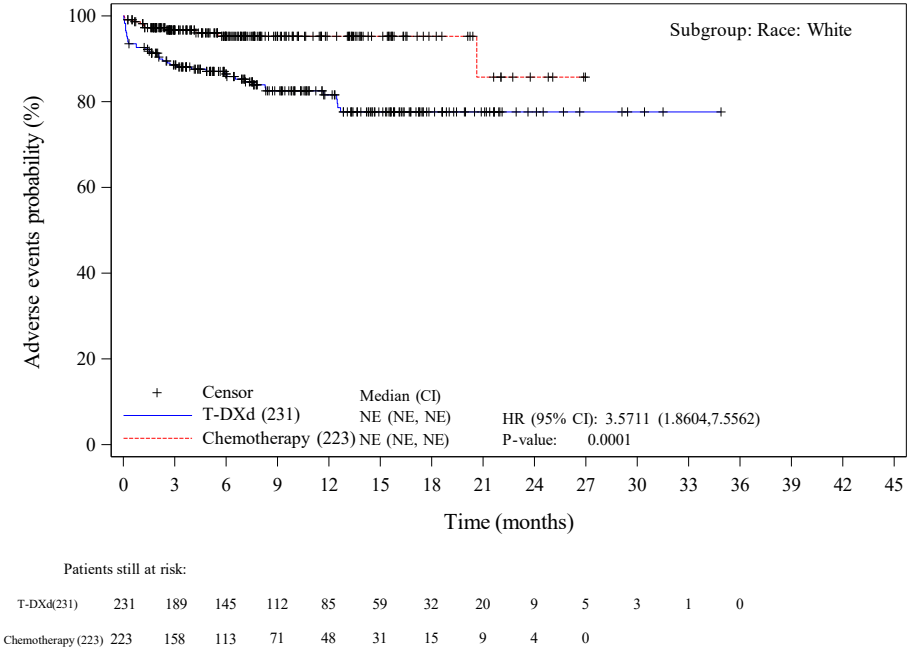
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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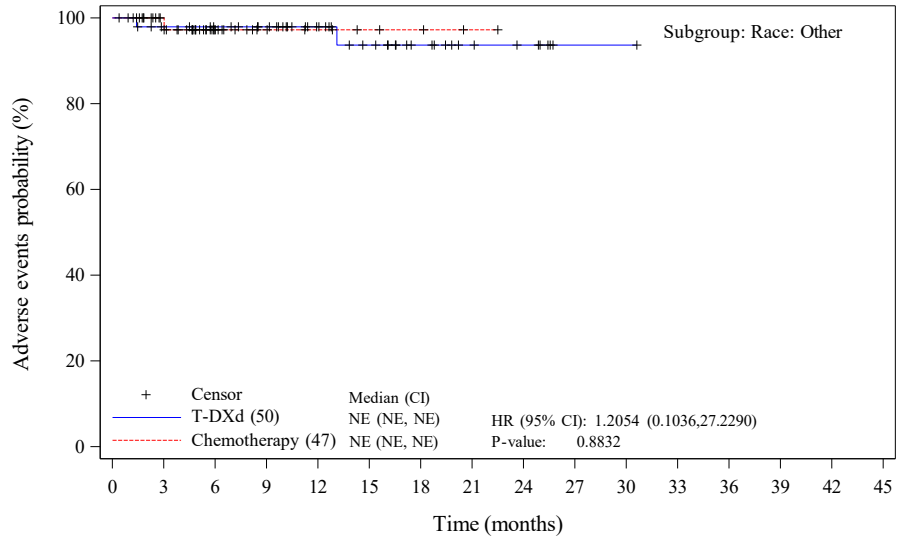
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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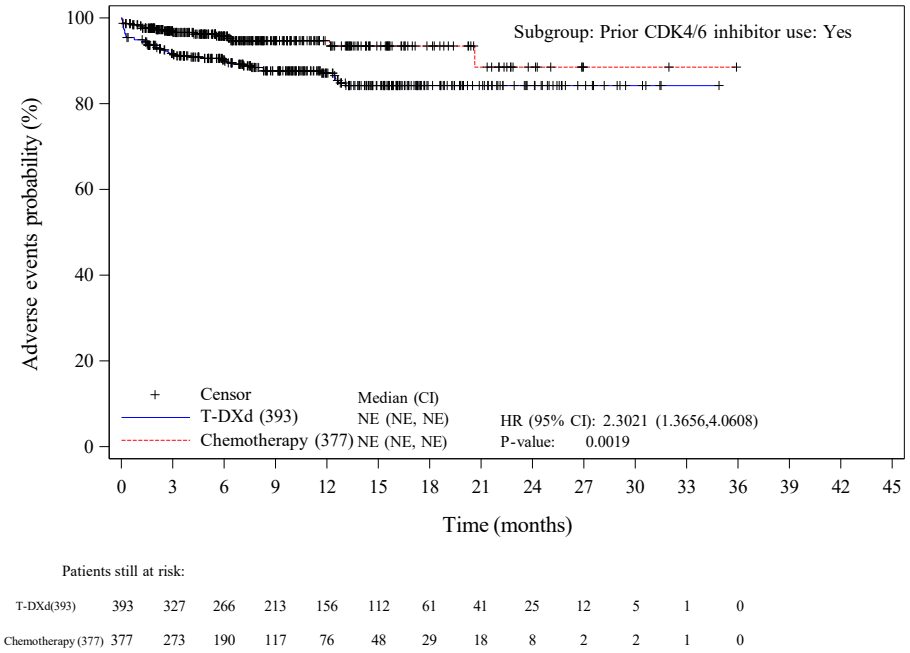
Run date: 13DEC2024 11:19; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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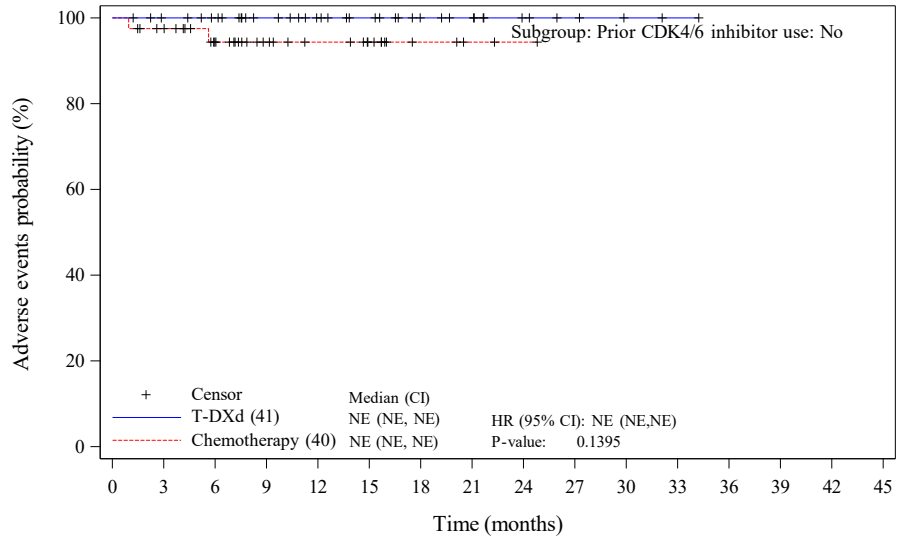
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia



Patients still at risk:

T-DXd(41)	41	38	35	28	23	19	13	11	6	4	2	1	0
Chemotherapy (40)	40	36	27	18	14	10	4	2	1	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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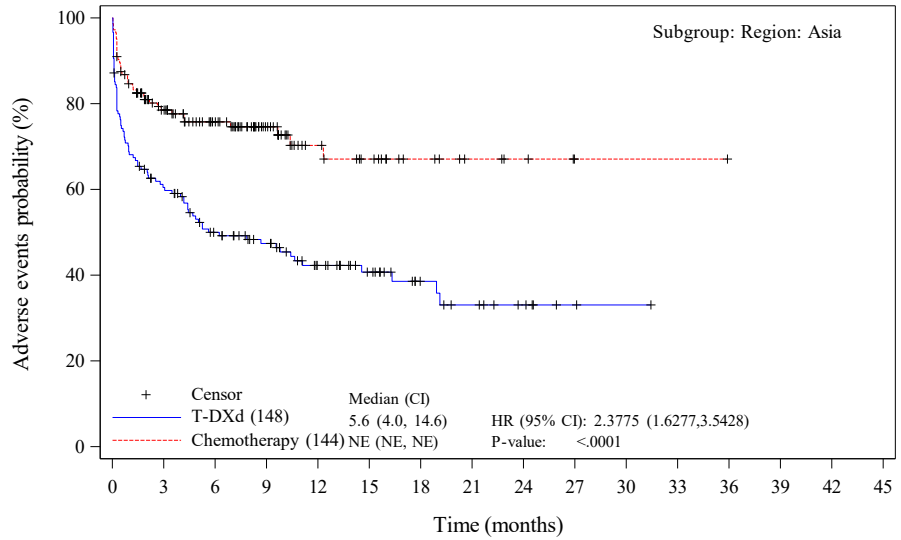
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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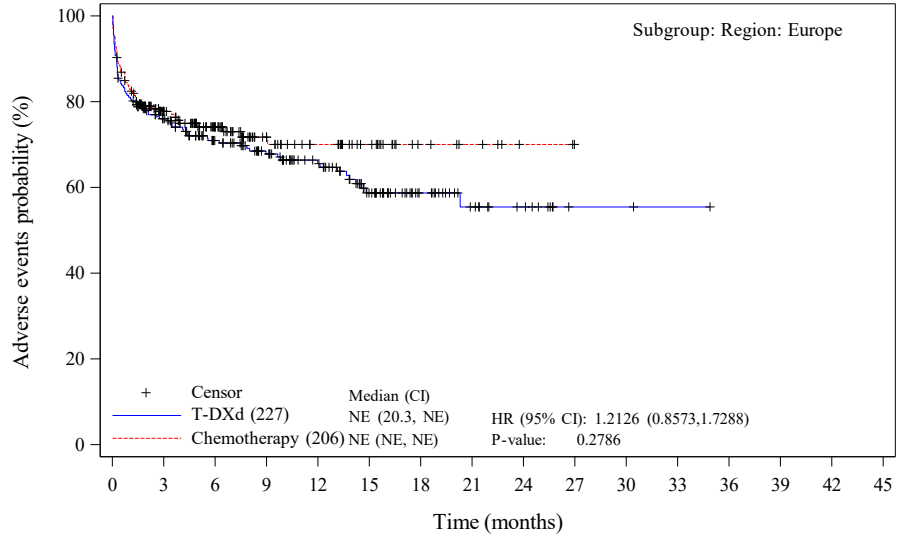
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Patients still at risk:

T-DXd(227)	227	159	122	100	78	51	28	16	10	2	2	1	0
Chemotherapy (206)	206	115	75	44	31	21	9	6	2	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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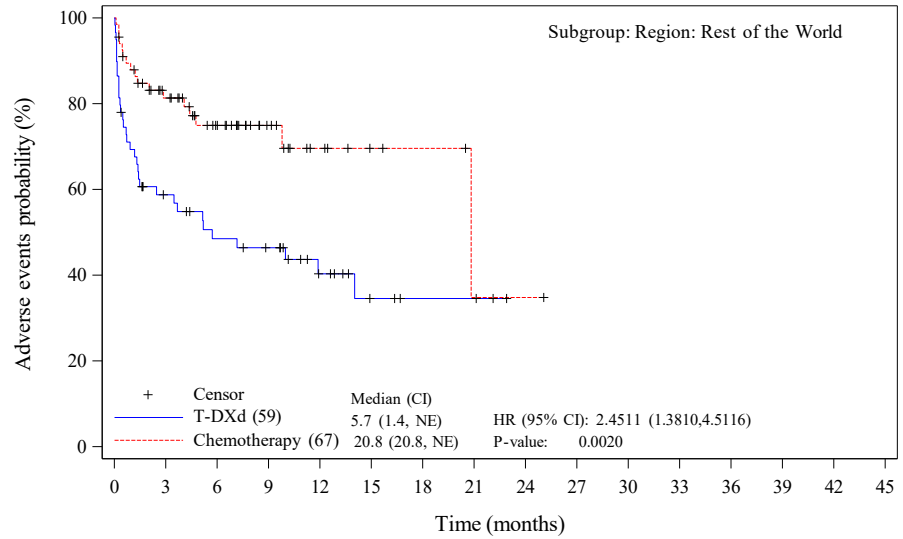
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Patients still at risk:

T-DXd(59)	59	30	23	20	11	5	3	3	0	
Chemotherapy (67)	67	45	30	16	8	4	3	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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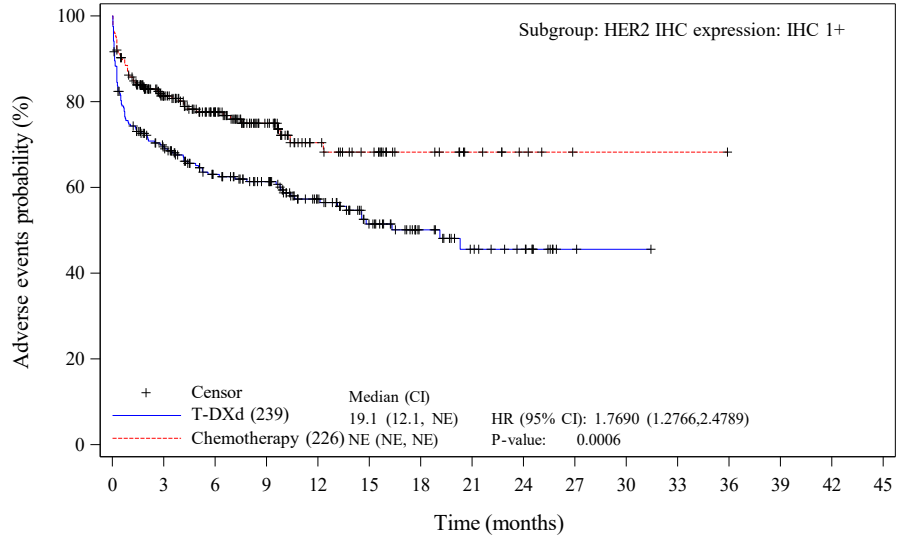
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Patients still at risk:

T-DXd(239)	239	151	118	100	71	46	27	17	12	2	1	0
Chemotherapy (226)	226	144	102	63	33	24	14	8	4	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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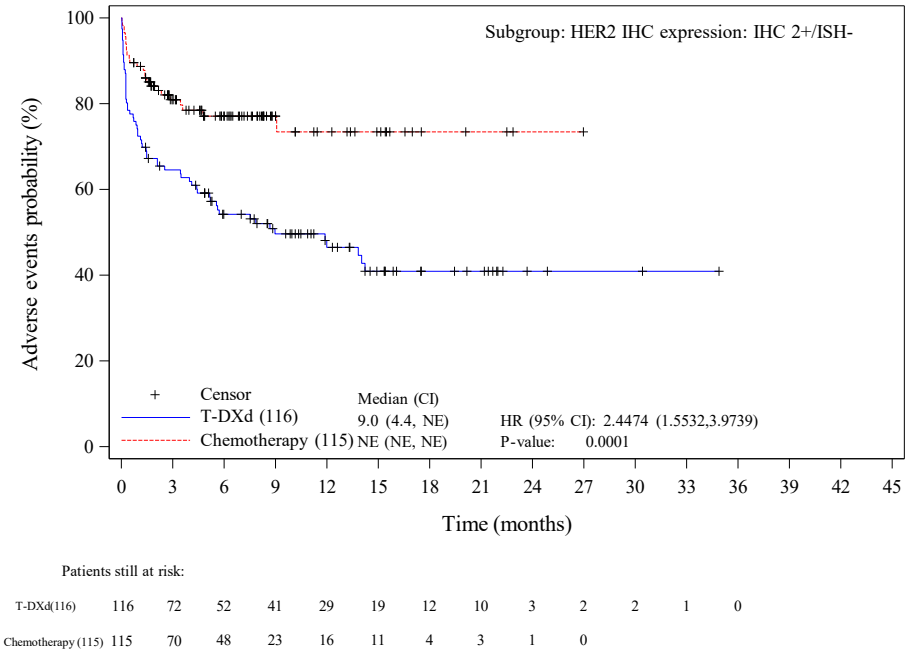
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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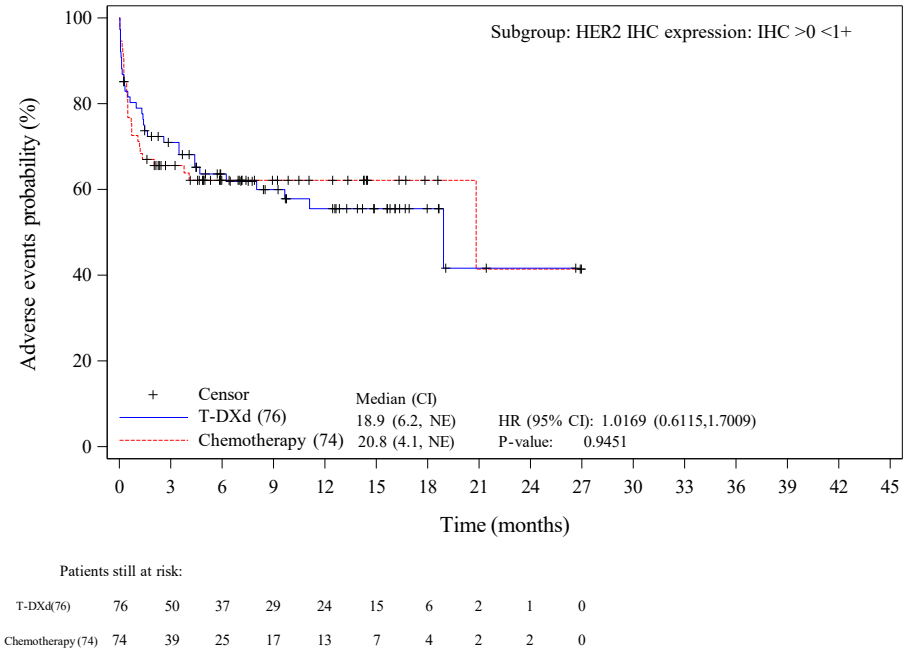
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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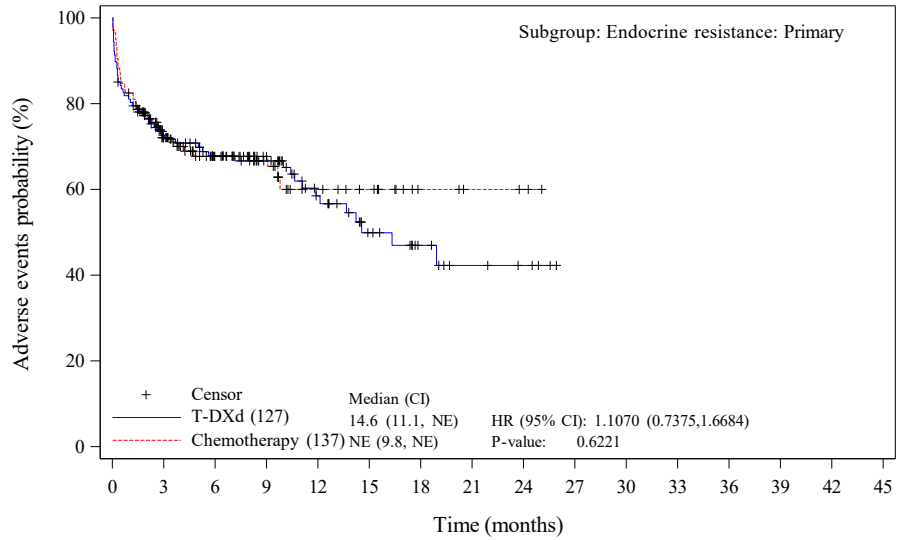
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Patients still at risk:

T-DXd(127)	127	80	64	50	32	19	11	6	4	0
Chemotherapy (137)	137	75	46	30	17	13	5	3	2	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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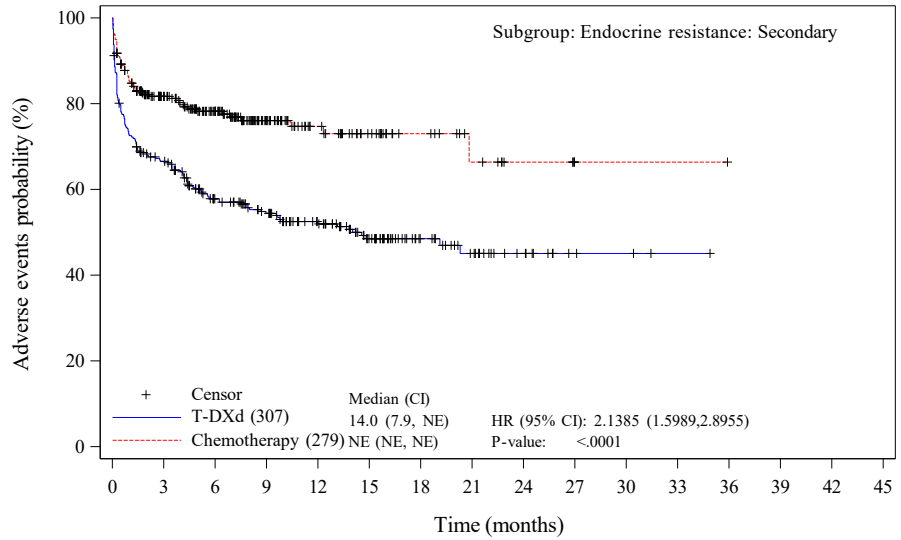
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Patients still at risk:

T-DXd(307)	307	194	144	121	93	62	34	23	12	4	3	1	0
Chemotherapy (279)	279	178	129	73	45	29	17	10	5	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)

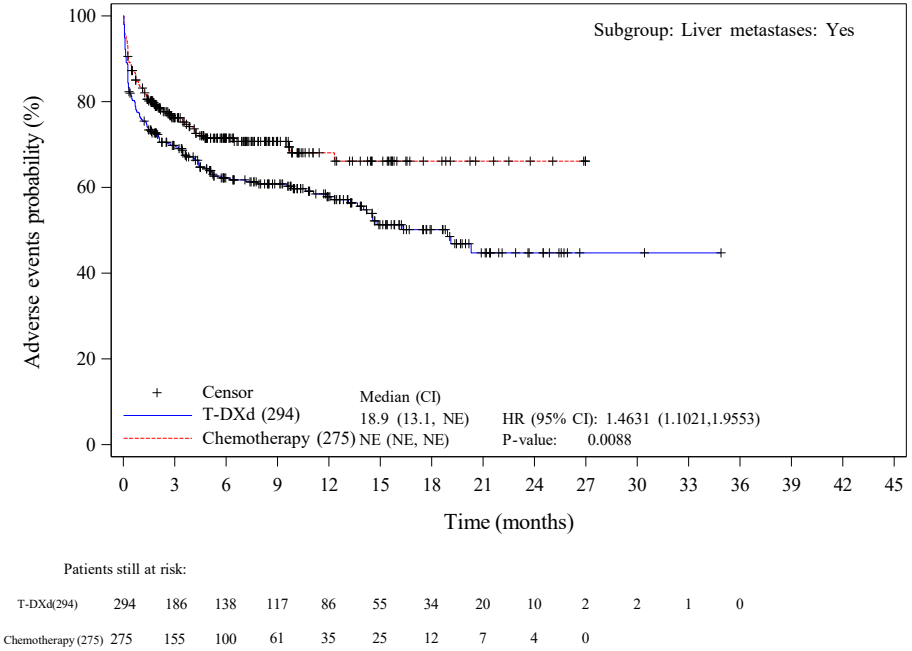

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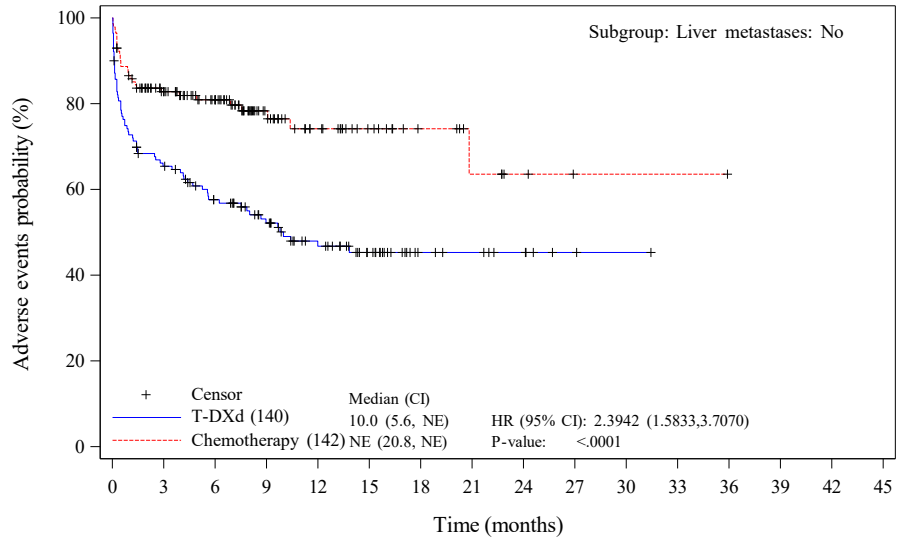
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Patients still at risk:

T-DXd(140)	140	88	70	54	39	26	11	9	6	2	1	0
Chemotherapy (142)	142	99	75	42	27	17	10	6	3	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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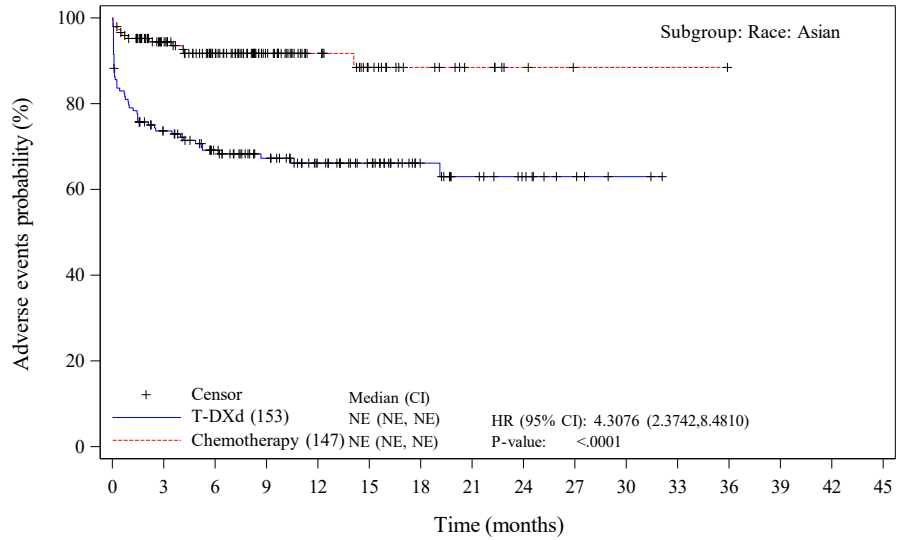
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



Patients still at risk:

T-DXd(153)	153	103	83	66	50	38	21	15	10	5	2	0
Chemotherapy (147)	147	113	85	54	32	20	12	7	3	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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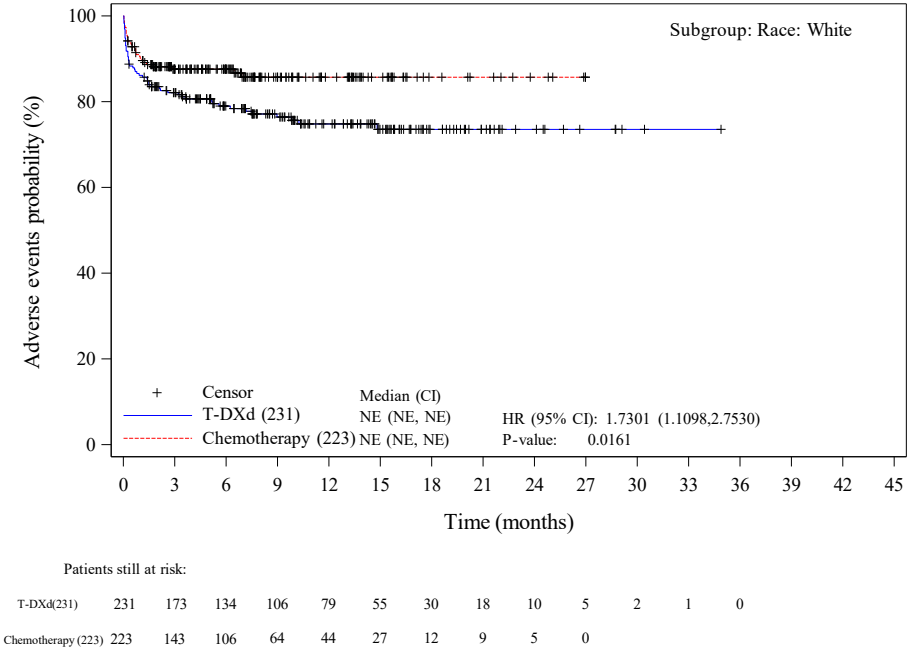
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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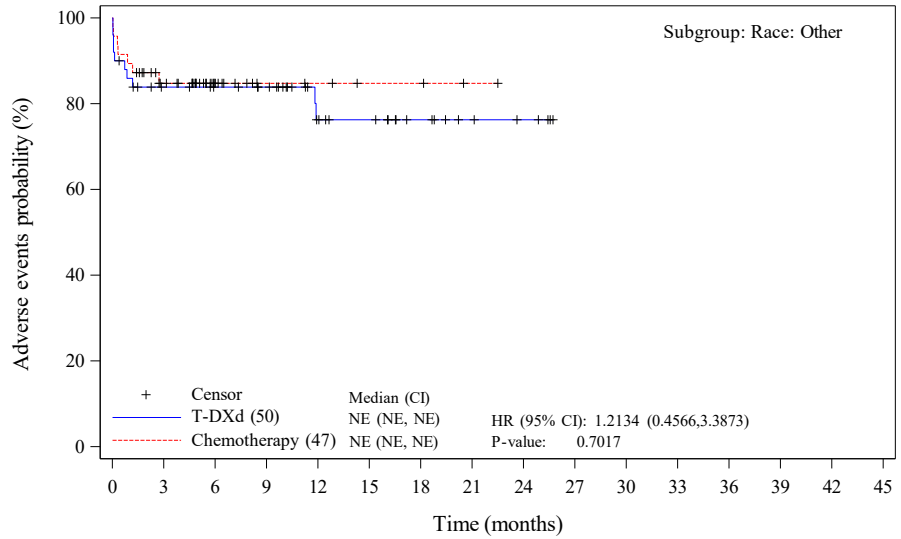
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



Patients still at risk:

T-DXd(50)	50	37	34	31	19	16	10	6	4	0
Chemotherapy (47)	47	32	14	6	5	3	3	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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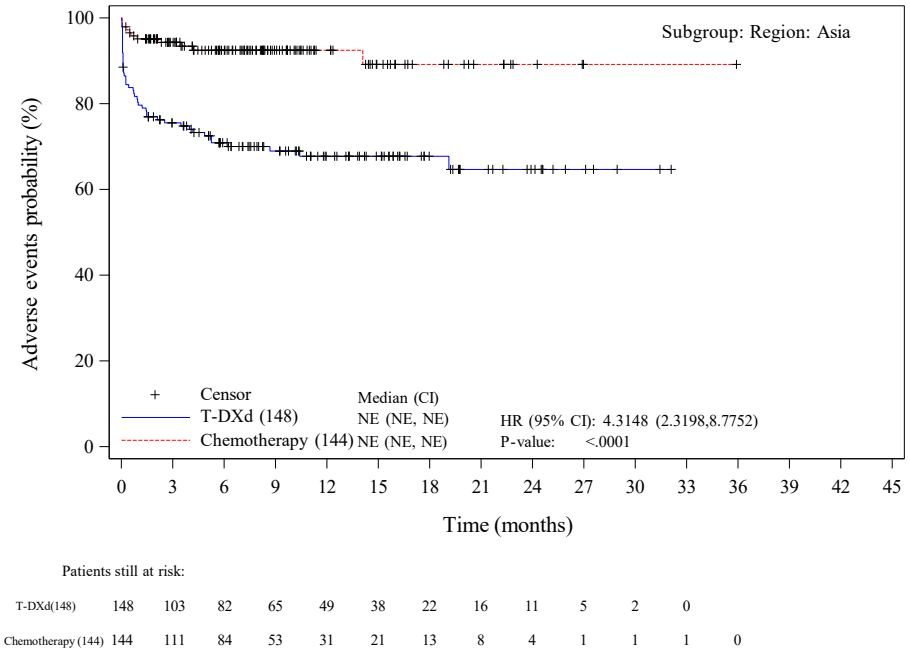
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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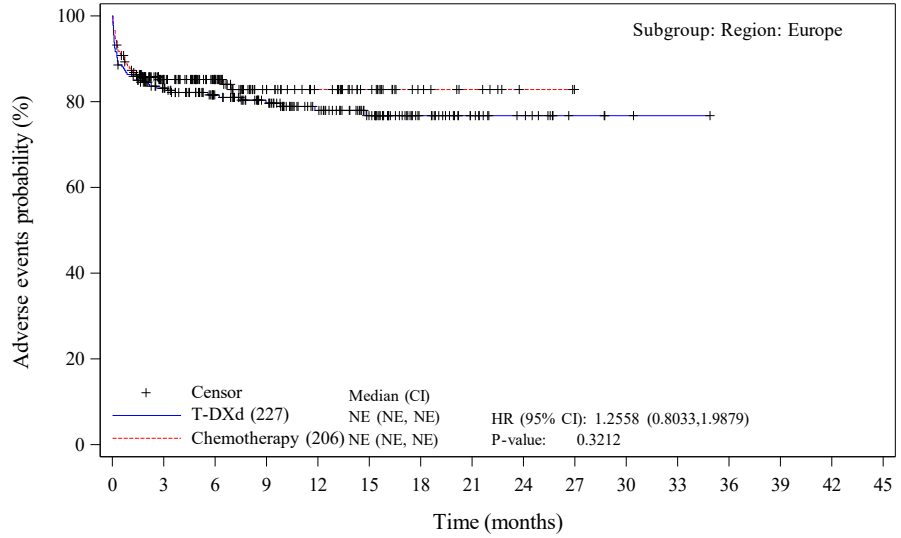
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



Patients still at risk:

T-DXd(227)	227	172	137	113	84	61	33	19	12	4	2	1	0
Chemotherapy (206)	206	127	86	52	38	24	11	7	2	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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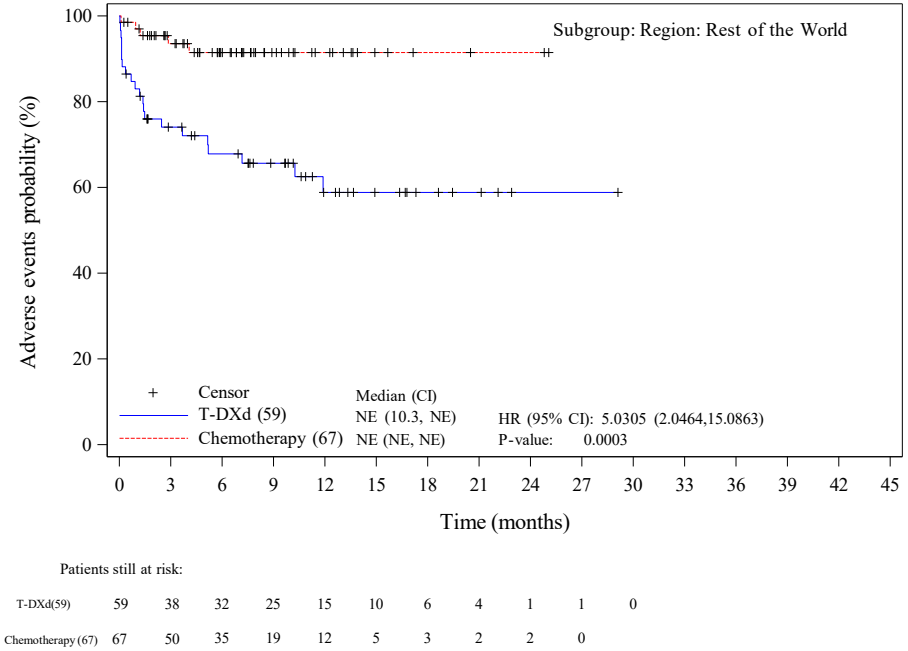
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



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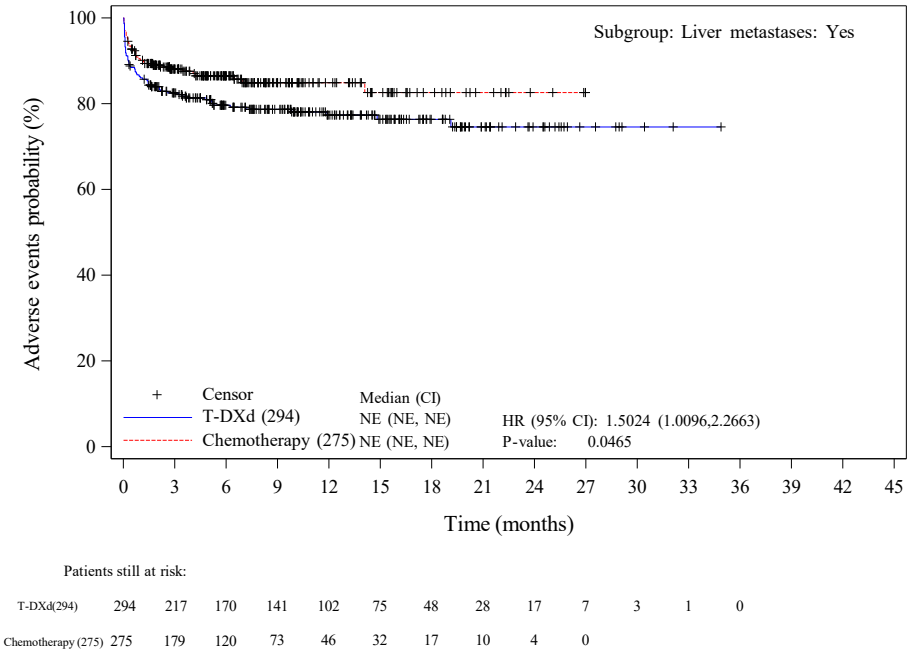
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



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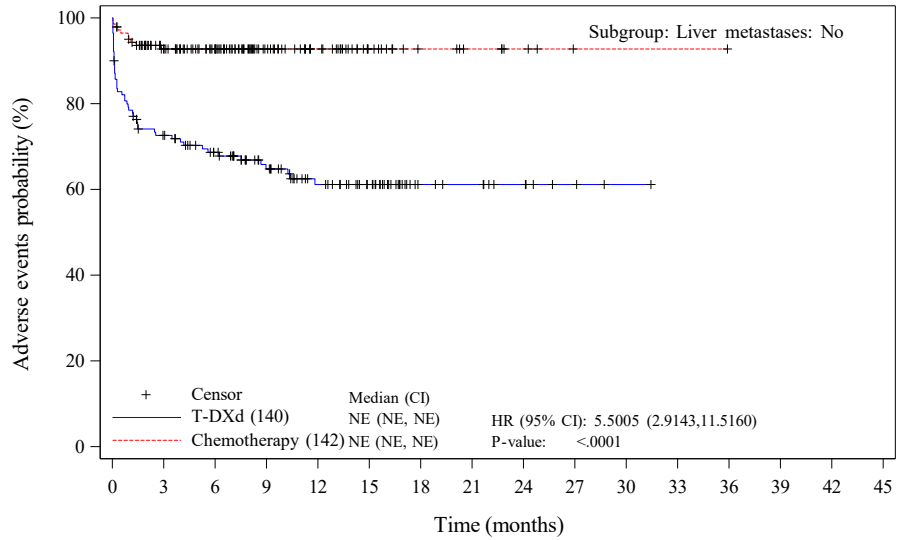
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



Patients still at risk:

T-DXd(140)	140	96	81	62	46	34	13	11	7	3	1	0
Chemotherapy (142)	142	109	85	51	35	18	10	7	4	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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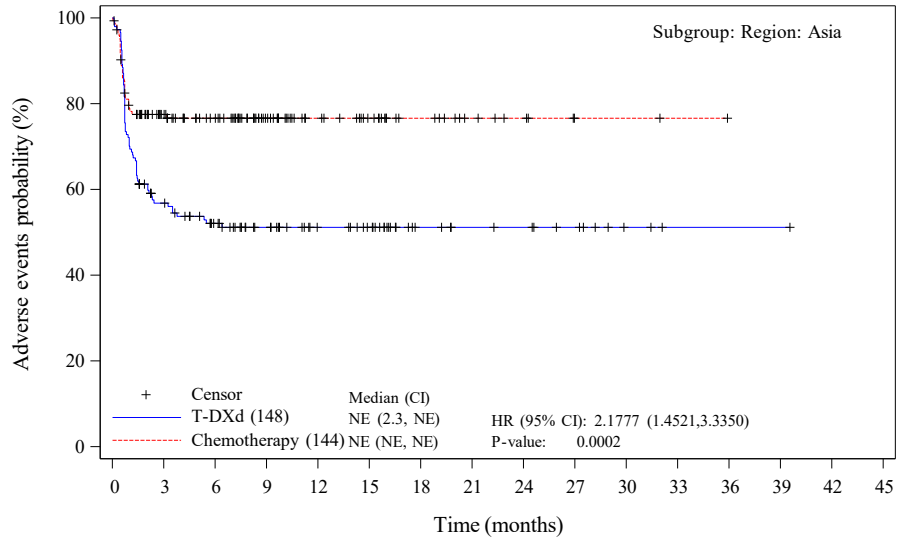
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Patients still at risk:

T-DXd(148)	148	75	59	45	34	29	15	12	11	8	3	1	1	1	0
Chemotherapy (144)	144	90	73	48	32	24	15	9	6	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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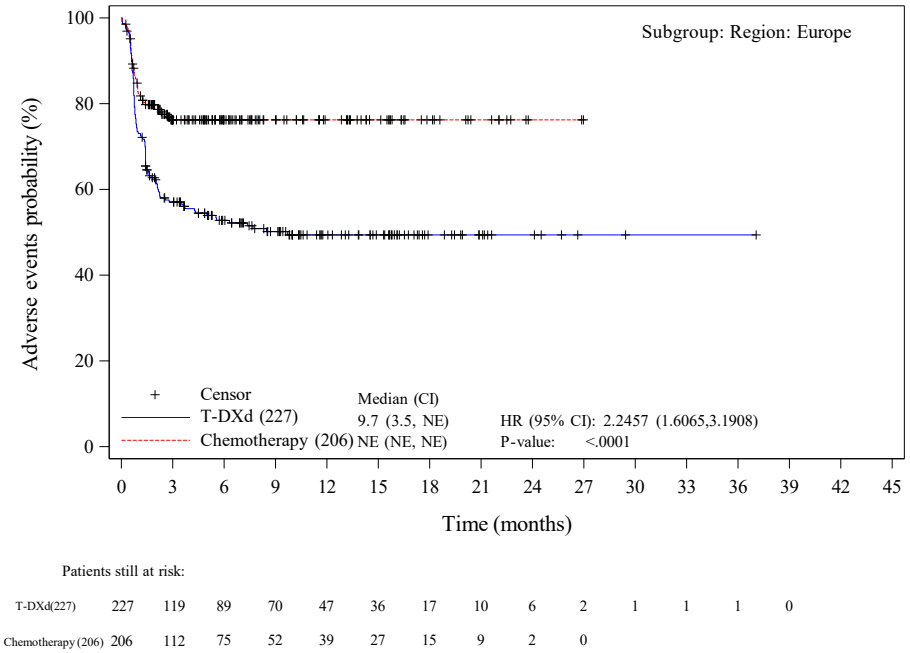
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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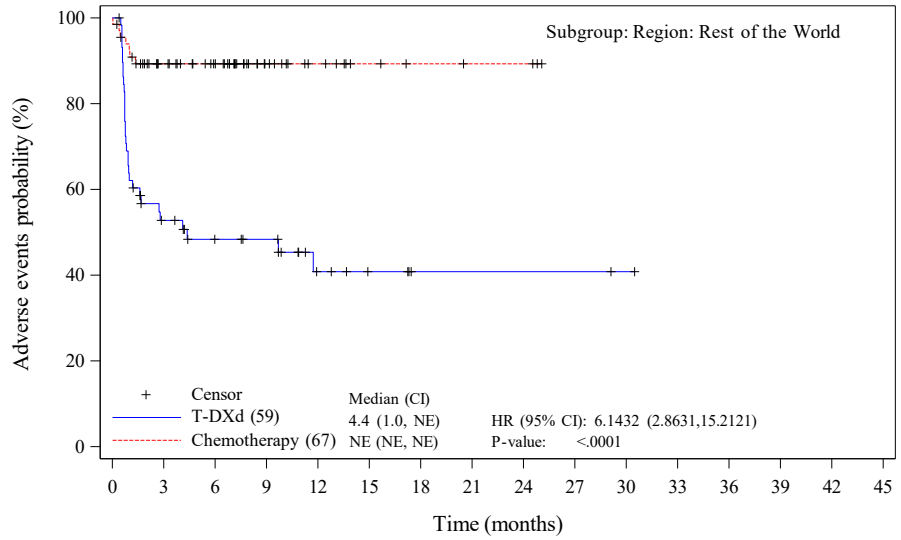
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Patients still at risk:

T-DXd(59)	59	26	19	17	8	5	2	2	2	2	1	0
Chemotherapy (67)	67	47	37	18	11	6	4	3	3	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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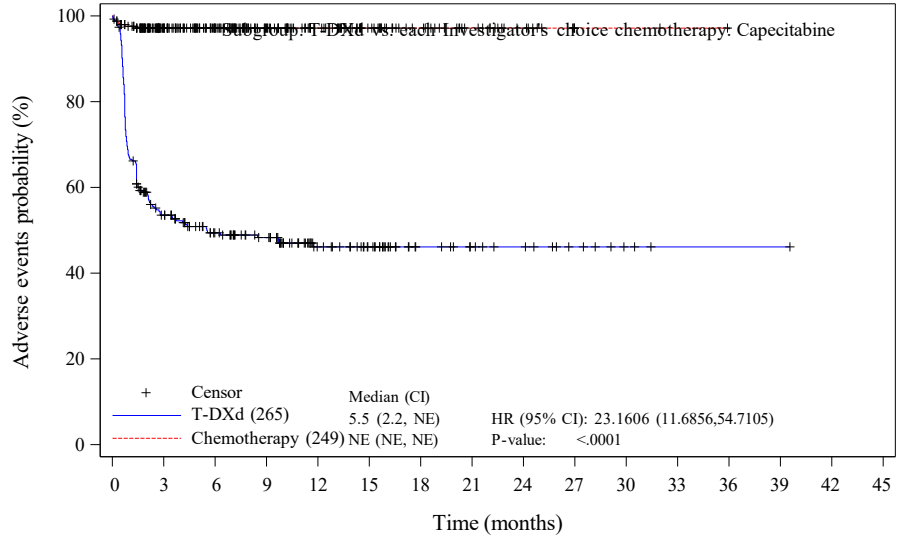
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Patients still at risk:

T-DXd(265)	265	128	97	81	50	38	20	15	12	7	3	1	1	1	0
Chemotherapy (249)	249	183	138	95	68	47	31	20	11	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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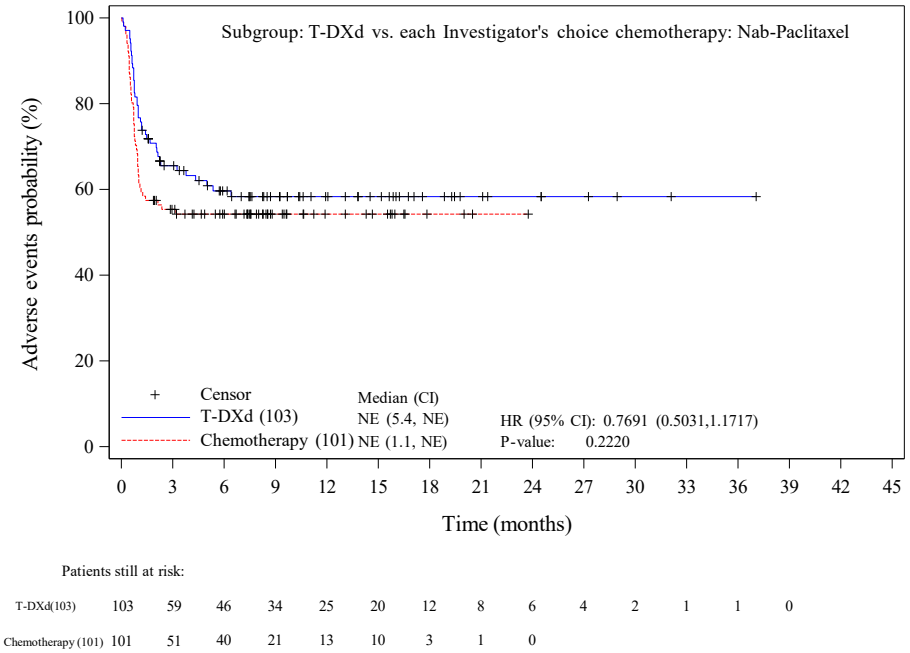
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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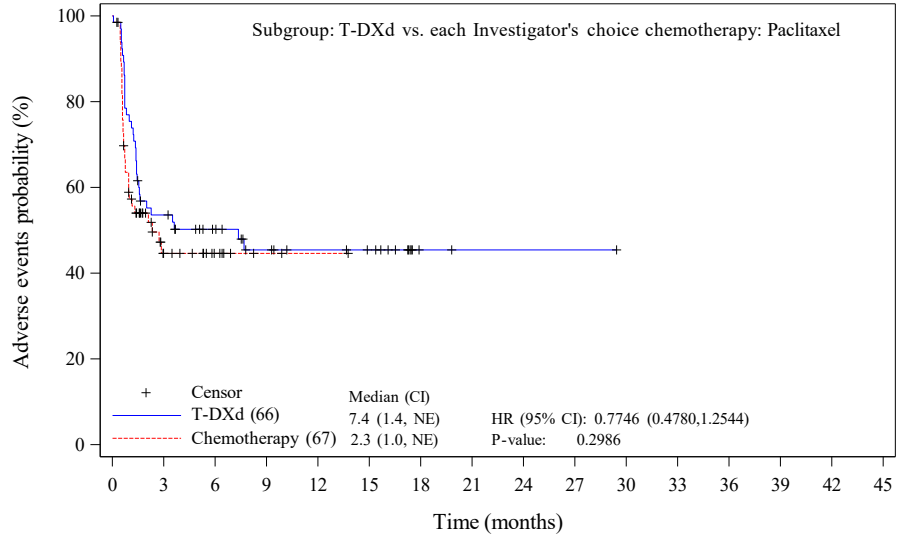
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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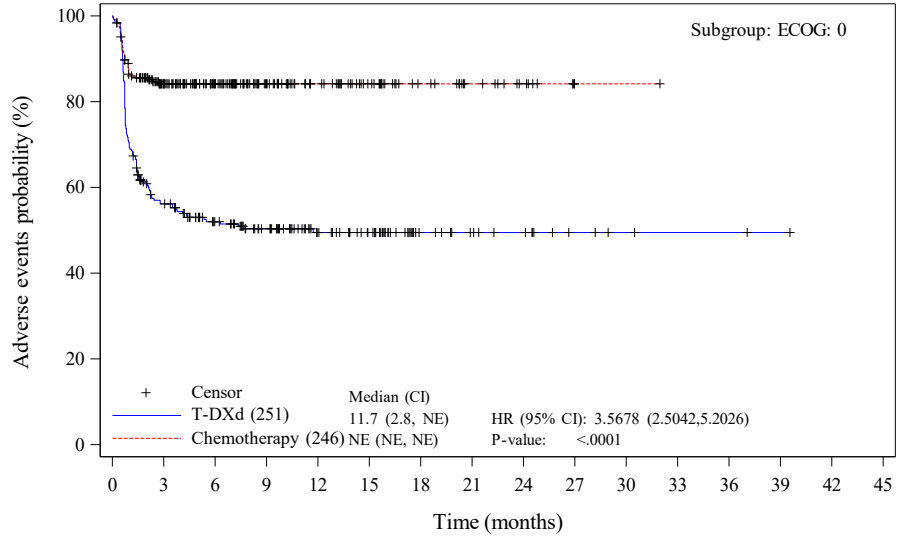
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Patients still at risk:

T-DXd(251)	251	131	100	80	55	43	19	14	11	5	3	2	2	1	0
Chemotherapy (246)	246	165	119	80	56	39	23	15	9	1	1	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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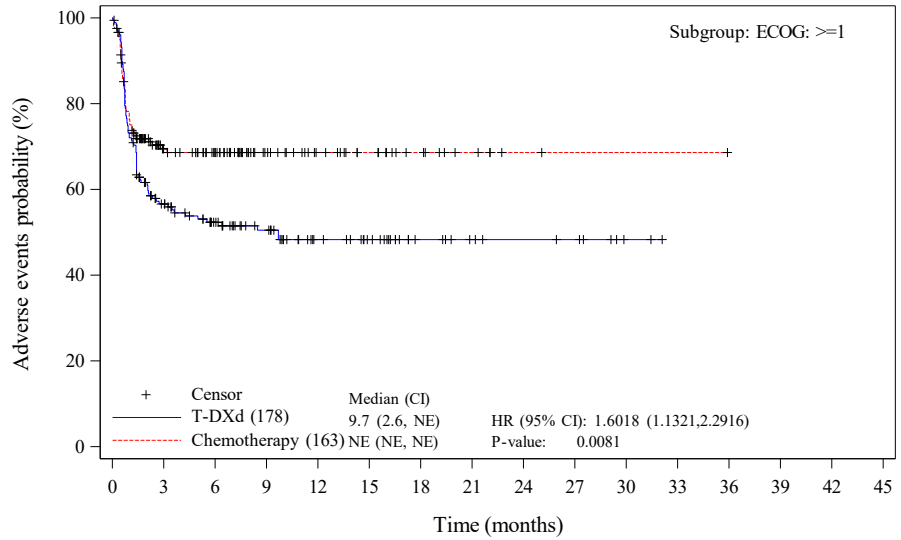
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Patients still at risk:

T-DXd(178)	178	86	65	50	33	26	14	10	8	7	2	0	
Chemotherapy (163)	163	79	62	36	25	18	11	6	2	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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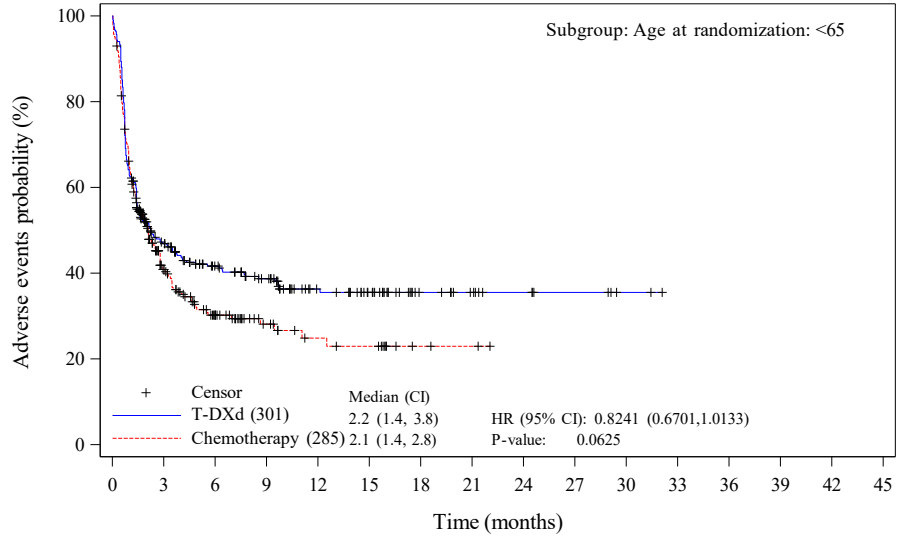
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)



Patients still at risk:

T-DXd(301)	301	126	90	71	46	35	17	12	8	5	2	0
Chemotherapy (285)	285	81	43	21	13	11	3	2	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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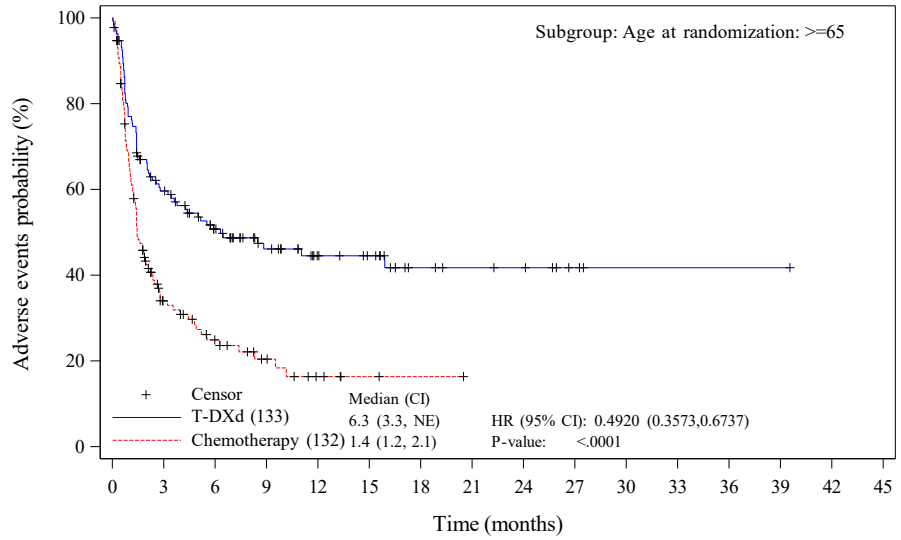
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)



Patients still at risk:

T-DXd(133)	133	72	51	35	24	20	10	8	7	3	1	1	1	1	0
Chemotherapy (132)	132	32	19	11	5	2	1	0							

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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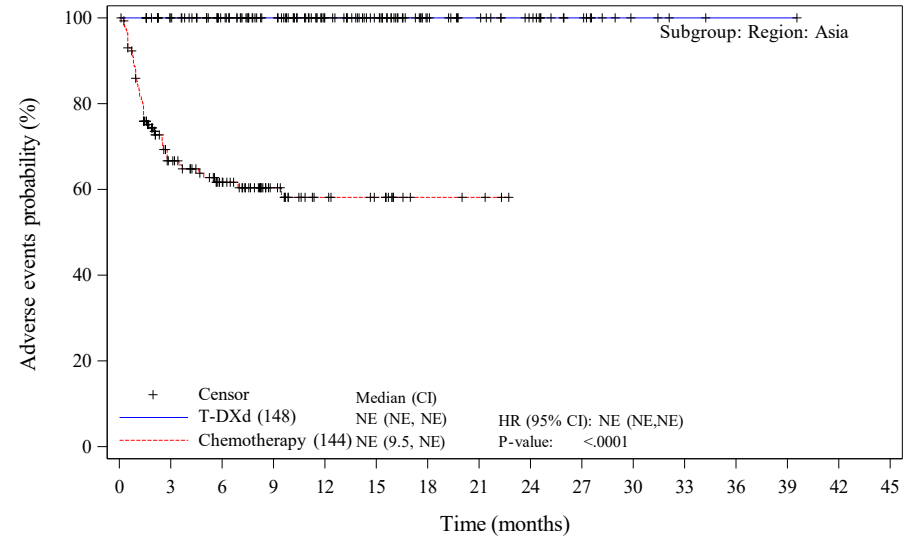
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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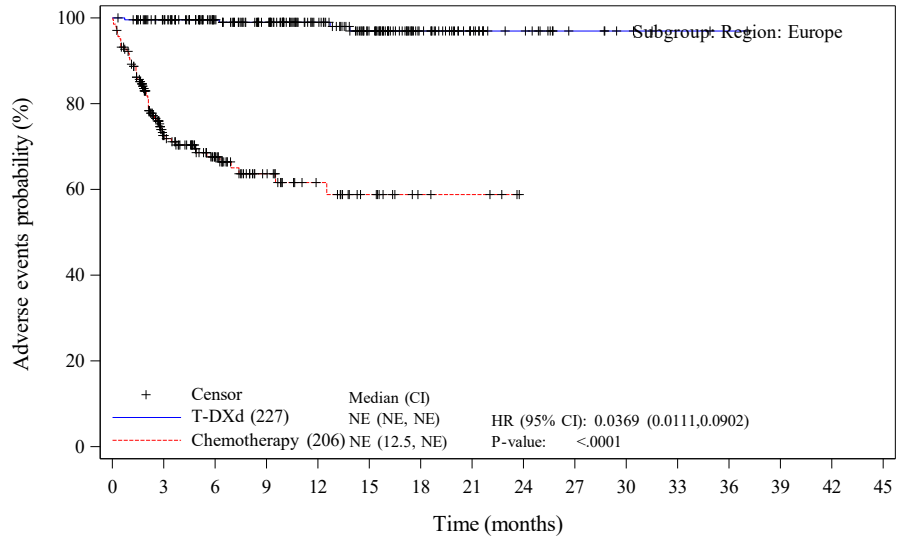
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome



Patients still at risk:

T-DXd(227)	227	208	169	144	108	79	44	25	16	7	4	2	1	0
Chemotherapy (206)	206	101	62	35	22	13	5	4	0					

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome

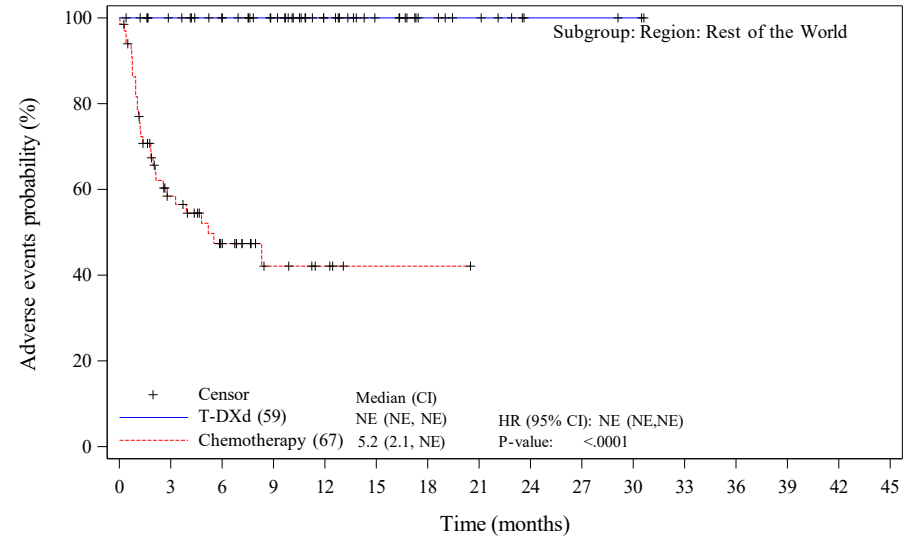

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Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)

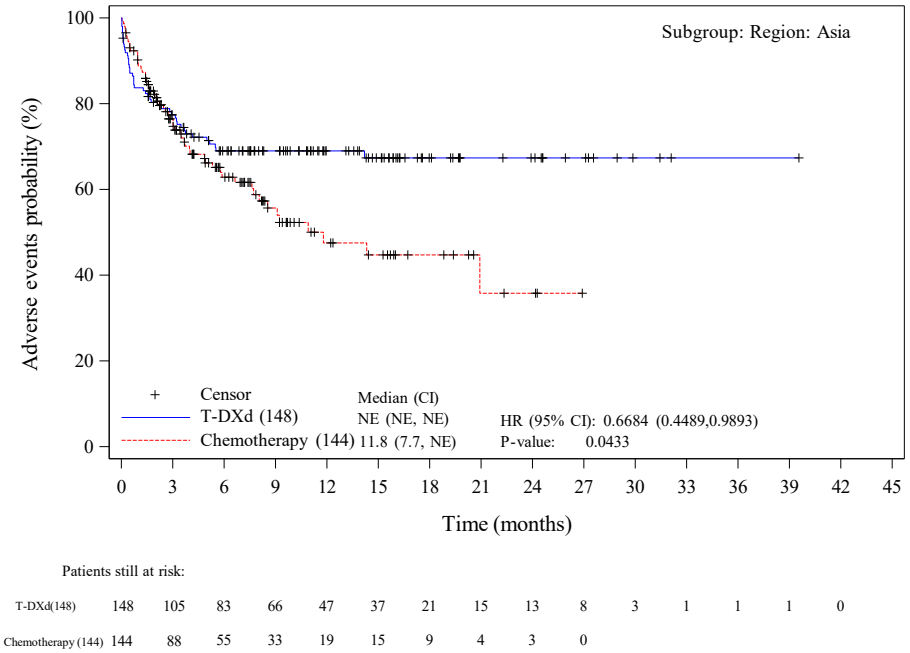

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Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)

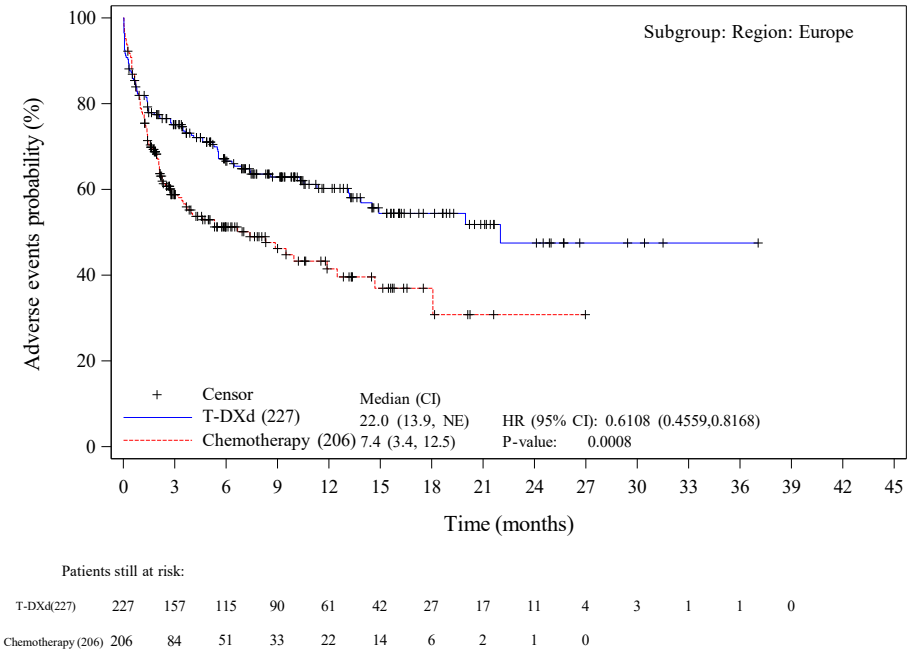

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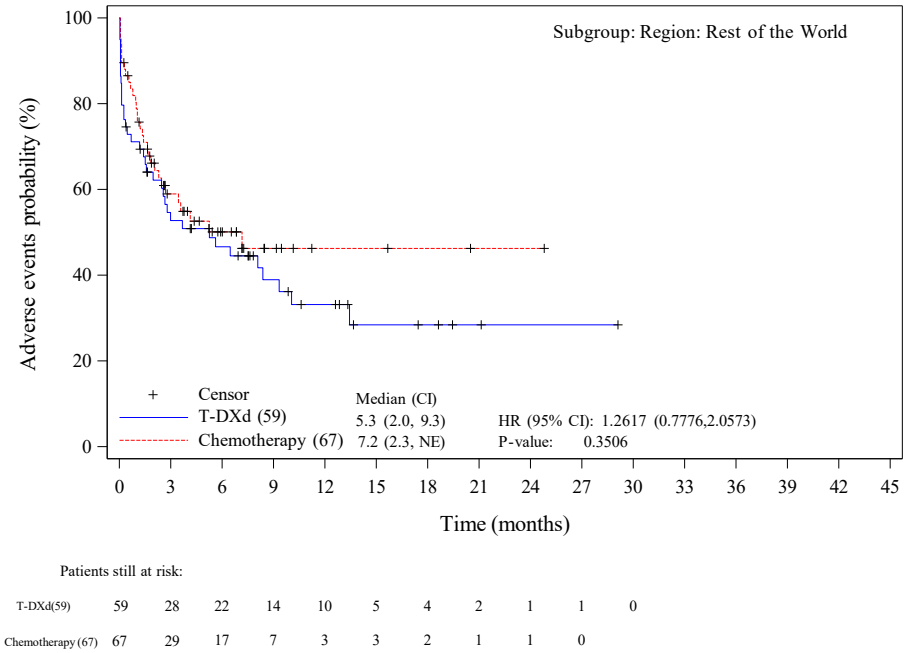
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)



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SOC: Nervous system disorders; PT: All (any PT)

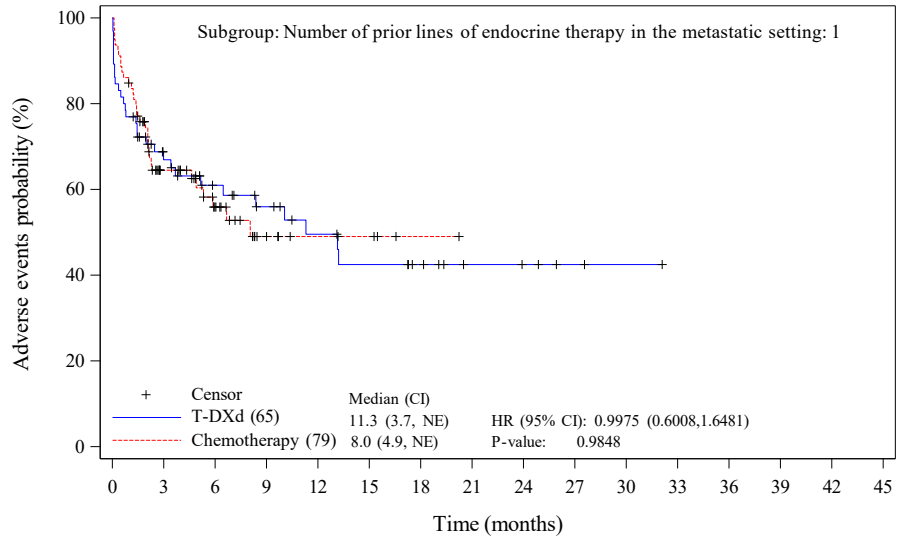

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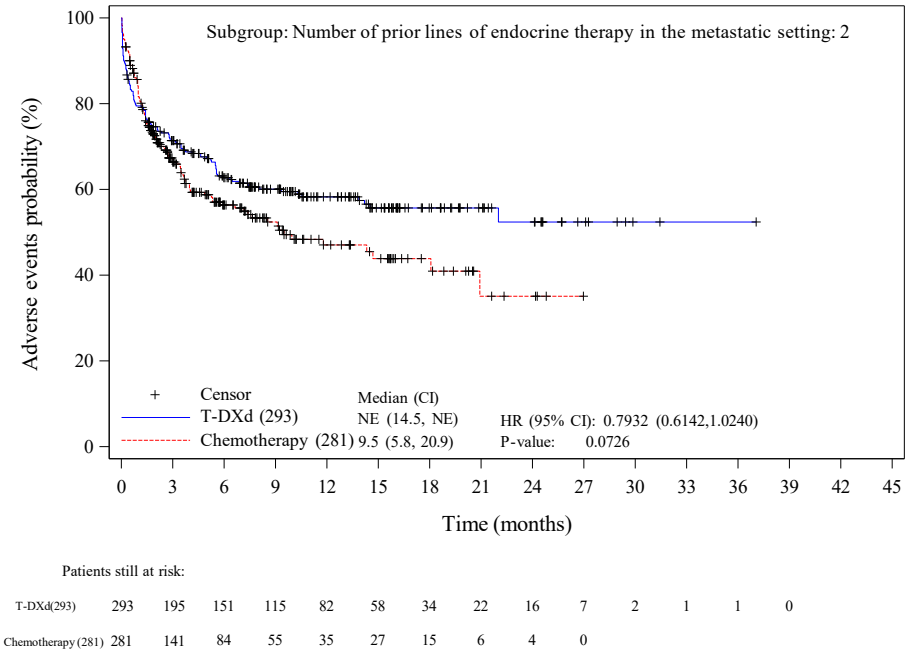
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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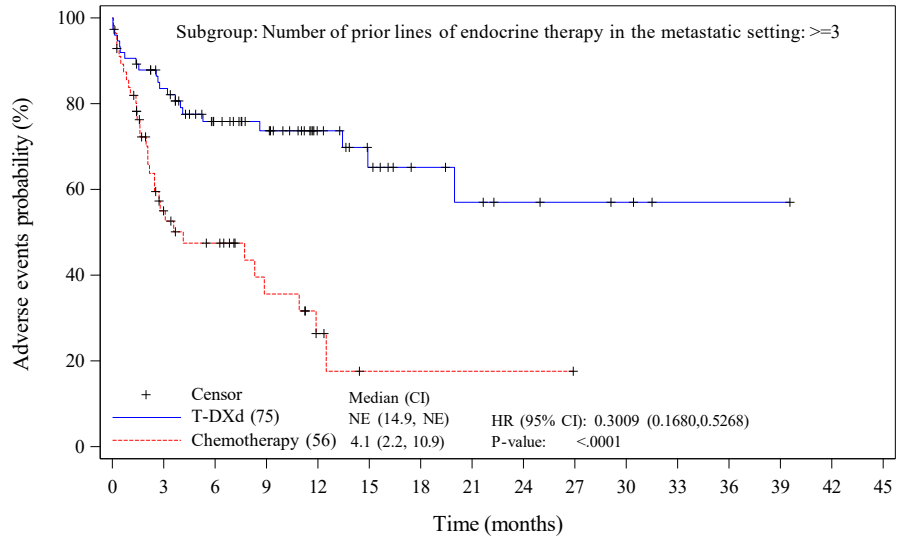
SOC: Nervous system disorders; PT: All (any PT)



Patients still at risk:

T-DXd(75)	75	58	42	34	21	14	9	7	5	4	3	1	1	1	0
Chemotherapy (56)	56	23	17	9	4	1	1	1	1	0					

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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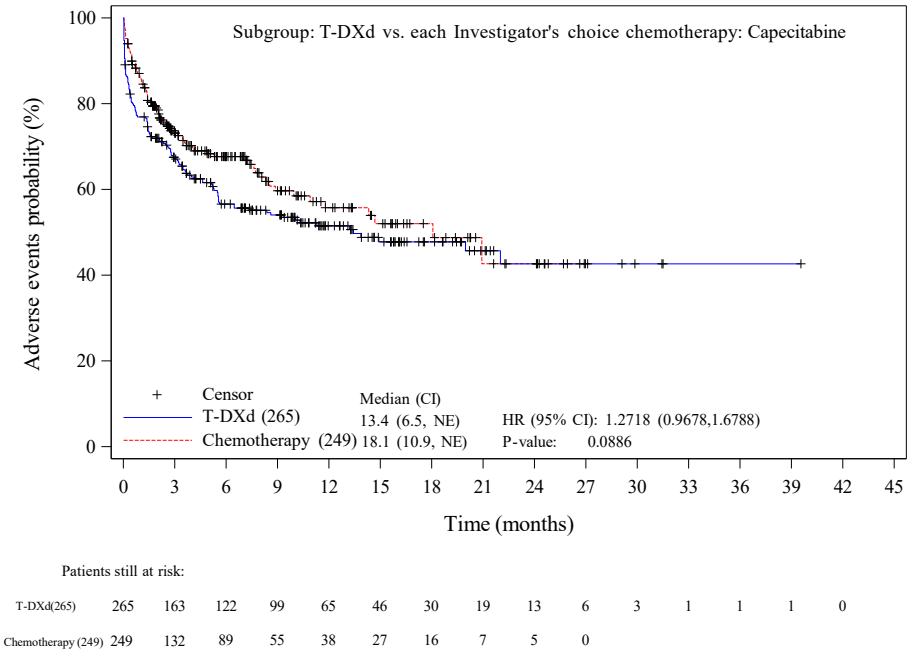
SOC: Nervous system disorders; PT: All (any PT)



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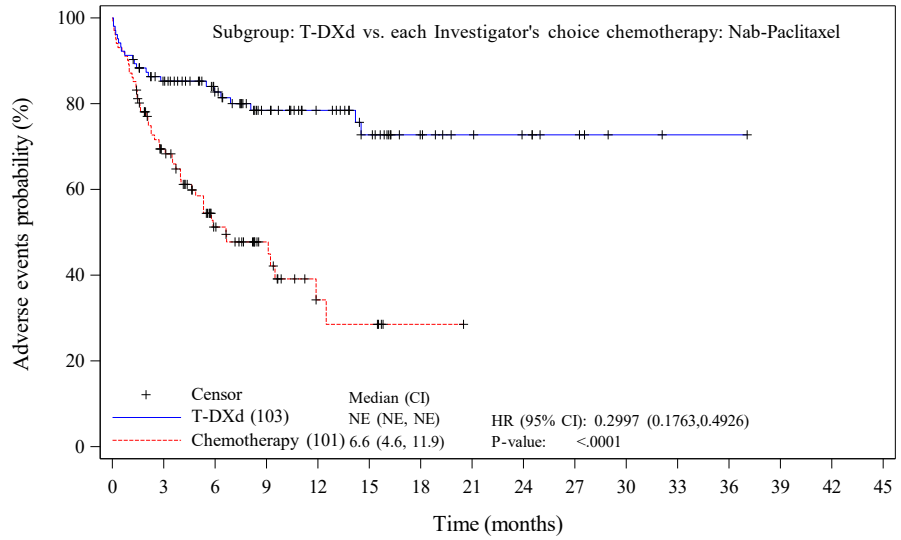
SOC: Nervous system disorders; PT: All (any PT)



Patients still at risk:

T-DXd(103)	103	80	63	45	34	24	14	10	8	5	2	1	1	0
Chemotherapy (101)	101	61	31	17	6	5	1	0						

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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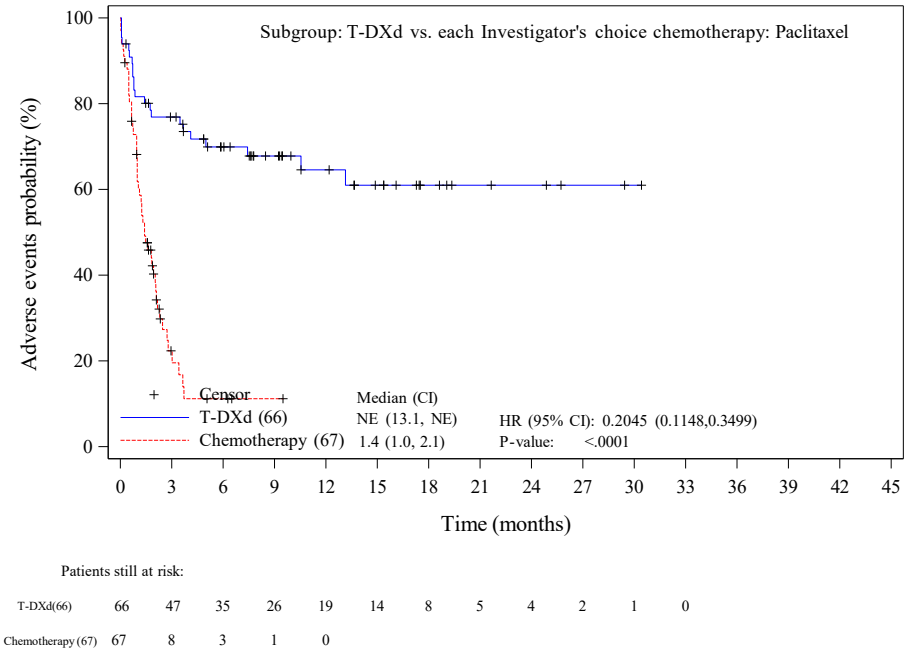
SOC: Nervous system disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)

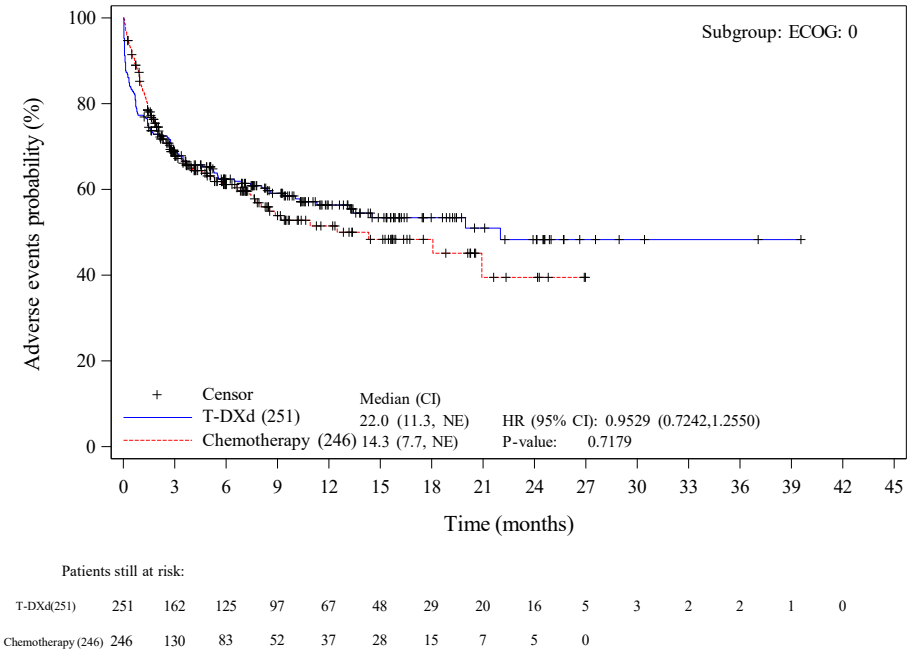

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Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)

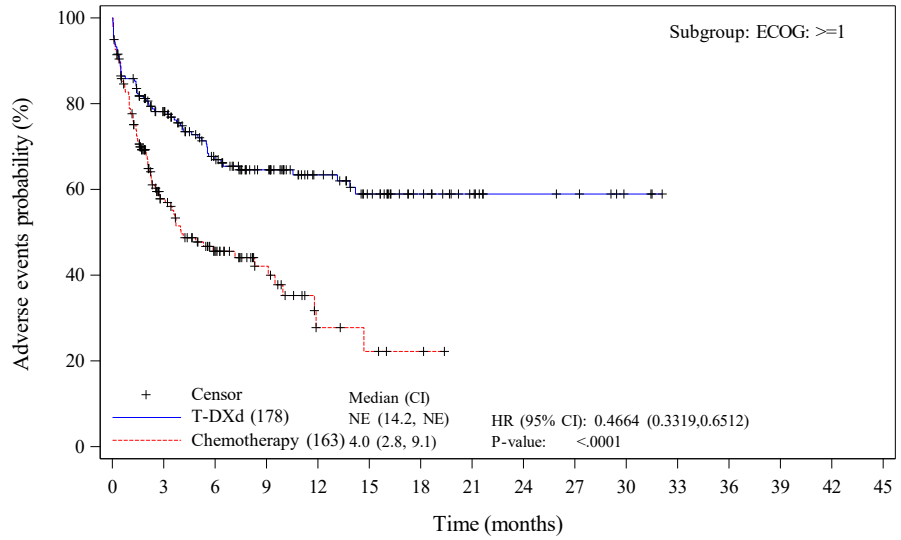

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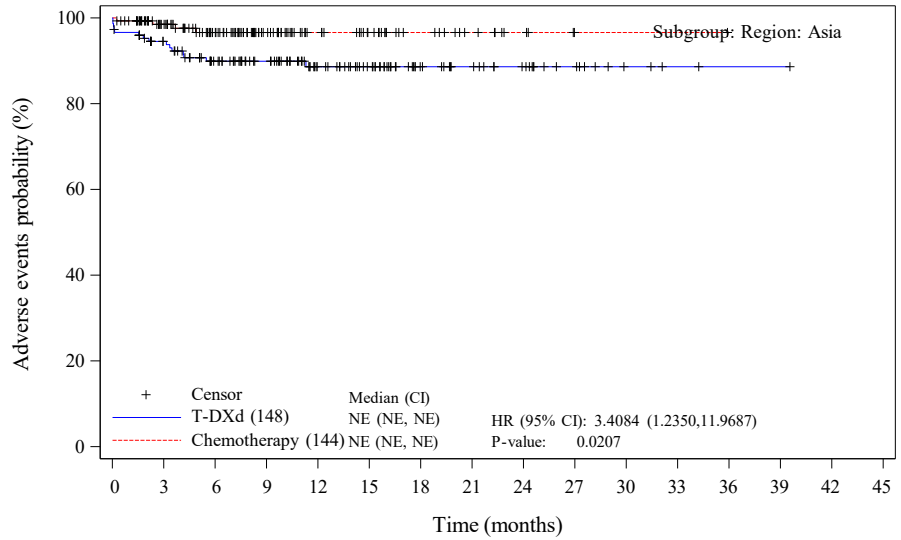
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Dysgeusia



Patients still at risk:

T-DXd(148)	148	126	104	86	62	49	29	23	17	10	4	2	1	1	0
Chemotherapy (144)	144	116	88	57	35	26	16	10	5	1	1	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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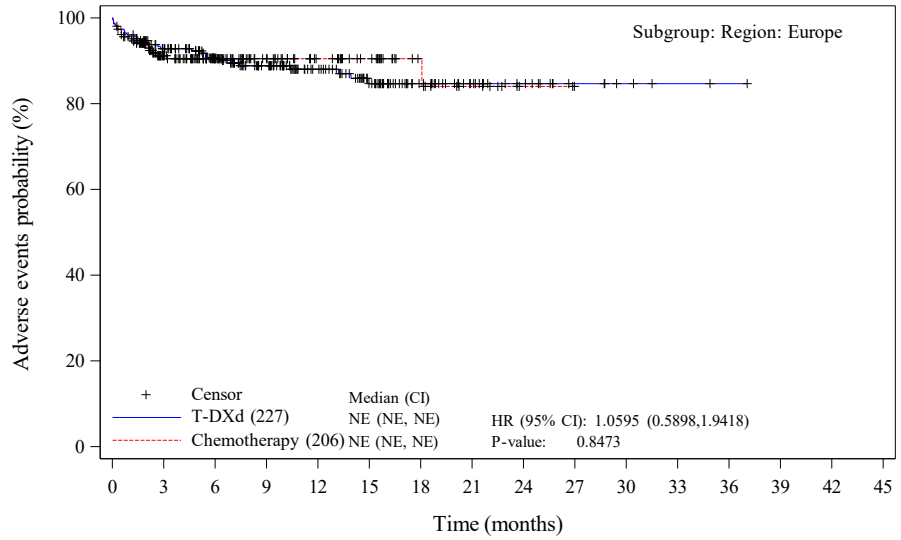
SOC: Nervous system disorders; PT: Dysgeusia



Patients still at risk:

T-DXd(227)	227	194	156	128	93	67	39	24	15	7	4	2	1	0
Chemotherapy (206)	206	132	89	57	40	29	14	8	2	0				

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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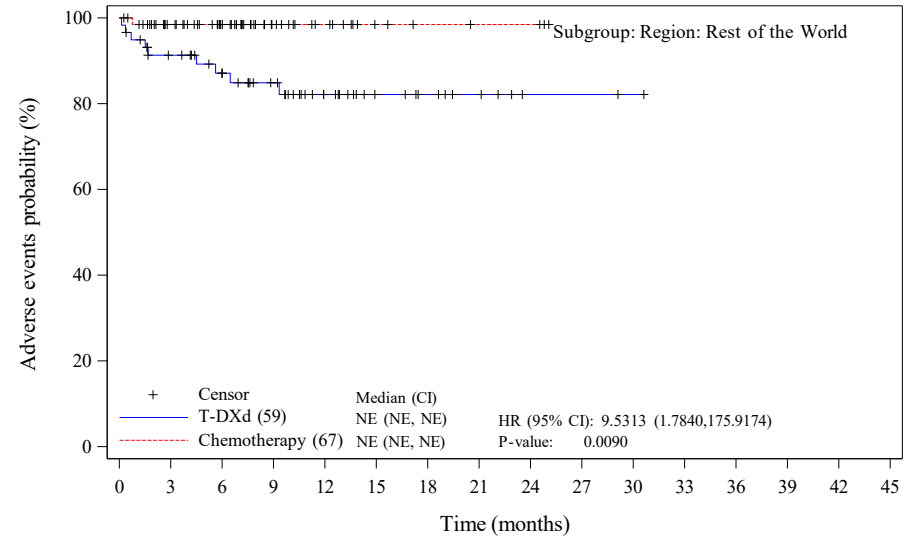
SOC: Nervous system disorders; PT: Dysgeusia



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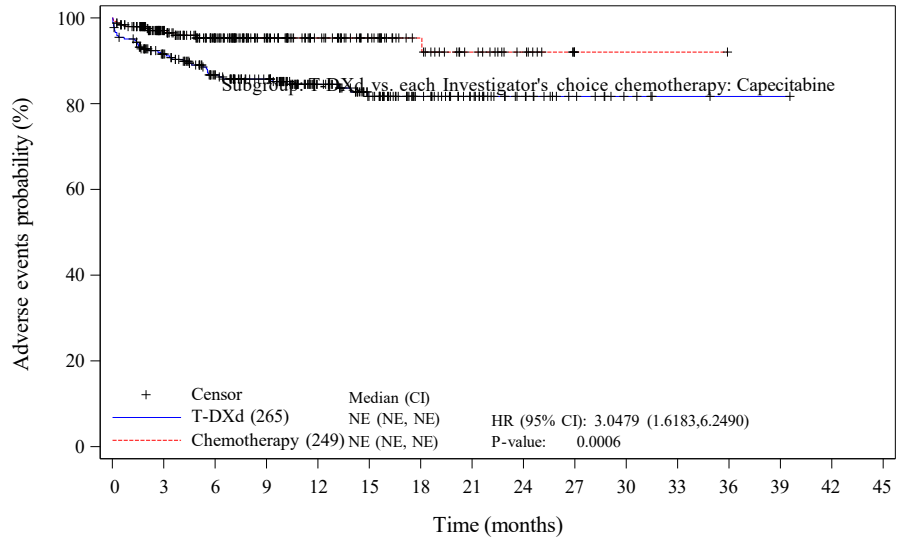

Patients still at risk:

T-DXd(265)	265	221	181	154	105	76	49	34	20	11	5	2	1	1	0
Chemotherapy (249)	249	180	133	91	64	45	29	18	10	1	1	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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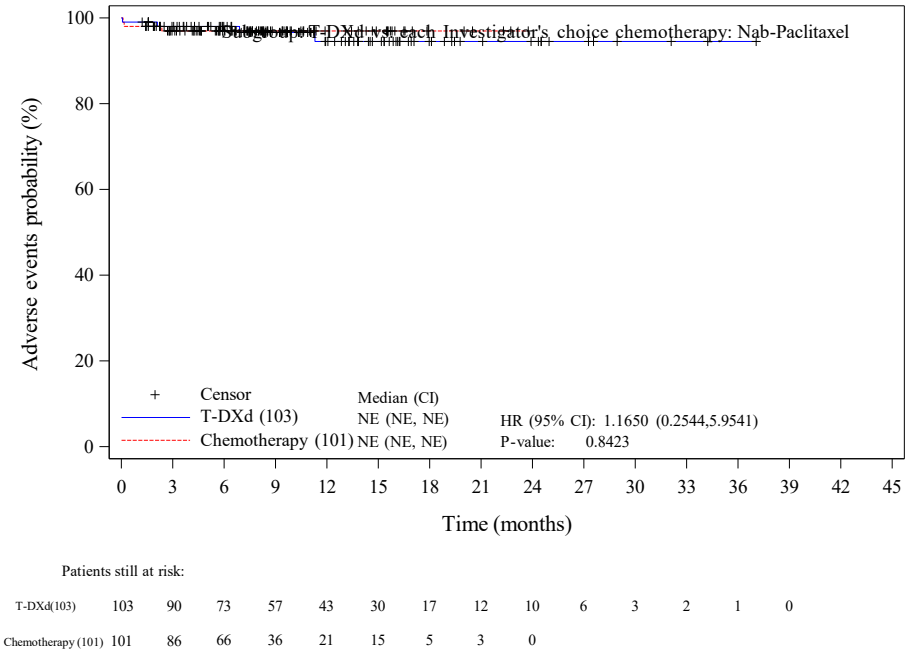

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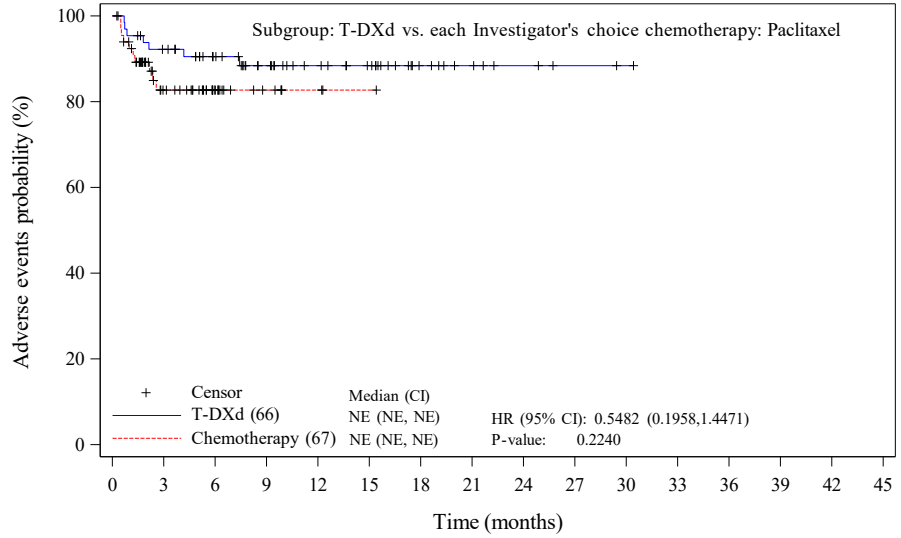
SOC: Nervous system disorders; PT: Dysgeusia



Patients still at risk:

T-DXd(66)	66	57	46	35	27	22	11	7	4	2	1	0
Chemotherapy (67)	67	34	17	7	3	1	0					

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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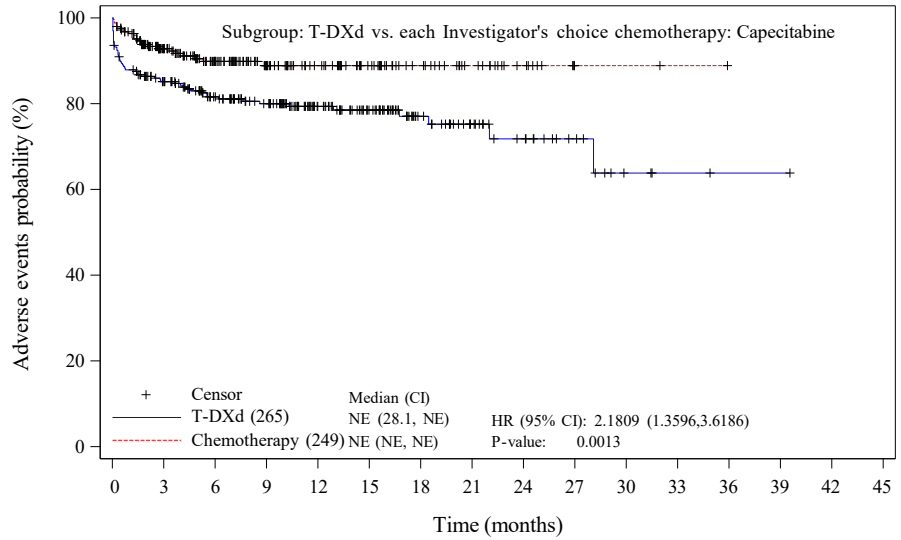
SOC: Nervous system disorders; PT: Headache



Patients still at risk:

T-DXd(265)	265	208	169	142	100	75	43	28	19	11	4	2	1	1	0
Chemotherapy (249)	249	173	125	88	65	47	31	20	11	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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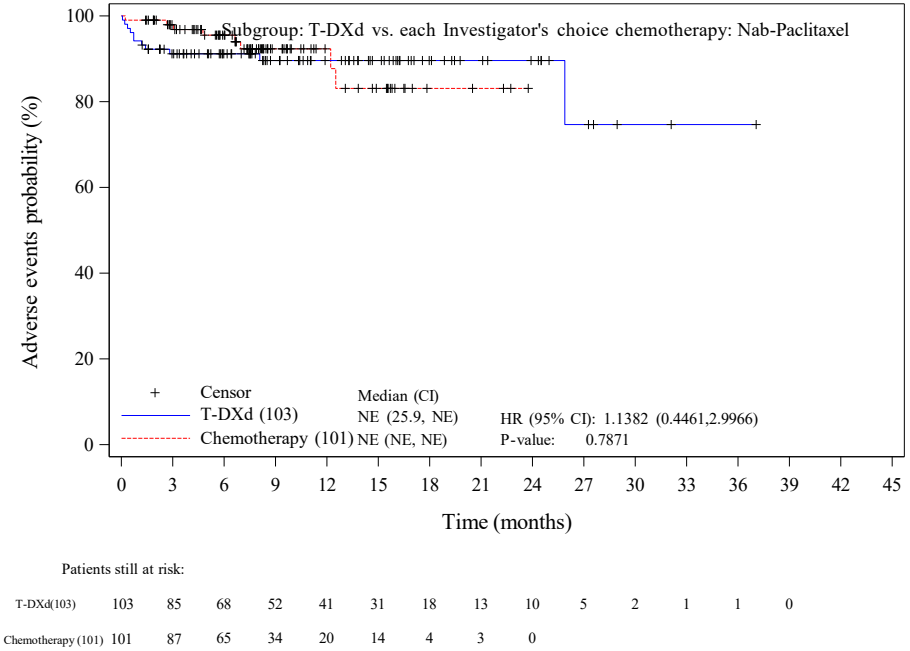

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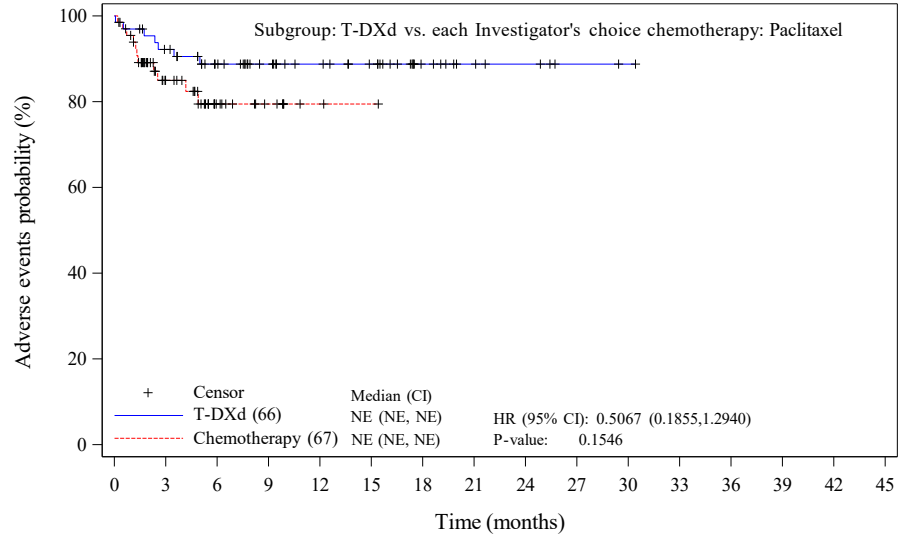
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Headache



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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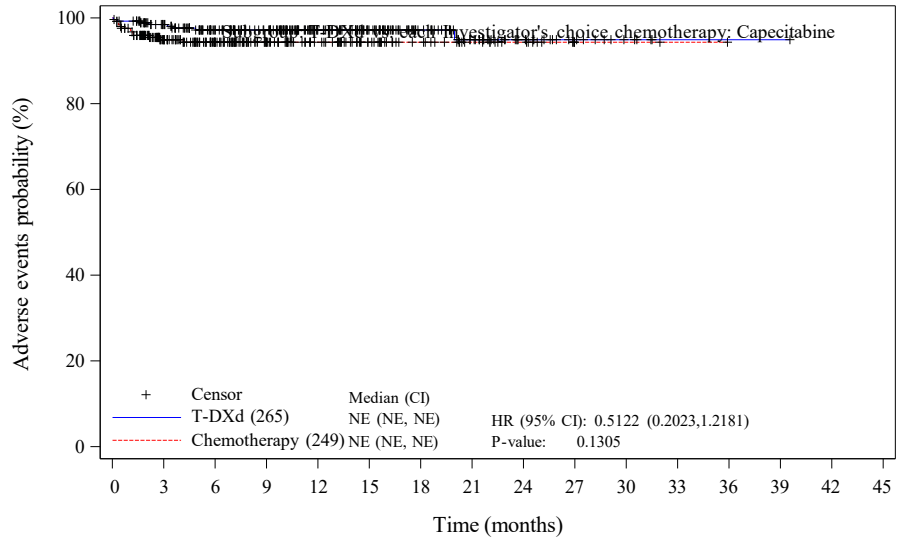
Run date: 13DEC2024 11:20; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy



Patients still at risk:

T-DXd(265)	265	238	199	172	121	90	55	37	20	11	5	1	1	1	0
Chemotherapy (249)	249	176	130	90	64	42	27	17	11	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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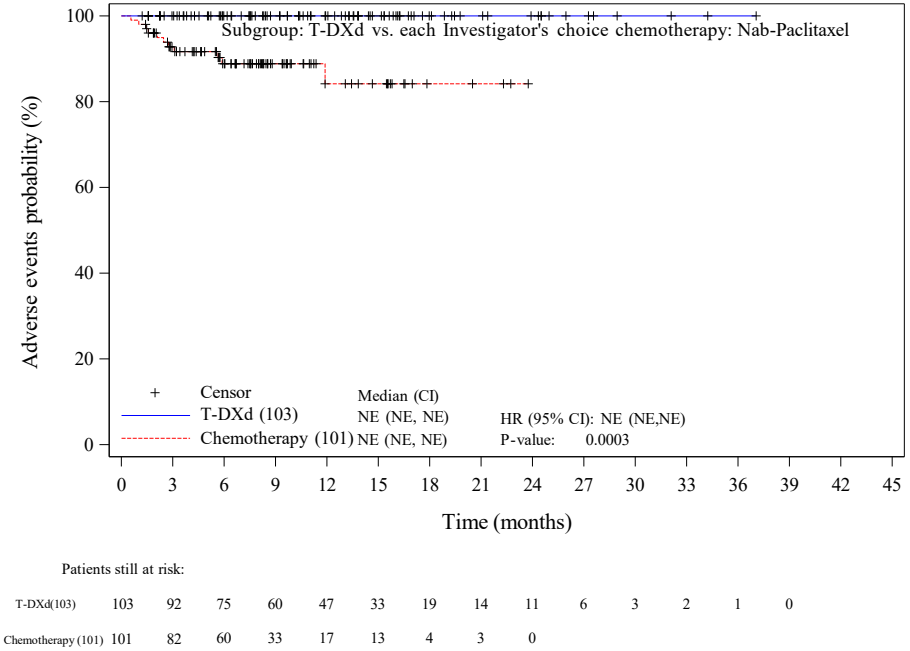
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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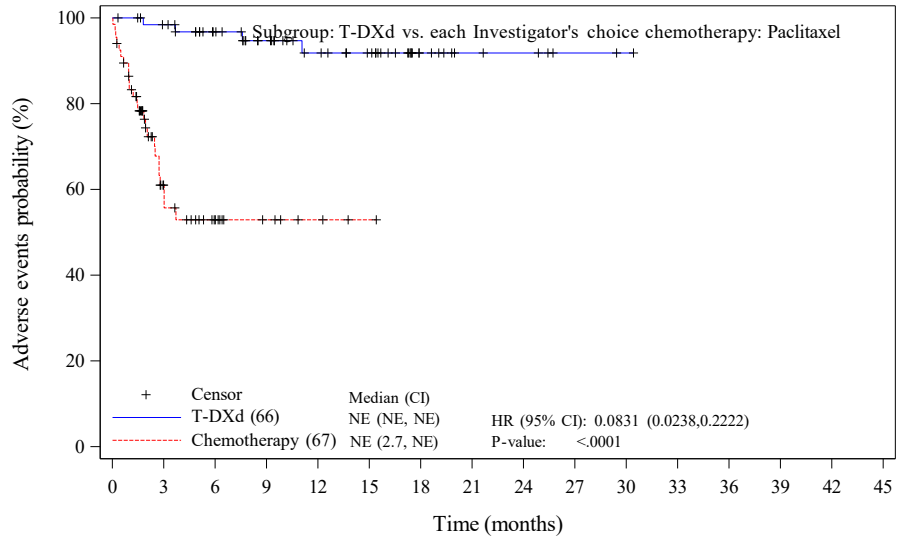
Run date: 13DEC2024 11:20; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy



Patients still at risk:

T-DXd(66)	66	61	50	40	31	26	11	6	5	2	1	0
Chemotherapy (67)	67	23	12	6	3	1	0					

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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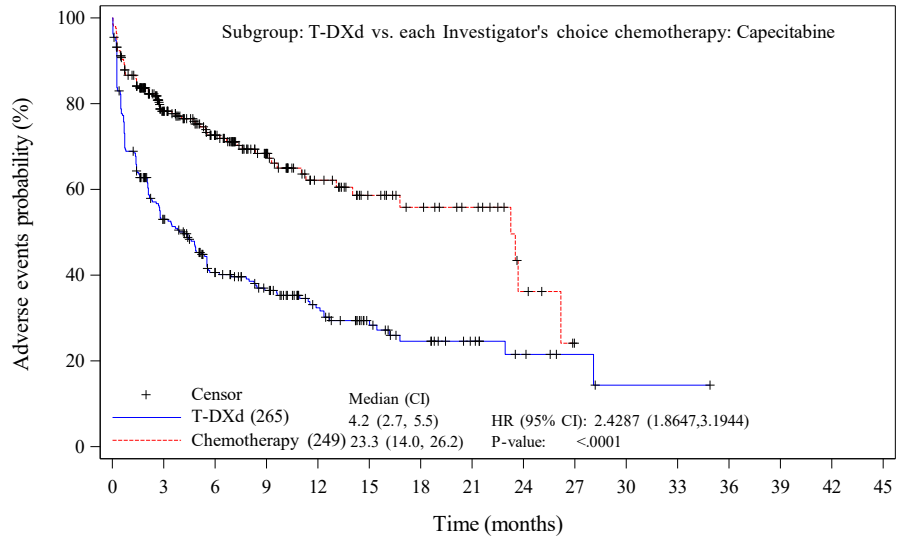
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Patients still at risk:

T-DXd(265)	265	128	85	66	44	27	18	11	6	3	1	1	0
Chemotherapy (249)	249	145	101	65	40	26	19	14	5	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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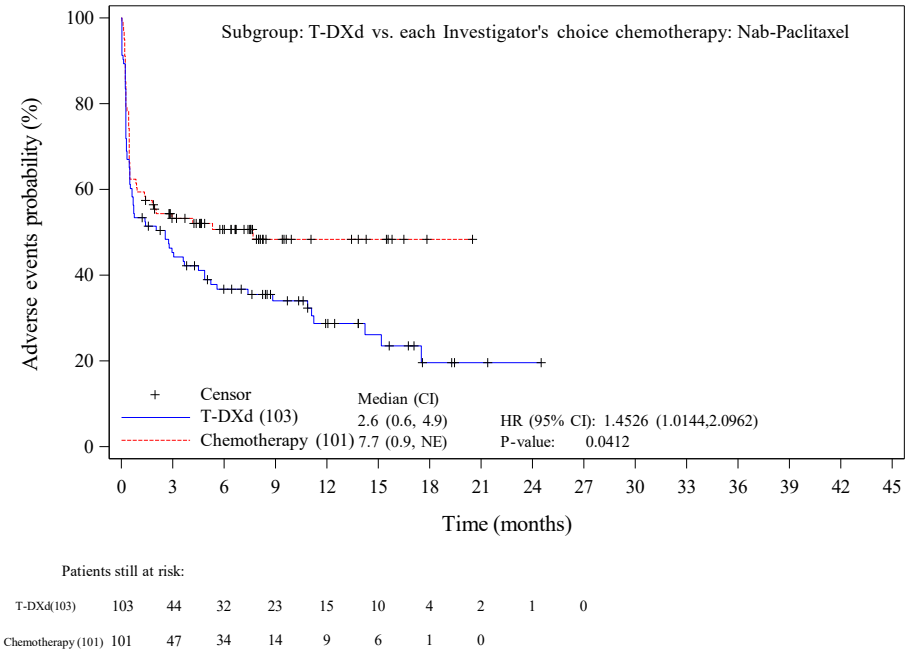
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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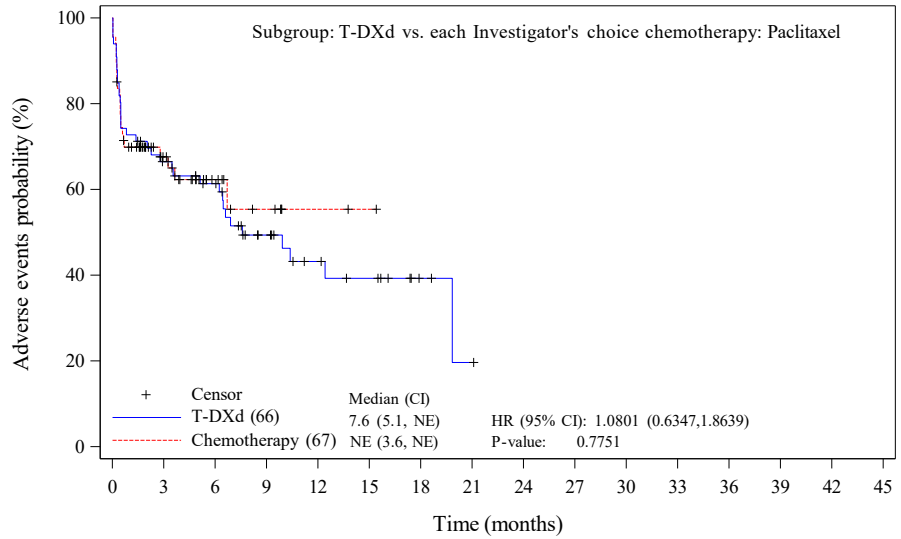
Run date: 13DEC2024 11:20; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Patients still at risk:

T-DXd(66)	66	41	33	19	12	9	3	1	0
Chemotherapy (67)	67	27	12	6	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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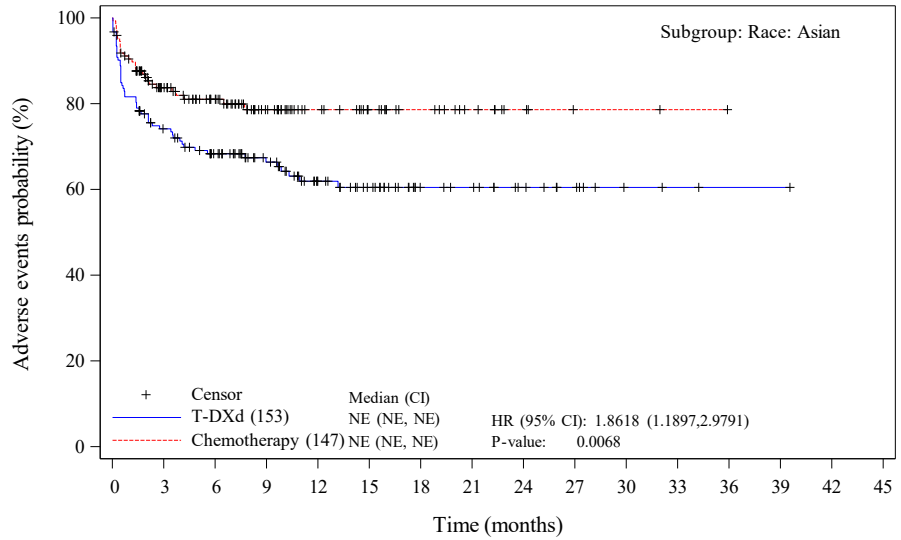
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Patients still at risk:

T-DXd(153)	153	104	86	65	45	35	20	18	12	8	3	2	1	1	0
Chemotherapy (147)	147	99	77	50	33	23	16	10	5	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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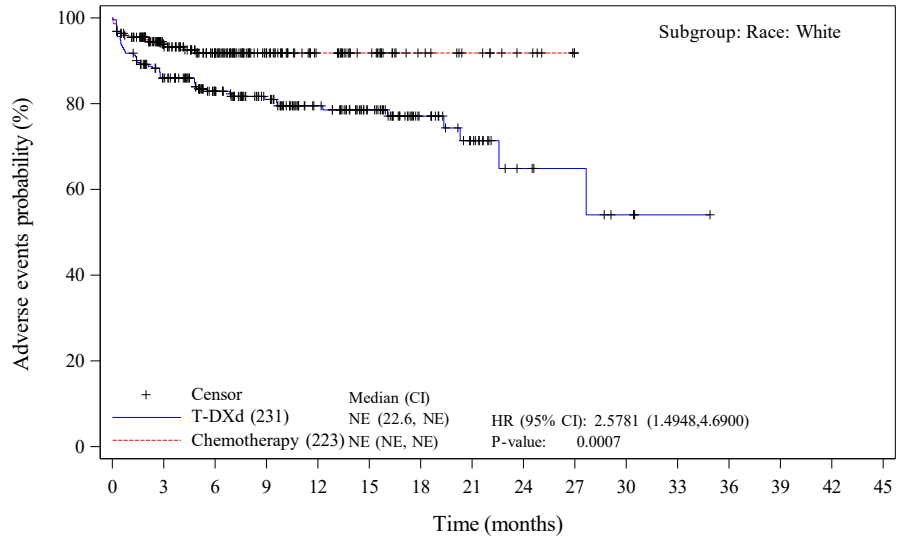
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Patients still at risk:

T-DXd(231)	231	186	144	114	85	62	35	20	8	6	3	1	0
Chemotherapy (223)	223	152	110	68	43	30	16	11	6	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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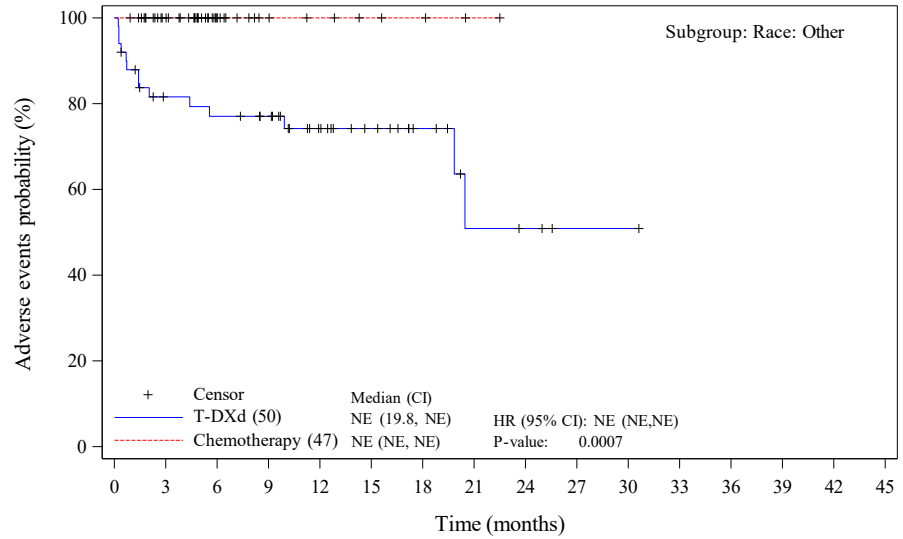
Run date: 13DEC2024 11:20; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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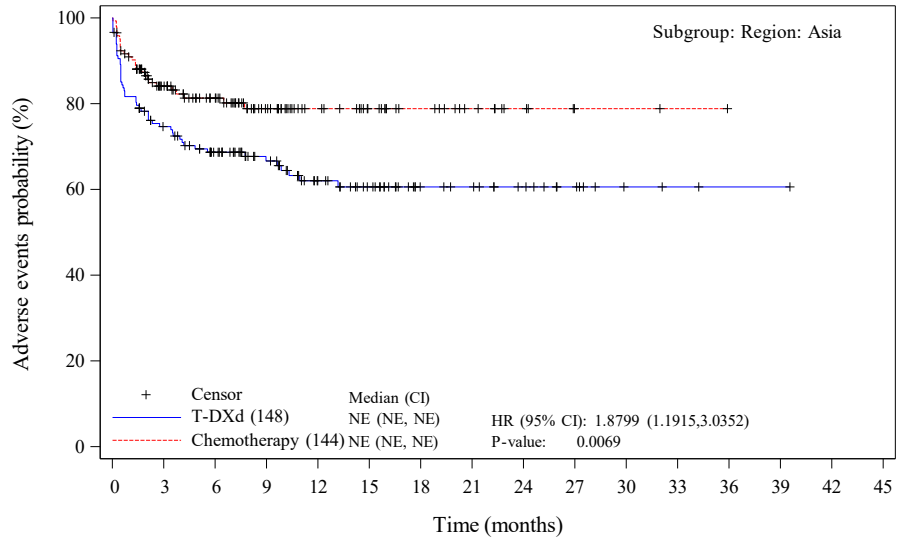
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Patients still at risk:

T-DXd(148)	148	102	83	63	45	35	20	18	13	8	3	2	1	1	0
Chemotherapy (144)	144	98	76	50	33	24	17	11	6	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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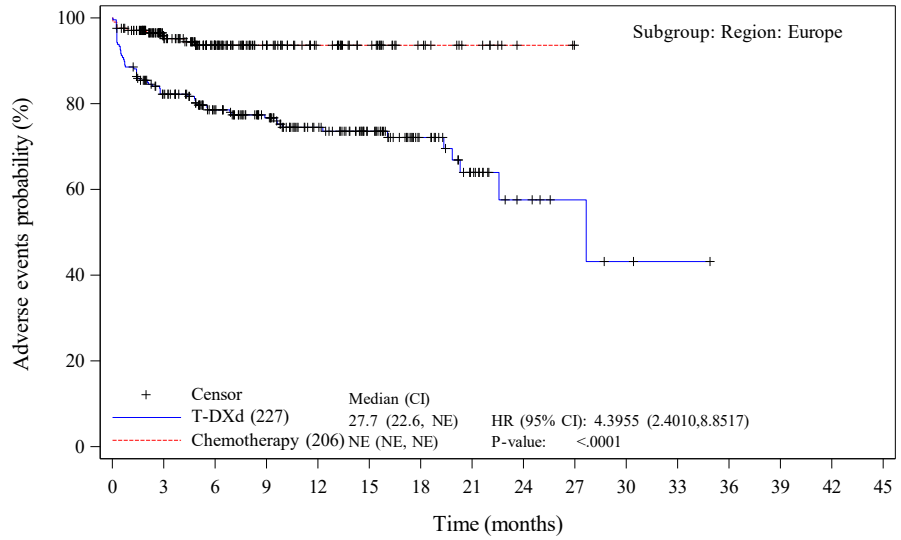
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Patients still at risk:

T-DXd(227)	227	174	138	111	83	60	34	18	7	4	2	1	0
Chemotherapy (206)	206	141	92	59	39	27	14	8	2	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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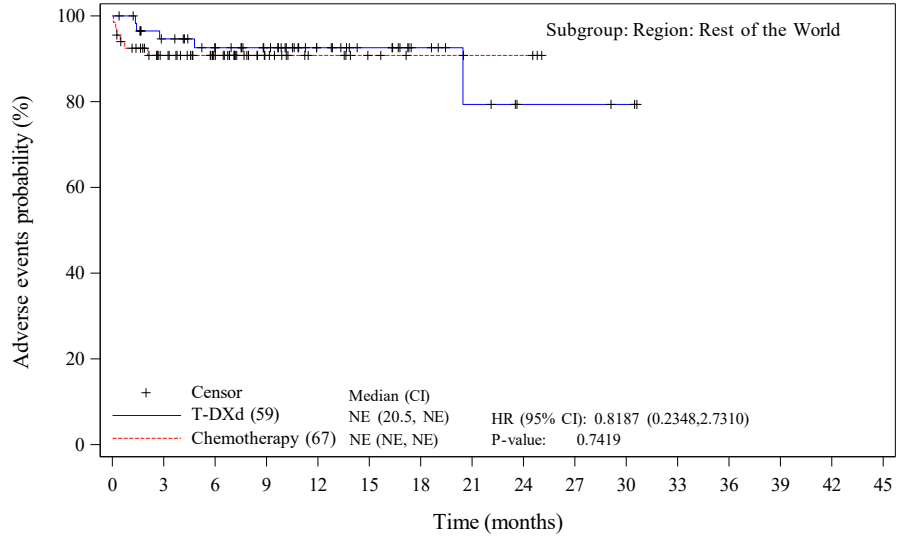
Run date: 13DEC2024 11:20; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Patients still at risk:

T-DXd(59)	59	50	43	36	23	17	10	6	3	3	2	0
Chemotherapy (67)	67	48	35	17	10	6	4	3	3	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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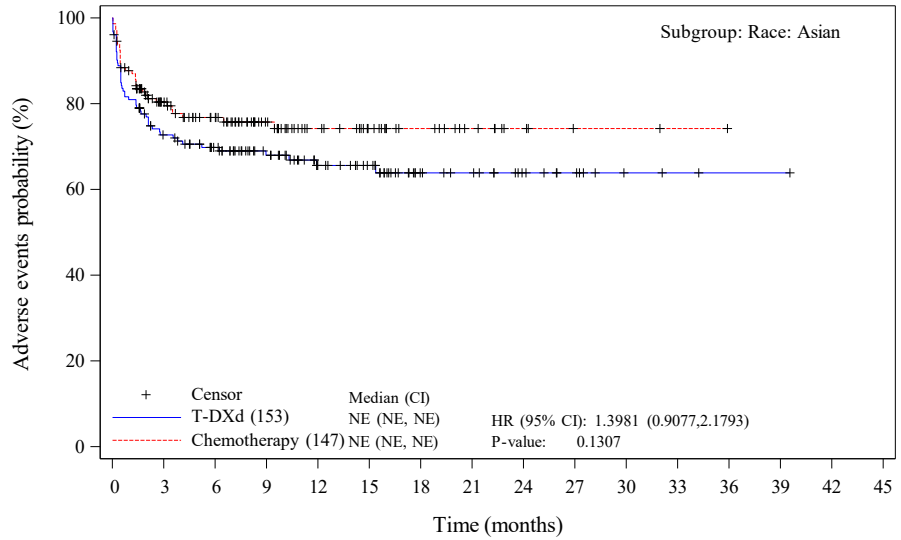
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Alanine aminotransferase increased



Patients still at risk:

T-DXd(153)	153	102	87	67	49	41	22	19	12	8	3	2	1	1	0
Chemotherapy (147)	147	94	75	51	34	24	16	10	5	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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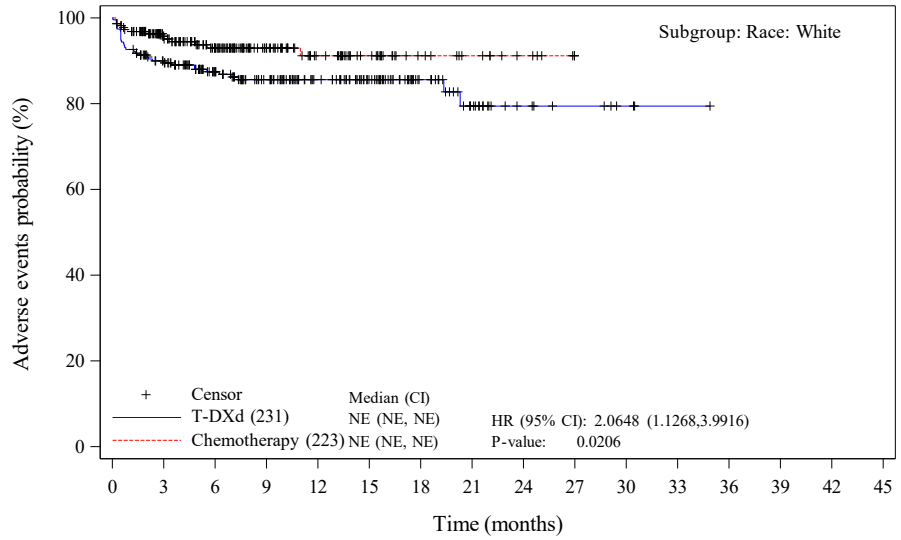
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Alanine aminotransferase increased



Patients still at risk:

T-DXd(231)	231	193	149	120	89	66	37	20	9	6	3	1	0
Chemotherapy (223)	223	156	112	70	44	30	16	11	6	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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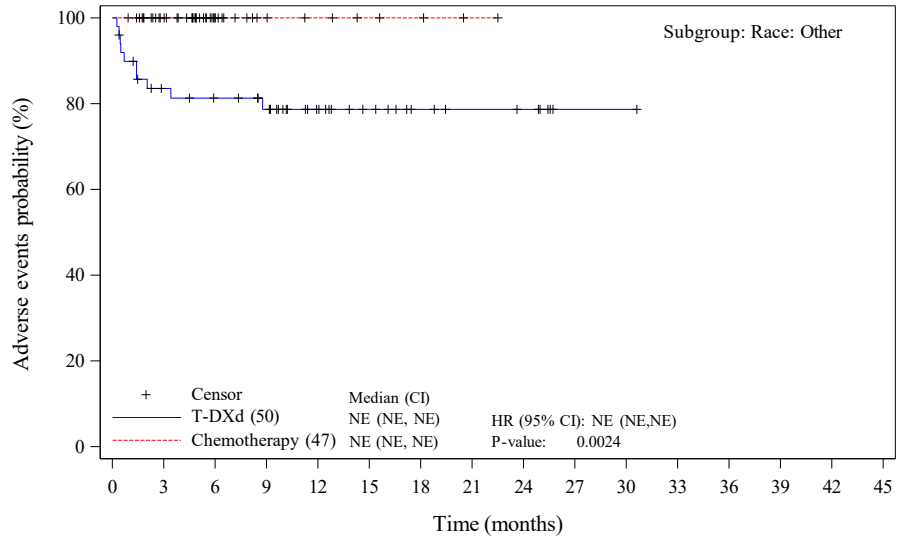
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Alanine aminotransferase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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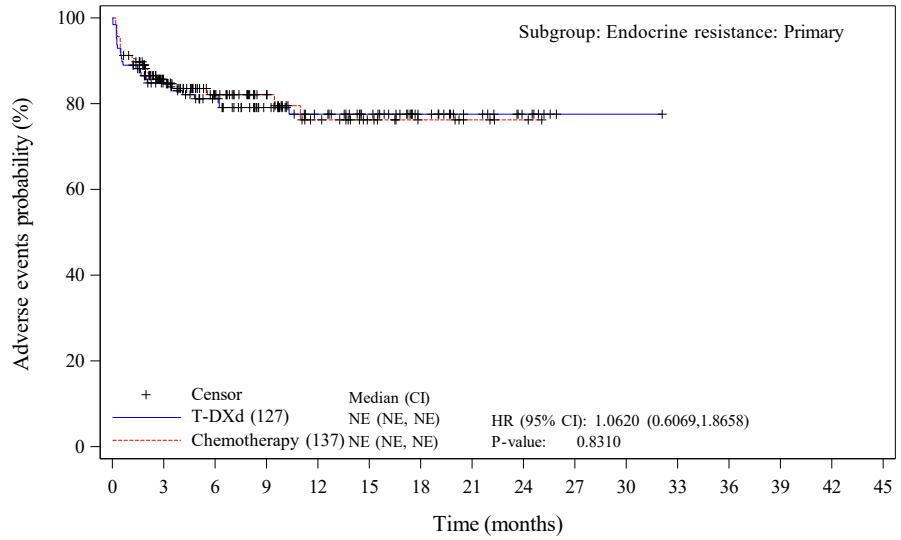
SOC: Investigations; PT: Alanine aminotransferase increased



Patients still at risk:

T-DXd(127)	127	95	80	61	46	36	21	13	7	1	1	0
Chemotherapy (137)	137	83	52	34	20	12	7	4	2	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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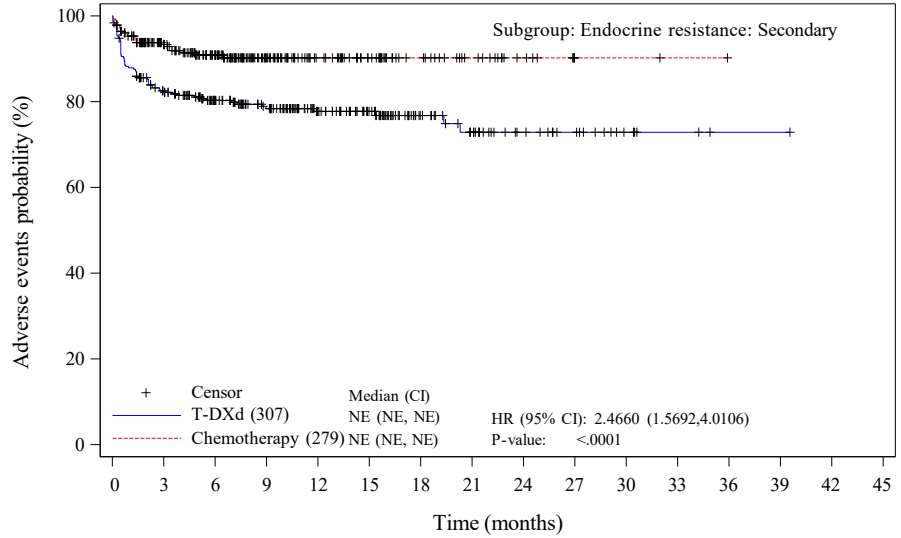
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Alanine aminotransferase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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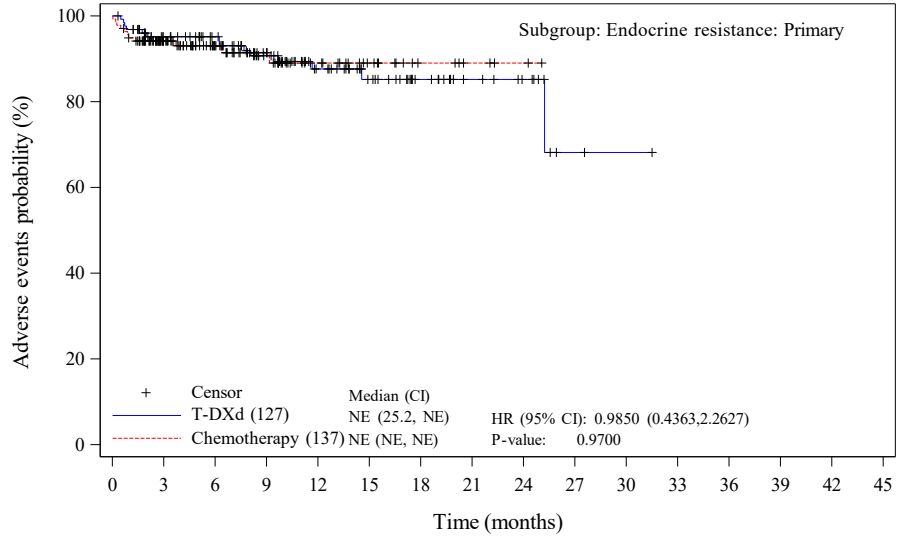
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Blood alkaline phosphatase increased



Patients still at risk:

T-DXd(127)	127	105	92	71	48	34	21	13	9	2	1	0
Chemotherapy (137)	137	93	60	40	24	15	7	4	2	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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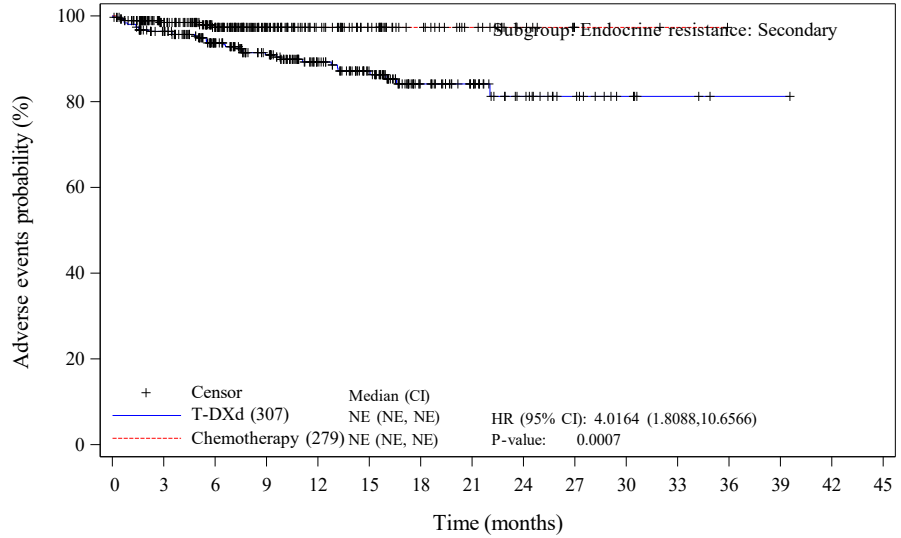
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Blood alkaline phosphatase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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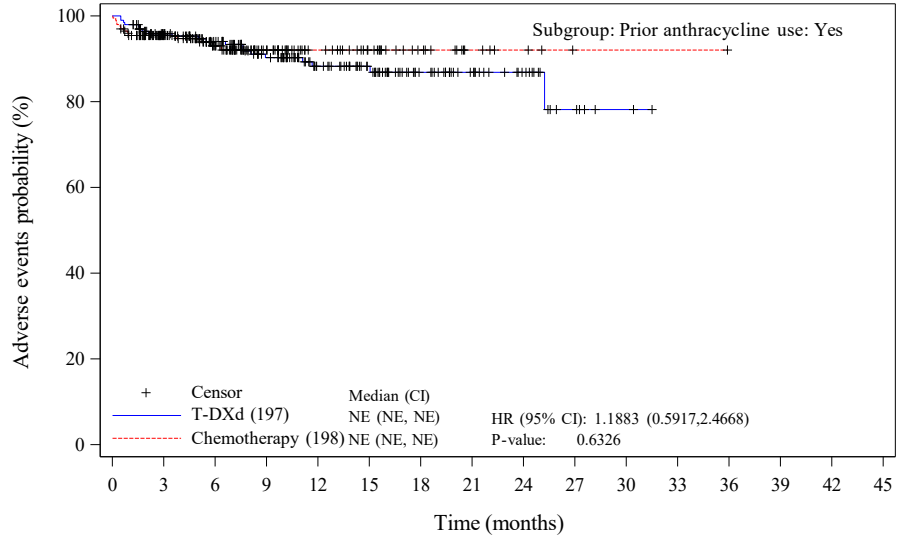
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Blood alkaline phosphatase increased



Patients still at risk:

T-DXd(197)	197	170	144	113	81	63	39	26	16	6	2	0
Chemotherapy (198)	198	140	99	60	37	26	15	7	4	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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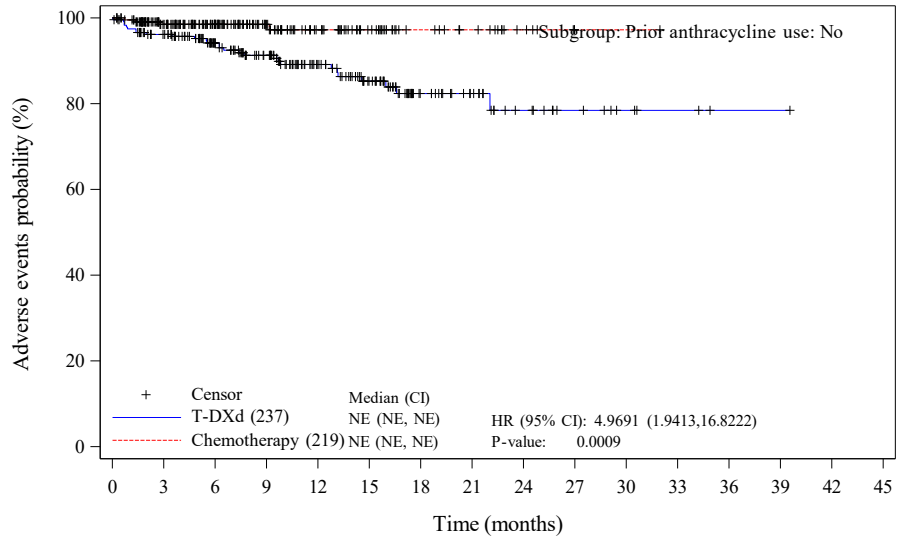
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Blood alkaline phosphatase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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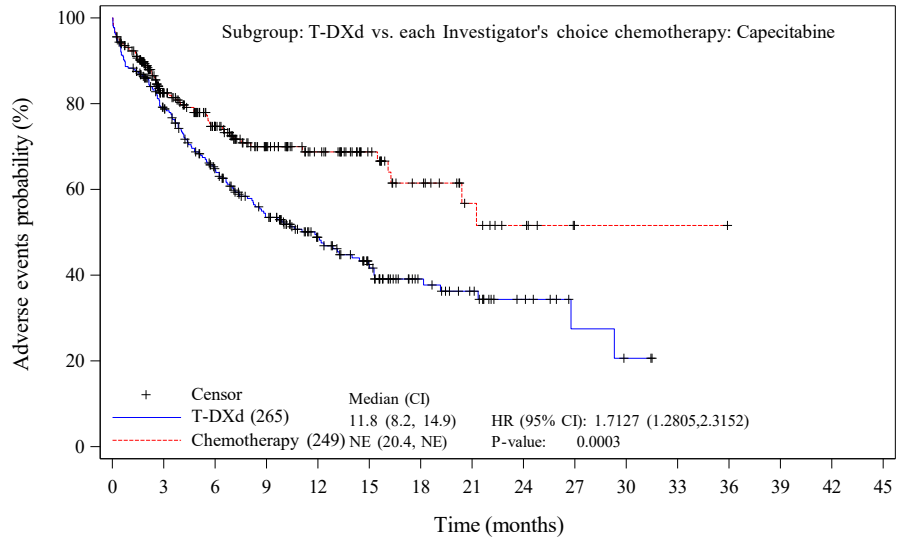
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)



Patients still at risk:

T-DXd(265)	265	195	145	108	74	51	28	20	10	4	2	0
Chemotherapy (249)	249	153	108	72	51	33	20	11	6	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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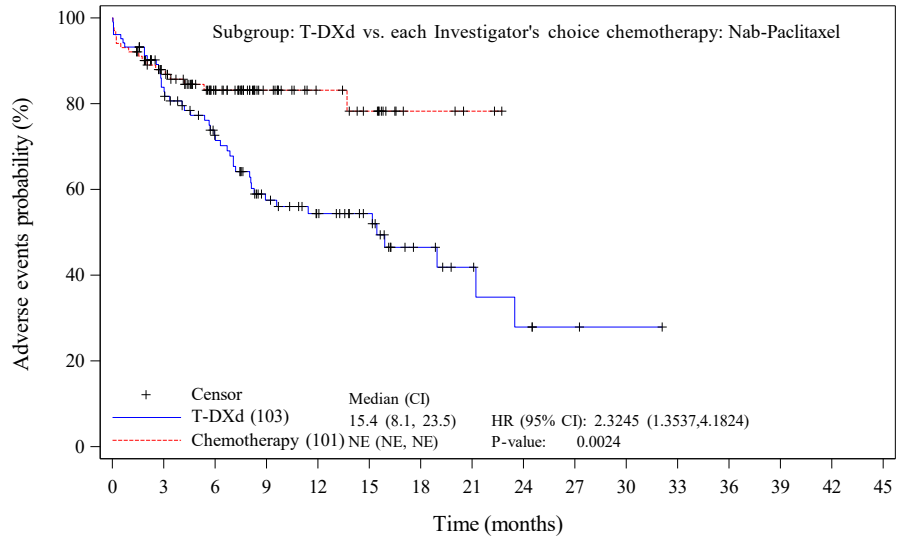
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)



Patients still at risk:

T-DXd(103)	103	79	60	40	31	23	11	7	4	2	1	0
Chemotherapy (101)	101	79	54	29	18	13	4	2	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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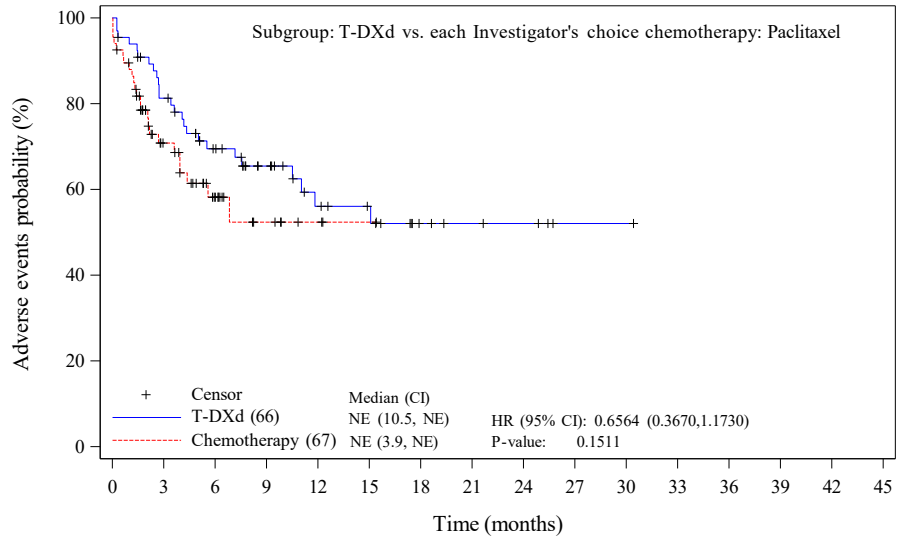
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)



Patients still at risk:

T-DXd(66)	66	51	37	26	17	14	7	5	4	1	1	0
Chemotherapy (67)	67	32	16	7	3	1	0					

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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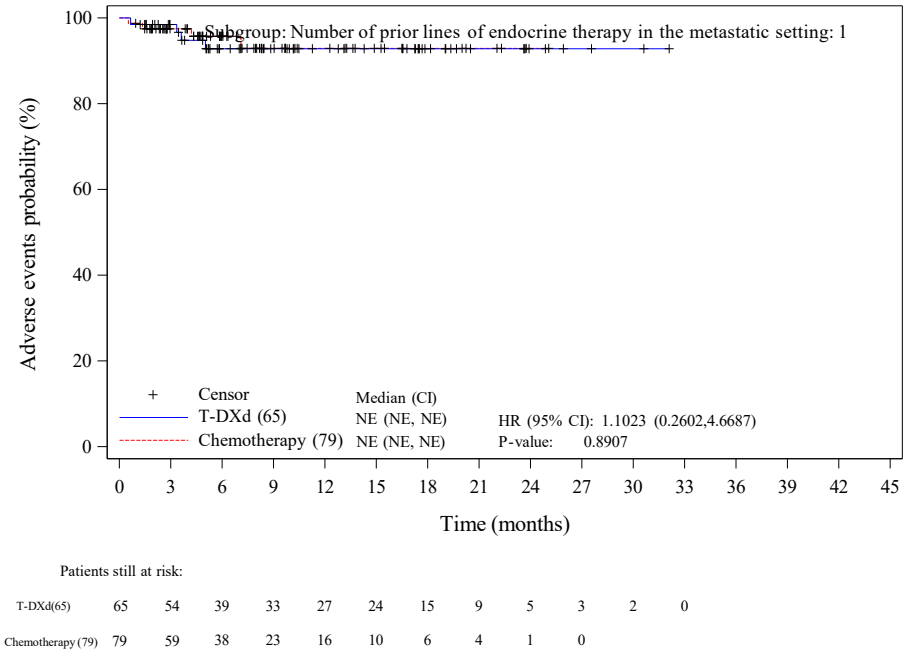
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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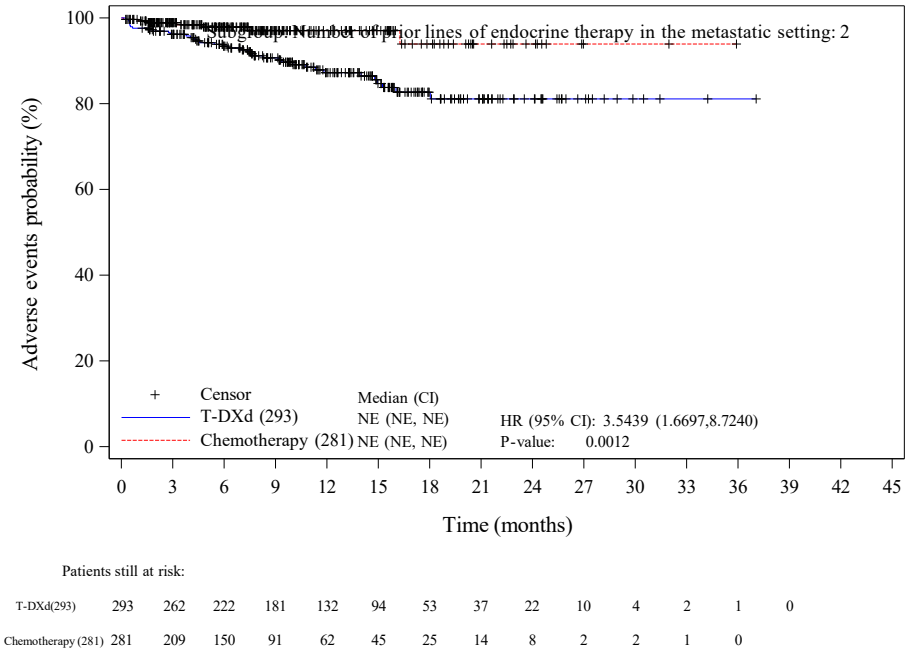
Run date: 13DEC2024 11:20; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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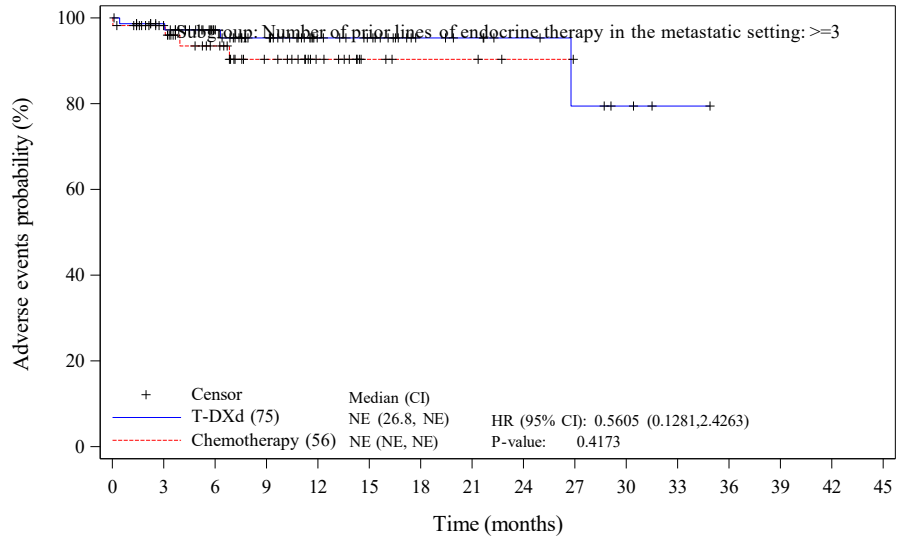
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis



Patients still at risk:

T-DXd(75)	75	68	53	42	27	22	12	10	7	5	3	1	0
Chemotherapy (56)	56	44	33	22	13	5	3	3	1	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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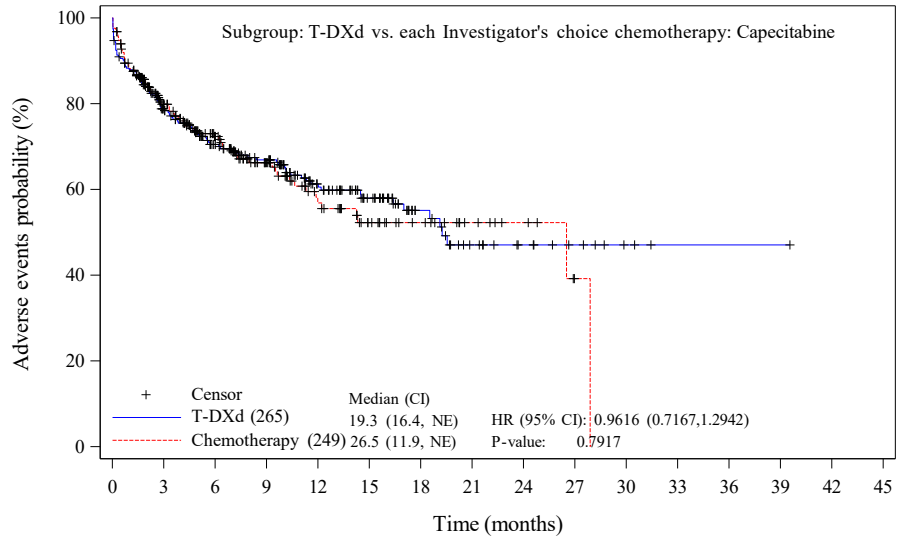
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)



Patients still at risk:

T-DXd(265)	265	192	145	123	84	57	29	17	11	7	3	1	1	1	0
Chemotherapy (249)	249	149	105	68	43	27	18	10	6	1	0				

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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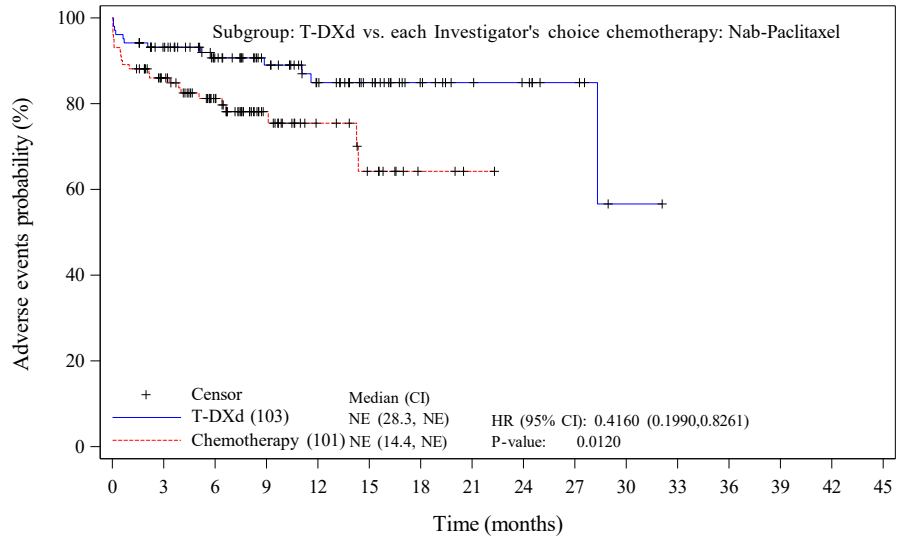
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)



Patients still at risk:

T-DXd(103)	103	86	68	53	39	28	16	11	9	5	1	0
Chemotherapy (101)	101	77	56	29	16	10	3	1	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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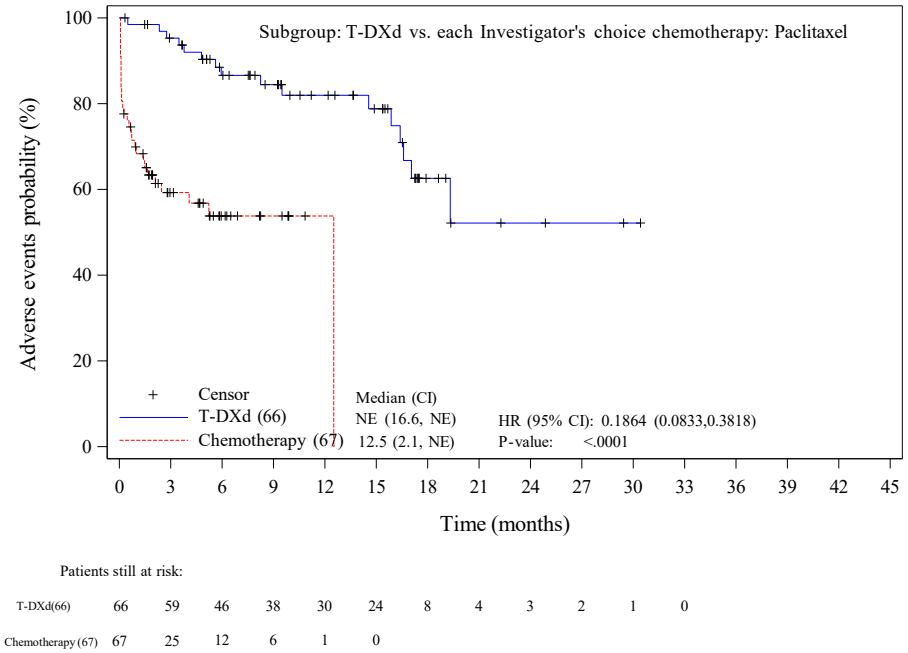
Run date: 13DEC2024 11:20; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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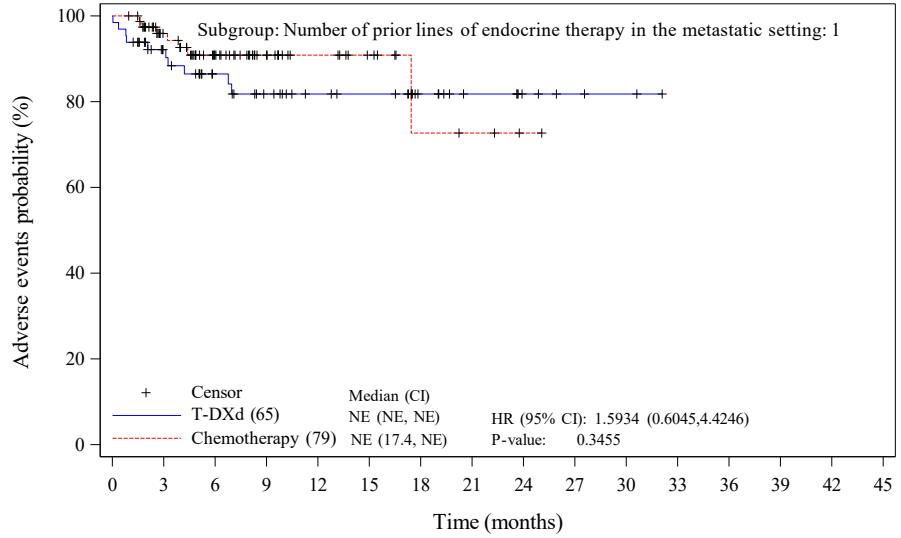
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Patients still at risk:

T-DXd(65)	65	49	37	30	24	22	14	9	5	3	2	0
Chemotherapy (79)	79	59	38	23	14	9	4	3	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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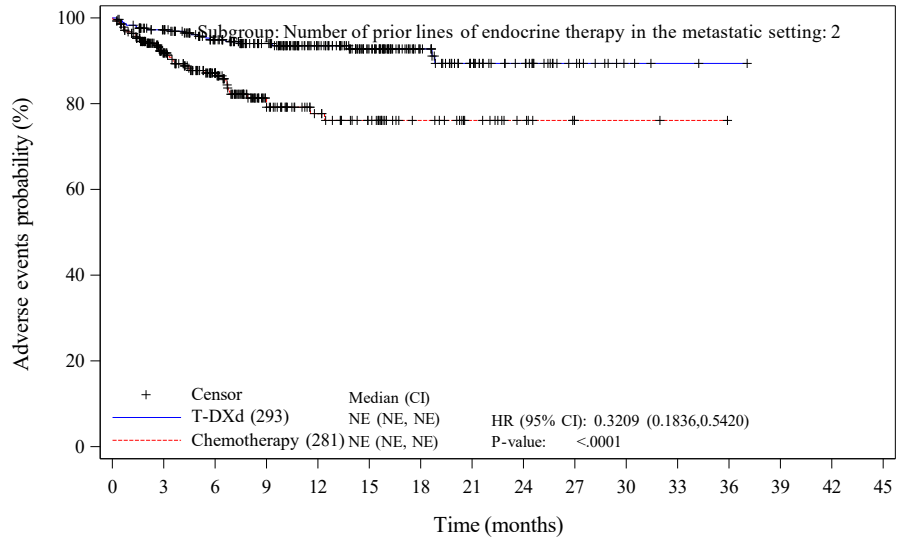
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Patients still at risk:

T-DXd(293)	293	267	229	191	144	103	60	39	26	12	4	2	1	0
Chemotherapy (281)	281	192	136	76	51	38	23	15	8	2	2	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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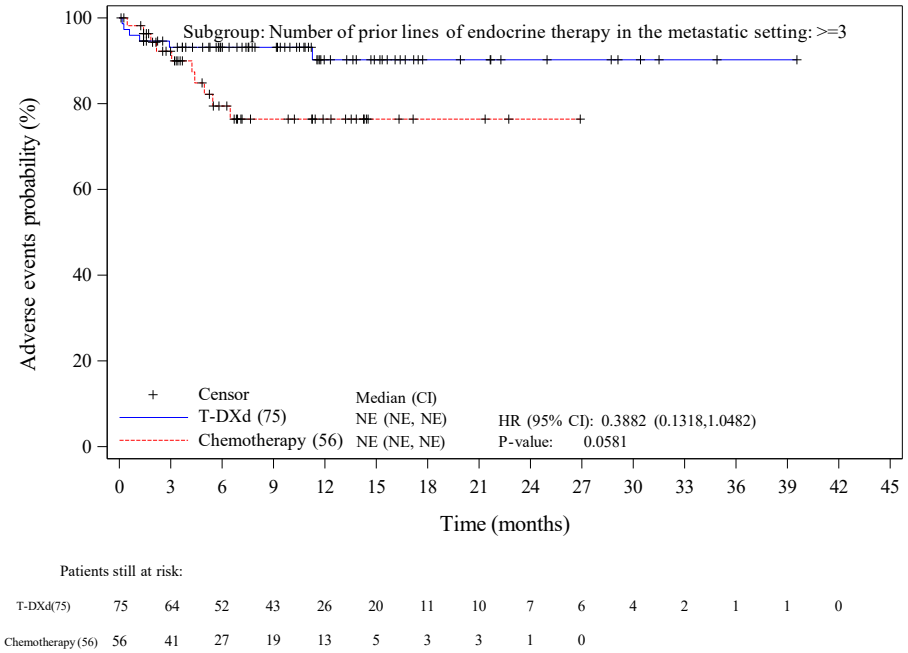
Run date: 13DEC2024 11:20; Program name: F.2.28.2_10PCTTEAE_SAF_SUB.sas; Output name: F.2.28.2_10PCTTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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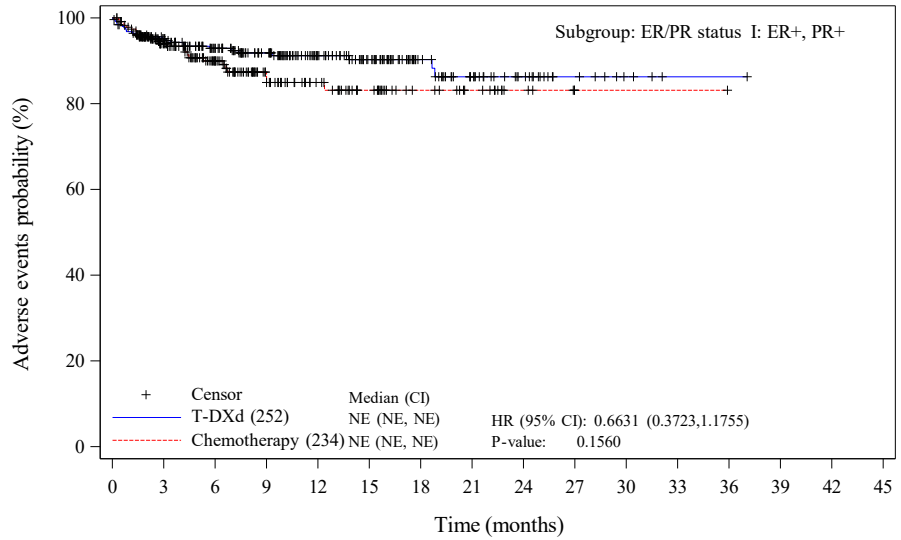
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Patients still at risk:

T-DXd(252)	252	221	186	151	112	85	47	31	19	9	4	1	1	0
Chemotherapy (234)	234	159	112	72	49	34	20	14	6	1	1	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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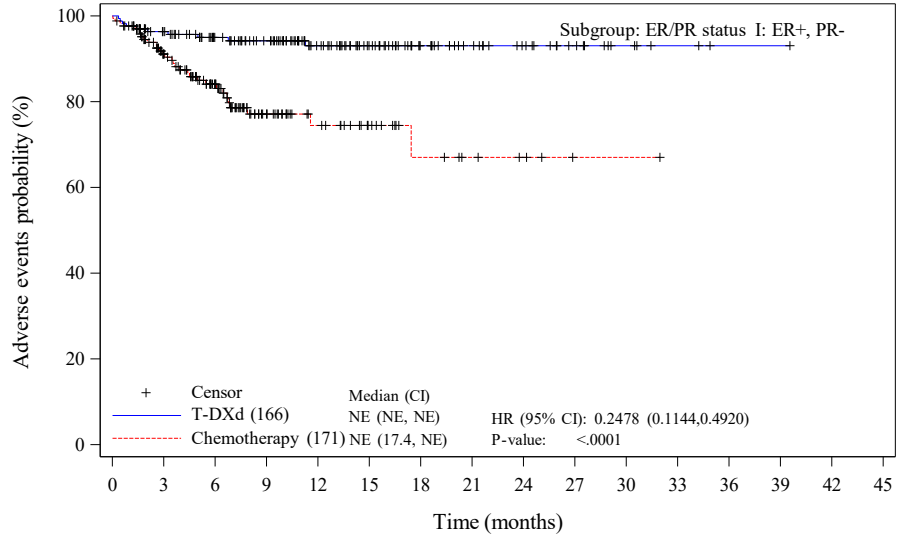
Figure 2.28.2 Adverse events by SOC and PT with incidence >= 10% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Patients still at risk:

T-DXd(166)	166	146	122	106	77	56	36	26	19	12	6	3	1	1	0
Chemotherapy (171)	171	126	85	44	28	17	9	6	4	1	1	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Tabelle 2.29.1 Unerwünschte Ereignisse nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – SAF

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders						
All (any PT)	376 (86.6)	0.1 [0.1; 0.1]	256 (61.4)	2.0 [1.2; 3.0]	2.2866 [1.9491; 2.6871] <.0001	<.0001
PT: Nausea	303 (69.8)	0.2 [0.1; 0.3]	126 (30.2)	NE [NE; NE]	3.4031 [2.7691; 4.2077] <.0001	<.0001
PT: Diarrhoea	148 (34.1)	NE [22.5; NE]	114 (27.3)	NE [21.0; NE]	1.0380 [0.8117; 1.3309] 0.7669	0.7669
PT: Vomiting	146 (33.6)	NE [NE; NE]	49 (11.8)	NE [NE; NE]	3.0522 [2.2247; 4.2605] <.0001	<.0001
PT: Constipation	137 (31.6)	NE [NE; NE]	62 (14.9)	NE [NE; NE]	2.0786 [1.5464; 2.8270] <.0001	<.0001
PT: Stomatitis	57 (13.1)	NE [NE; NE]	37 (8.9)	NE [NE; NE]	1.2099 [0.7998; 1.8514] 0.3719	0.3691
PT: Dyspepsia	50 (11.5)	NE [NE; NE]	20 (4.8)	NE [NE; NE]	2.0828 [1.2576; 3.5877] 0.0058	0.0048
PT: Abdominal pain	45 (10.4)	NE [NE; NE]	35 (8.4)	NE [NE; NE]	1.0878 [0.6997; 1.7060] 0.7102	0.7097

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Abdominal pain upper	35 (8.1)	NE [NE; NE]	20 (4.8)	NE [NE; NE]	1.4537 [0.8445; 2.5709] 0.1850	0.1826
PT: Dry mouth	24 (5.5)	NE [NE; NE]	16 (3.8)	NE [NE; NE]	1.1774 [0.6274; 2.2684] 0.6155	0.6149
PT: Abdominal distension	21 (4.8)	NE [NE; NE]	16 (3.8)	NE [NE; NE]	0.9803 [0.5101; 1.9187] 0.9525	0.9523
PT: Gastrooesophageal reflux disease	17 (3.9)	NE [NE; NE]	7 (1.7)	NE [NE; NE]	2.0175 [0.8684; 5.2312] 0.1192	0.1117
PT: Haemorrhoids	15 (3.5)	NE [NE; NE]	2 (0.5)	NE [NE; NE]	5.7188 [1.6056; 36.3601] 0.0208	0.0091
PT: Abdominal discomfort	12 (2.8)	NE [NE; NE]	3 (0.7)	NE [NE; NE]	3.1362 [0.9899; 13.8136] 0.0778	0.0631
PT: Flatulence	10 (2.3)	NE [NE; NE]	4 (1.0)	NE [NE; NE]	2.0680 [0.6888; 7.5665] 0.2210	0.2109
PT: Mouth ulceration	7 (1.6)	NE [NE; NE]	7 (1.7)	NE [NE; NE]	0.8003 [0.2732; 2.3438] 0.6778	0.6771
PT: Toothache	7 (1.6)	NE [NE; NE]	8 (1.9)	NE [NE; NE]	0.5945 [0.2054; 1.6801] 0.3223	0.3169

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Gastrointestinal pain	6 (1.4)	NE [NE; NE]	4 (1.0)	NE [NE; NE]	1.3609 [0.3882; 5.3285] 0.6334	0.6321
SOC: Investigations						
All (any PT)	281 (64.7)	4.2 [2.8; 5.5]	151 (36.2)	23.3 [13.1; 26.2]	1.8584 [1.5272; 2.2705] <.0001	<.0001
PT: Aspartate aminotransferase increased	117 (27.0)	NE [27.7; NE]	44 (10.6)	NE [NE; NE]	2.3750 [1.6908; 3.3967] <.0001	<.0001
PT: Neutrophil count decreased	99 (22.8)	NE [NE; NE]	66 (15.8)	NE [NE; NE]	1.2938 [0.9480; 1.7768] 0.1073	0.1091
PT: Alanine aminotransferase increased	93 (21.4)	NE [NE; NE]	48 (11.5)	NE [NE; NE]	1.7704 [1.2555; 2.5290] 0.0013	0.0012
PT: White blood cell count decreased	79 (18.2)	NE [NE; NE]	53 (12.7)	NE [NE; NE]	1.3086 [0.9261; 1.8639] 0.1307	0.1303
PT: Platelet count decreased	61 (14.1)	NE [NE; NE]	15 (3.6)	NE [26.2; NE]	3.4582 [2.0160; 6.3255] <.0001	<.0001
PT: Blood alkaline phosphatase increased	48 (11.1)	NE [NE; NE]	17 (4.1)	NE [NE; NE]	2.0811 [1.2165; 3.7359] 0.0099	0.0085

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Gamma-glutamyltransferase increased	40 (9.2)	NE [NE; NE]	9 (2.2)	NE [NE; NE]	3.3099 [1.6742; 7.3057] 0.0013	0.0007
PT: Ejection fraction decreased	35 (8.1)	NE [NE; NE]	12 (2.9)	NE [NE; NE]	1.9717 [1.0488; 3.9748] 0.0438	0.0401
PT: Weight decreased	32 (7.4)	NE [NE; NE]	8 (1.9)	NE [NE; NE]	2.9397 [1.4169; 6.8779] 0.0067	0.0045
PT: Blood bilirubin increased	30 (6.9)	NE [NE; NE]	20 (4.8)	NE [26.0; NE]	0.9739 [0.5539; 1.7491] 0.9277	0.9282
PT: Lymphocyte count decreased	27 (6.2)	NE [NE; NE]	11 (2.6)	NE [NE; NE]	1.9451 [0.9855; 4.1135] 0.0651	0.0603
PT: Blood lactate dehydrogenase increased	17 (3.9)	NE [NE; NE]	18 (4.3)	NE [NE; NE]	0.6820 [0.3443; 1.3433] 0.2664	0.2639
PT: Weight increased	14 (3.2)	NE [NE; NE]	10 (2.4)	NE [NE; NE]	1.0010 [0.4446; 2.3365] 0.9981	0.9983
PT: Bilirubin conjugated increased	8 (1.8)	NE [NE; NE]	2 (0.5)	NE [NE; NE]	2.9656 [0.7355; 19.7543] 0.1714	0.1516
PT: Transaminases increased	8 (1.8)	NE [NE; NE]	4 (1.0)	NE [NE; NE]	1.6208 [0.5053; 6.1148] 0.4339	0.4295

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Blood cholesterol increased	7 (1.6)	NE [NE; NE]	3 (0.7)	NE [NE; NE]	1.4460 [0.3952; 6.7930] 0.5974	0.5954
PT: Blood creatinine increased	7 (1.6)	NE [NE; NE]	7 (1.7)	NE [NE; NE]	0.7535 [0.2529; 2.2375] 0.6031	0.6018
SOC: General disorders and administration site conditions						
All (any PT)	275 (63.4)	3.5 [2.1; 4.7]	230 (55.2)	4.5 [3.2; 6.0]	1.1547 [0.9690; 1.3784] 0.1093	0.1231
PT: Fatigue	117 (27.0)	NE [NE; NE]	83 (19.9)	NE [NE; NE]	1.3263 [1.0021; 1.7633] 0.0497	0.0511
PT: Asthenia	99 (22.8)	NE [NE; NE]	71 (17.0)	NE [NE; NE]	1.2483 [0.9209; 1.7005] 0.1556	0.1588
PT: Pyrexia	52 (12.0)	NE [NE; NE]	30 (7.2)	NE [NE; NE]	1.2272 [0.7840; 1.9546] 0.3777	0.3768
PT: Oedema peripheral	36 (8.3)	NE [NE; NE]	59 (14.1)	NE [NE; NE]	0.4446 [0.2902; 0.6720] 0.0001	0.0001
PT: Malaise	35 (8.1)	NE [NE; NE]	18 (4.3)	NE [NE; NE]	1.7235 [0.9866; 3.1163] 0.0617	0.0592

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 09DEC2024 10:14; Program name: T.2.29.1_10TEAE_SAF.sas; Output name: T.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Mucosal inflammation	15 (3.5)	NE [NE; NE]	15 (3.6)	NE [NE; NE]	0.7979 [0.3848; 1.6534] 0.5395	0.5389
PT: Influenza like illness	12 (2.8)	NE [NE; NE]	3 (0.7)	NE [NE; NE]	2.3719 [0.7438; 10.4916] 0.1847	0.1720
PT: Chest discomfort	9 (2.1)	NE [NE; NE]	7 (1.7)	NE [NE; NE]	1.0705 [0.3973; 3.0070] 0.8929	0.8925
PT: Peripheral swelling	6 (1.4)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	0.7723 [0.2302; 2.7050] 0.6724	0.6716
SOC: Skin and subcutaneous tissue disorders						
All (any PT)	250 (57.6)	3.3 [2.1; 5.5]	278 (66.7)	1.9 [1.4; 2.3]	0.7071 [0.5949; 0.8400] 0.0001	0.0001
PT: Alopecia	210 (48.4)	9.7 [3.7; NE]	87 (20.9)	NE [NE; NE]	2.5250 [1.9752; 3.2593] <.0001	<.0001
PT: Rash	26 (6.0)	NE [NE; NE]	31 (7.4)	NE [NE; NE]	0.5726 [0.3355; 0.9695] 0.0384	0.0362
PT: Dry skin	22 (5.1)	NE [NE; NE]	15 (3.6)	NE [NE; NE]	1.1801 [0.6145; 2.3282] 0.6229	0.6225

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Pruritus	17 (3.9)	NE [NE; NE]	11 (2.6)	NE [NE; NE]	1.1449 [0.5393; 2.5315] 0.7286	0.7284
PT: Nail disorder	11 (2.5)	NE [NE; NE]	17 (4.1)	NE [NE; NE]	0.4800 [0.2173; 1.0173] 0.0593	0.0539
PT: Erythema	6 (1.4)	NE [NE; NE]	11 (2.6)	NE [NE; NE]	0.3874 [0.1321; 1.0299] 0.0647	0.0558
PT: Palmar-plantar erythrodysaesthesia syndrome	4 (0.9)	NE [NE; NE]	146 (35.0)	NE [12.5; NE]	0.0174 [0.0053; 0.0413] <.0001	<.0001
PT: Skin hyperpigmentation	4 (0.9)	NE [NE; NE]	8 (1.9)	NE [NE; NE]	0.3763 [0.0996; 1.2070] 0.1136	0.1005
PT: Skin fissures	3 (0.7)	NE [NE; NE]	7 (1.7)	NE [NE; NE]	0.3382 [0.0722; 1.2296] 0.1191	0.1026
PT: Nail discolouration	2 (0.5)	NE [NE; NE]	10 (2.4)	NE [NE; NE]	0.1480 [0.0227; 0.5639] 0.0139	0.0044
SOC: Infections and infestations						
All (any PT)	233 (53.7)	10.1 [7.7; 12.0]	161 (38.6)	11.5 [8.1; 13.7]	1.0949 [0.8954; 1.3421] 0.3795	0.3793

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: COVID-19	106 (24.4)	NE [20.0; NE]	52 (12.5)	NE [NE; NE]	1.4053 [1.0112; 1.9773] 0.0462	0.0454
PT: Urinary tract infection	28 (6.5)	NE [NE; NE]	20 (4.8)	NE [NE; NE]	1.0294 [0.5800; 1.8601] 0.9219	0.9219
PT: Nasopharyngitis	24 (5.5)	NE [NE; NE]	15 (3.6)	NE [NE; NE]	0.9685 [0.5088; 1.9029] 0.9237	0.9241
PT: Upper respiratory tract infection	21 (4.8)	NE [NE; NE]	10 (2.4)	NE [NE; NE]	1.3833 [0.6616; 3.0909] 0.4038	0.4019
PT: Pneumonia	20 (4.6)	NE [NE; NE]	9 (2.2)	NE [NE; NE]	1.3446 [0.6218; 3.1365] 0.4674	0.4658
PT: Influenza	13 (3.0)	NE [NE; NE]	6 (1.4)	NE [NE; NE]	1.3946 [0.5473; 3.9910] 0.5032	0.5013
PT: Cystitis	12 (2.8)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	1.8512 [0.6821; 5.8489] 0.2501	0.2427
PT: COVID-19 pneumonia	11 (2.5)	NE [NE; NE]	2 (0.5)	NE [NE; NE]	3.8505 [1.0218; 25.0293] 0.0813	0.0611
PT: Sinusitis	11 (2.5)	NE [NE; NE]	3 (0.7)	NE [NE; NE]	2.3093 [0.7128; 10.2801] 0.2022	0.1899

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Bronchitis	9 (2.1)	NE [NE; NE]	6 (1.4)	NE [NE; NE]	0.8584 [0.3041; 2.6014] 0.7758	0.7757
PT: Herpes zoster	9 (2.1)	NE [NE; NE]	6 (1.4)	NE [NE; NE]	0.9370 [0.3292; 2.8529] 0.9040	0.9046
PT: Conjunctivitis	8 (1.8)	NE [NE; NE]	8 (1.9)	NE [NE; NE]	0.6585 [0.2401; 1.8049] 0.4078	0.4046
PT: Gastroenteritis	6 (1.4)	NE [NE; NE]	6 (1.4)	NE [NE; NE]	0.7364 [0.2277; 2.3788] 0.6000	0.5987
PT: Paronychia	5 (1.2)	NE [NE; NE]	9 (2.2)	NE [NE; NE]	0.3695 [0.1128; 1.0782] 0.0764	0.0654
PT: Cellulitis	2 (0.5)	NE [NE; NE]	10 (2.4)	NE [NE; NE]	0.1204 [0.0183; 0.4678] 0.0070	0.0015
SOC: Respiratory, thoracic and mediastinal disorders						
All (any PT)	209 (48.2)	12.4 [9.9; 15.3]	106 (25.4)	NE [20.4; NE]	1.5584 [1.2357; 1.9771] 0.0002	0.0002
PT: Cough	69 (15.9)	NE [NE; NE]	38 (9.1)	NE [NE; NE]	1.3504 [0.9118; 2.0301] 0.1400	0.1387

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Epistaxis	44 (10.1)	NE [NE; NE]	15 (3.6)	NE [NE; NE]	2.0866 [1.1834; 3.8903] 0.0146	0.0126
PT: Interstitial lung disease	30 (6.9)	NE [NE; NE]	2 (0.5)	NE [NE; NE]	10.2821 [3.0918; 63.6938] 0.0015	0.0001
PT: Pneumonitis	30 (6.9)	NE [NE; NE]	0 (0.0)	NE [NE; NE]	NE [NE; NE]	<.0001
PT: Dyspnoea	27 (6.2)	NE [NE; NE]	41 (9.8)	NE [NE; NE]	0.5205 [0.3157; 0.8444] 0.0090	0.0079
PT: Oropharyngeal pain	16 (3.7)	NE [NE; NE]	8 (1.9)	NE [NE; NE]	1.5358 [0.6711; 3.8072] 0.3252	0.3217
PT: Rhinorrhoea	12 (2.8)	NE [NE; NE]	9 (2.2)	NE [NE; NE]	0.9153 [0.3839; 2.2603] 0.8426	0.8426
PT: Nasal congestion	11 (2.5)	NE [NE; NE]	4 (1.0)	NE [NE; NE]	1.6401 [0.5560; 5.9581] 0.4001	0.3952
PT: Productive cough	8 (1.8)	NE [NE; NE]	4 (1.0)	NE [NE; NE]	1.3458 [0.4192; 5.0841] 0.6307	0.6295
PT: Pulmonary embolism	8 (1.8)	NE [NE; NE]	9 (2.2)	NE [NE; NE]	0.6377 [0.2379; 1.6783] 0.3579	0.3540

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Pleural effusion	5 (1.2)	NE [NE; NE]	7 (1.7)	NE [NE; NE]	0.5390 [0.1578; 1.7068] 0.2961	0.2889
SOC: Blood and lymphatic system disorders						
All (any PT)	203 (46.8)	14.3 [8.5; NE]	152 (36.5)	NE [NE; NE]	1.1722 [0.9501; 1.4492] 0.1399	0.1445
PT: Anaemia	159 (36.6)	NE [21.5; NE]	107 (25.7)	NE [NE; NE]	1.2861 [1.0070; 1.6489] 0.0452	0.0465
PT: Neutropenia	76 (17.5)	NE [NE; NE]	63 (15.1)	NE [NE; NE]	1.0306 [0.7378; 1.4446] 0.8602	0.8590
PT: Leukopenia	30 (6.9)	NE [NE; NE]	17 (4.1)	NE [NE; NE]	1.3863 [0.7702; 2.5768] 0.2855	0.2837
PT: Thrombocytopenia	27 (6.2)	NE [NE; NE]	7 (1.7)	NE [NE; NE]	2.7850 [1.2735; 6.9765] 0.0165	0.0125
PT: Lymphopenia	21 (4.8)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	3.2282 [1.3081; 9.7059] 0.0191	0.0133
PT: Febrile neutropenia	5 (1.2)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	0.8461 [0.2348; 3.0493] 0.7921	0.7918

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
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CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders						
All (any PT)	197 (45.4)	14.6 [11.1; NE]	107 (25.7)	NE [NE; NE]	1.7241 [1.3645; 2.1906] <.0001	<.0001
PT: Decreased appetite	114 (26.3)	NE [NE; NE]	48 (11.5)	NE [NE; NE]	2.2716 [1.6320; 3.2140] <.0001	<.0001
PT: Hypokalaemia	56 (12.9)	NE [NE; NE]	15 (3.6)	NE [NE; NE]	2.8471 [1.6479; 5.2339] 0.0003	0.0002
PT: Hypoalbuminaemia	25 (5.8)	NE [NE; NE]	12 (2.9)	NE [NE; NE]	1.6627 [0.8485; 3.4430] 0.1506	0.1464
PT: Hypocalcaemia	18 (4.1)	NE [NE; NE]	16 (3.8)	NE [NE; NE]	0.9833 [0.4991; 1.9542] 0.9611	0.9606
PT: Hyperglycaemia	15 (3.5)	NE [NE; NE]	6 (1.4)	NE [NE; NE]	1.8886 [0.7606; 5.3345] 0.1920	0.1848
PT: Hyponatraemia	13 (3.0)	NE [NE; NE]	13 (3.1)	NE [NE; NE]	0.8243 [0.3765; 1.8038] 0.6246	0.6236
PT: Hypomagnesaemia	12 (2.8)	NE [NE; NE]	8 (1.9)	NE [NE; NE]	1.2282 [0.5048; 3.1511] 0.6546	0.6541

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
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Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Hypercalcaemia	10 (2.3)	NE [NE; NE]	9 (2.2)	NE [NE; NE]	0.7602 [0.3001; 1.9481] 0.5596	0.5582
PT: Hypophosphataemia	10 (2.3)	NE [NE; NE]	10 (2.4)	NE [NE; NE]	0.8190 [0.3350; 2.0016] 0.6564	0.6553
PT: Dehydration	7 (1.6)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	0.9442 [0.2937; 3.2584] 0.9236	0.9231
PT: Hyperuricaemia	6 (1.4)	NE [NE; NE]	12 (2.9)	NE [NE; NE]	0.4132 [0.1428; 1.0722] 0.0796	0.0707
SOC: Nervous system disorders						
All (any PT)	169 (38.9)	NE [14.9; NE]	188 (45.1)	8.5 [5.9; 11.9]	0.7134 [0.5778; 0.8799] 0.0016	0.0015
PT: Headache	74 (17.1)	NE [NE; NE]	42 (10.1)	NE [NE; NE]	1.5429 [1.0597; 2.2757] 0.0257	0.0251
PT: Dysgeusia	51 (11.8)	NE [NE; NE]	24 (5.8)	NE [NE; NE]	1.7927 [1.1145; 2.9668] 0.0188	0.0172
PT: Dizziness	37 (8.5)	NE [NE; NE]	26 (6.2)	NE [23.0; NE]	1.1209 [0.6786; 1.8776] 0.6587	0.6596

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
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Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Paraesthesia	12 (2.8)	NE [NE; NE]	19 (4.6)	NE [NE; NE]	0.4442 [0.2072; 0.9151] 0.0305	0.0265
PT: Peripheral sensory neuropathy	12 (2.8)	NE [NE; NE]	49 (11.8)	NE [NE; NE]	0.1949 [0.0987; 0.3548] <.0001	<.0001
PT: Neuropathy peripheral	8 (1.8)	NE [NE; NE]	36 (8.6)	NE [NE; NE]	0.1694 [0.0730; 0.3471] <.0001	<.0001
PT: Hypoaesthesia	5 (1.2)	NE [NE; NE]	12 (2.9)	NE [NE; NE]	0.3099 [0.0980; 0.8410] 0.0287	0.0209
PT: Somnolence	4 (0.9)	NE [NE; NE]	6 (1.4)	NE [NE; NE]	0.4597 [0.1160; 1.6325] 0.2341	0.2233
SOC: Musculoskeletal and connective tissue disorders						
All (any PT)	129 (29.7)	NE [19.3; NE]	133 (31.9)	26.5 [14.3; NE]	0.6953 [0.5435; 0.8892] 0.0038	0.0037
PT: Back pain	36 (8.3)	NE [NE; NE]	36 (8.6)	NE [NE; NE]	0.7354 [0.4601; 1.1752] 0.1970	0.1952
PT: Arthralgia	32 (7.4)	NE [NE; NE]	45 (10.8)	NE [NE; NE]	0.4925 [0.3090; 0.7761] 0.0025	0.0020

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Pain in extremity	26 (6.0)	NE [NE; NE]	24 (5.8)	NE [26.5; NE]	0.7648 [0.4348; 1.3500] 0.3507	0.3492
PT: Musculoskeletal chest pain	21 (4.8)	NE [NE; NE]	13 (3.1)	NE [NE; NE]	1.2242 [0.6166; 2.5222] 0.5697	0.5691
PT: Myalgia	19 (4.4)	NE [NE; NE]	27 (6.5)	NE [NE; NE]	0.5816 [0.3176; 1.0436] 0.0721	0.0690
PT: Muscle spasms	15 (3.5)	NE [NE; NE]	7 (1.7)	NE [NE; NE]	1.5042 [0.6290; 3.9657] 0.3767	0.3735
PT: Musculoskeletal pain	10 (2.3)	NE [NE; NE]	4 (1.0)	NE [NE; NE]	1.3433 [0.4449; 4.9353] 0.6207	0.6195
PT: Neck pain	9 (2.1)	NE [NE; NE]	2 (0.5)	NE [NE; NE]	2.5289 [0.6394; 16.7471] 0.2398	0.2241
PT: Bone pain	5 (1.2)	NE [NE; NE]	8 (1.9)	NE [NE; NE]	0.5256 [0.1585; 1.5801] 0.2605	0.2526
PT: Muscular weakness	5 (1.2)	NE [NE; NE]	6 (1.4)	NE [NE; NE]	0.6229 [0.1781; 2.0847] 0.4378	0.4337

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 09DEC2024 10:14; Program name: T.2.29.1_10TEAE_SAF.sas; Output name: T.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Eye disorders						
All (any PT)	89 (20.5)	NE [NE; NE]	58 (13.9)	NE [NE; NE]	1.1553 [0.8297; 1.6208] 0.3970	0.3972
PT: Dry eye	28 (6.5)	NE [NE; NE]	18 (4.3)	NE [NE; NE]	1.2077 [0.6700; 2.2319] 0.5358	0.5352
PT: Vision blurred	17 (3.9)	NE [NE; NE]	8 (1.9)	NE [NE; NE]	1.7193 [0.7609; 4.2302] 0.2087	0.2031
PT: Cataract	9 (2.1)	NE [NE; NE]	1 (0.2)	NE [NE; NE]	5.0437 [0.9410; 93.2103] 0.1256	0.0889
PT: Lacrimation increased	7 (1.6)	NE [NE; NE]	9 (2.2)	NE [NE; NE]	0.5482 [0.1943; 1.4835] 0.2371	0.2304
PT: Visual impairment	7 (1.6)	NE [NE; NE]	3 (0.7)	NE [NE; NE]	1.5439 [0.4228; 7.2349] 0.5332	0.5300
SOC: Vascular disorders						
All (any PT)	60 (13.8)	NE [NE; NE]	52 (12.5)	NE [NE; NE]	0.9233 [0.6357; 1.3459] 0.6757	0.6767
PT: Hypertension	27 (6.2)	NE [NE; NE]	23 (5.5)	NE [NE; NE]	0.9192 [0.5247; 1.6241] 0.7687	0.7698

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 09DEC2024 10:14; Program name: T.2.29.1_10TEAE_SAF.sas; Output name: T.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Hypotension	10 (2.3)	NE [NE; NE]	4 (1.0)	NE [NE; NE]	2.0505 [0.6822; 7.5079] 0.2268	0.2169
PT: Hot flush	8 (1.8)	NE [NE; NE]	3 (0.7)	NE [NE; NE]	2.0424 [0.5836; 9.3944] 0.2953	0.2855
PT: Lymphoedema	7 (1.6)	NE [NE; NE]	6 (1.4)	NE [NE; NE]	0.8854 [0.2935; 2.7555] 0.8271	0.8270
PT: Deep vein thrombosis	0 (0.0)	NE [NE; NE]	10 (2.4)	NE [NE; NE]	NE [NE; NE]	0.0003
SOC: Psychiatric disorders						
All (any PT)	53 (12.2)	NE [31.3; NE]	32 (7.7)	NE [NE; NE]	1.2846 [0.8307; 2.0179] 0.2667	0.2651
PT: Insomnia	32 (7.4)	NE [NE; NE]	19 (4.6)	NE [NE; NE]	1.2814 [0.7305; 2.3094] 0.3953	0.3941
PT: Anxiety	12 (2.8)	NE [31.3; NE]	2 (0.5)	NE [NE; NE]	4.2946 [1.1579; 27.7541] 0.0578	0.0391
PT: Depression	10 (2.3)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	1.4419 [0.5086; 4.6555] 0.5068	0.5045

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Injury, poisoning and procedural complications						
All (any PT)	45 (10.4)	NE [NE; NE]	38 (9.1)	NE [NE; NE]	0.8461 [0.5471; 1.3151] 0.4535	0.4535
PT: Fall	9 (2.1)	NE [NE; NE]	9 (2.2)	NE [NE; NE]	0.6565 [0.2530; 1.7021] 0.3787	0.3755
PT: Infusion related reaction	7 (1.6)	NE [NE; NE]	3 (0.7)	NE [NE; NE]	1.9126 [0.5225; 8.9679] 0.3525	0.3444
PT: Contusion	5 (1.2)	NE [NE; NE]	7 (1.7)	NE [NE; NE]	0.4407 [0.1291; 1.3966] 0.1660	0.1551
SOC: Cardiac disorders						
All (any PT)	35 (8.1)	NE [NE; NE]	25 (6.0)	NE [NE; NE]	1.1142 [0.6672; 1.8874] 0.6820	0.6822
PT: Tachycardia	6 (1.4)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	0.8342 [0.2488; 2.9202] 0.7666	0.7664
SOC: Renal and urinary disorders						
All (any PT)	30 (6.9)	NE [NE; NE]	18 (4.3)	NE [NE; NE]	1.2572 [0.7040; 2.3086] 0.4468	0.4461

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 09DEC2024 10:14; Program name: T.2.29.1_10TEAE_SAF.sas; Output name: T.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Dysuria	12 (2.8)	NE [NE; NE]	4 (1.0)	NE [NE; NE]	2.2183 [0.7639; 7.9941] 0.1713	0.1608
SOC: Hepatobiliary disorders						
All (any PT)	24 (5.5)	NE [NE; NE]	15 (3.6)	NE [NE; NE]	1.1744 [0.6181; 2.3021] 0.6289	0.6287
PT: Hypertransaminasaemia	5 (1.2)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	0.8300 [0.2298; 2.9972] 0.7692	0.7689
SOC: Reproductive system and breast disorders						
All (any PT)	21 (4.8)	NE [NE; NE]	14 (3.4)	NE [NE; NE]	1.0145 [0.5171; 2.0512] 0.9671	0.9670
SOC: Ear and labyrinth disorders						
All (any PT)	17 (3.9)	NE [NE; NE]	18 (4.3)	NE [NE; NE]	0.7060 [0.3580; 1.3856] 0.3090	0.3070
PT: Vertigo	7 (1.6)	NE [NE; NE]	7 (1.7)	NE [NE; NE]	0.7687 [0.2585; 2.2779] 0.6282	0.6271

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.29.1 Adverse events by SOC and PT observed for = 10 patients (in total) and = 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Immune system disorders						
All (any PT)	7 (1.6)	NE [NE; NE]	11 (2.6)	NE [NE; NE]	0.4636 [0.1693; 1.1868] 0.1150	0.1069

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 09DEC2024 10:14; Program name: T.2.29.1_10TEAE_SAF.sas; Output name: T.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.29.2 Unerwünschte Ereignisse nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Subgruppenanalyse – SAF

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: All (any PT)						
Age at randomization						0.0174
<65 years of age	269 / 301 (89.4)	0.1 [0.1; 0.1]	174 / 285 (61.1)	2.1 [1.2; 3.3]	2.5850 [2.1324; 3.1424] <.0001	
>=65 years of age	107 / 133 (80.5)	0.2 [0.1; 0.4]	82 / 132 (62.1)	1.2 [0.7; 4.3]	1.7520 [1.3144; 2.3438] 0.0001	
Race						0.1319
Asian	134 / 153 (87.6)	0.1 [0.1; 0.2]	82 / 147 (55.8)	4.8 [2.0; 7.3]	3.0634 [2.3226; 4.0641] <.0001	
White	198 / 231 (85.7)	0.1 [0.1; 0.2]	142 / 223 (63.7)	1.3 [0.7; 2.7]	1.9805 [1.5956; 2.4646] <.0001	
Other	44 / 50 (88.0)	0.1 [0.1; 0.2]	32 / 47 (68.1)	0.7 [0.3; 3.0]	1.9684 [1.2481; 3.1382] 0.0040	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2577
Asia	128 / 148 (86.5)	0.1 [0.1; 0.2]	81 / 144 (56.3)	3.4 [1.4; 6.2]	2.8804 [2.1781; 3.8339] <.0001	
Europe	194 / 227 (85.5)	0.1 [0.1; 0.1]	131 / 206 (63.6)	1.2 [0.6; 2.7]	1.9596 [1.5697; 2.4539] <.0001	
Rest of the World	54 / 59 (91.5)	0.1 [0.1; 0.2]	44 / 67 (65.7)	1.6 [0.7; 4.6]	2.4843 [1.6553; 3.7527] <.0001	
HER2 IHC expression						0.8672
IHC 1+	198 / 239 (82.8)	0.1 [0.1; 0.2]	132 / 226 (58.4)	2.7 [1.2; 5.6]	2.1996 [1.7634; 2.7526] <.0001	
IHC 2+/ISH-	106 / 116 (91.4)	0.1 [0.1; 0.1]	77 / 115 (67.0)	1.3 [0.5; 3.3]	2.4897 [1.8530; 3.3615] <.0001	
IHC >0 <1+	69 / 76 (90.8)	0.1 [0.1; 0.2]	46 / 74 (62.2)	1.1 [0.5; 5.6]	2.3051 [1.5855; 3.3822] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8750
Yes	342 / 393 (87.0)	0.1 [0.1; 0.1]	234 / 377 (62.1)	1.4 [1.0; 2.8]	2.2681 [1.9187; 2.6860] <.0001	
No	34 / 41 (82.9)	0.2 [0.1; 1.0]	22 / 40 (55.0)	6.2 [2.1; NE]	2.5757 [1.5083; 4.4901] 0.0005	
Prior Taxane Use In The Non-Metastatic Setting						0.5347
Yes	152 / 177 (85.9)	0.1 [0.1; 0.2]	102 / 172 (59.3)	2.7 [1.3; 5.6]	2.4353 [1.8928; 3.1468] <.0001	
No	224 / 257 (87.2)	0.1 [0.1; 0.1]	154 / 245 (62.9)	1.3 [0.7; 2.8]	2.1819 [1.7755; 2.6883] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1118
1	59 / 65 (90.8)	0.1 [0.1; 0.2]	48 / 79 (60.8)	2.7 [1.1; 6.2]	3.1756 [2.1419; 4.7305] <.0001	
2	254 / 293 (86.7)	0.1 [0.1; 0.1]	169 / 281 (60.1)	2.1 [1.1; 3.3]	2.2502 [1.8513; 2.7421] <.0001	
>=3	62 / 75 (82.7)	0.2 [0.1; 0.2]	39 / 56 (69.6)	0.7 [0.3; 5.1]	1.6871 [1.1312; 2.5458] 0.0114	
ER/PR status I						0.8185
ER+, PR+	213 / 252 (84.5)	0.1 [0.1; 0.2]	136 / 234 (58.1)	2.8 [1.2; 4.8]	2.2315 [1.7985; 2.7781] <.0001	
ER+, PR-	148 / 166 (89.2)	0.1 [0.1; 0.2]	113 / 171 (66.1)	1.4 [0.6; 2.5]	2.3293 [1.8203; 2.9894] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4065
ER <=10%	17 / 21 (81.0)	0.1 [0.1; 2.1]	9 / 14 (64.3)	1.1 [0.2; NE]	1.9131 [0.8651; 4.5236] 0.1379	
ER >10%	314 / 362 (86.7)	0.1 [0.1; 0.2]	201 / 343 (58.6)	2.7 [1.4; 4.7]	2.4392 [2.0419; 2.9207] <.0001	
Positive	45 / 51 (88.2)	0.1 [0.1; 0.1]	46 / 60 (76.7)	0.4 [0.2; 1.1]	1.8446 [1.2109; 2.8086] 0.0051	
Endocrine Resistance						0.5601
Primary	109 / 127 (85.8)	0.1 [0.1; 0.1]	83 / 137 (60.6)	2.1 [0.8; 5.2]	2.3929 [1.7943; 3.2039] <.0001	
Secondary	267 / 307 (87.0)	0.1 [0.1; 0.2]	172 / 279 (61.6)	2.0 [1.1; 3.3]	2.2490 [1.8556; 2.7331] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0781
Capecitabine	239 / 265 (90.2)	0.1 [0.1; 0.1]	174 / 249 (69.9)	1.1 [0.7; 1.4]	2.0672 [1.6981; 2.5215] <.0001	
Nab-Paclitaxel	78 / 103 (75.7)	0.2 [0.1; 0.9]	47 / 101 (46.5)	8.9 [5.1; NE]	2.4741 [1.7263; 3.5841] <.0001	
Paclitaxel	59 / 66 (89.4)	0.1 [0.1; 0.1]	35 / 67 (52.2)	3.9 [0.6; NE]	3.2987 [2.1635; 5.1019] <.0001	
Prior anthracycline use						0.8418
Yes	172 / 197 (87.3)	0.1 [0.1; 0.2]	120 / 198 (60.6)	2.5 [1.2; 5.2]	2.3562 [1.8638; 2.9886] <.0001	
No	204 / 237 (86.1)	0.1 [0.1; 0.1]	136 / 219 (62.1)	1.3 [0.7; 2.9]	2.2264 [1.7906; 2.7771] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5625
Yes	256 / 294 (87.1)	0.1 [0.1; 0.1]	165 / 275 (60.0)	2.1 [1.2; 3.4]	2.3398 [1.9227; 2.8555] <.0001	
No	120 / 140 (85.7)	0.1 [0.1; 0.2]	91 / 142 (64.1)	1.6 [1.0; 4.6]	2.1799 [1.6570; 2.8778] <.0001	
ECOG						0.0592
0	221 / 251 (88.0)	0.1 [0.1; 0.1]	148 / 246 (60.2)	2.5 [1.4; 4.3]	2.6064 [2.1143; 3.2236] <.0001	
>=1	150 / 178 (84.3)	0.2 [0.1; 0.2]	102 / 163 (62.6)	1.0 [0.6; 3.0]	1.9106 [1.4852; 2.4677] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Nausea						
Age at randomization						0.5410
<65 years of age	222 / 301 (73.8)	0.1 [0.1; 0.2]	91 / 285 (31.9)	NE [NE; NE]	3.5210 [2.7641; 4.5230] <.0001	
>=65 years of age	81 / 133 (60.9)	1.4 [0.3; 3.9]	35 / 132 (26.5)	NE [NE; NE]	3.1603 [2.1427; 4.7598] <.0001	
Race						0.1072
Asian	101 / 153 (66.0)	0.3 [0.1; 0.8]	30 / 147 (20.4)	NE [NE; NE]	4.8575 [3.2666; 7.4412] <.0001	
White	166 / 231 (71.9)	0.2 [0.1; 0.3]	77 / 223 (34.5)	NE [NE; NE]	2.9994 [2.2951; 3.9547] <.0001	
Other	36 / 50 (72.0)	0.1 [0.1; 0.8]	19 / 47 (40.4)	NE [2.8; NE]	2.6727 [1.5454; 4.7707] 0.0004	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.3086
Asia	95 / 148 (64.2)	0.3 [0.2; 1.6]	31 / 144 (21.5)	NE [NE; NE]	4.3651 [2.9395; 6.6636] <.0001	
Europe	161 / 227 (70.9)	0.2 [0.1; 0.3]	71 / 206 (34.5)	NE [NE; NE]	2.9369 [2.2289; 3.9099] <.0001	
Rest of the World	47 / 59 (79.7)	0.2 [0.1; 0.2]	24 / 67 (35.8)	NE [4.7; NE]	3.7798 [2.3176; 6.3241] <.0001	
HER2 IHC expression						0.8505
IHC 1+	158 / 239 (66.1)	0.3 [0.2; 1.4]	64 / 226 (28.3)	NE [NE; NE]	3.2610 [2.4493; 4.3959] <.0001	
IHC 2+/ISH-	87 / 116 (75.0)	0.1 [0.1; 0.3]	40 / 115 (34.8)	NE [9.4; NE]	3.3852 [2.3385; 4.9848] <.0001	
IHC >0 <1+	55 / 76 (72.4)	0.2 [0.1; 0.3]	21 / 74 (28.4)	NE [11.8; NE]	4.0040 [2.4516; 6.7899] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1082
Yes	280 / 393 (71.2)	0.2 [0.1; 0.2]	122 / 377 (32.4)	NE [NE; NE]	3.2810 [2.6561; 4.0770] <.0001	
No	23 / 41 (56.1)	2.4 [0.3; NE]	4 / 40 (10.0)	NE [NE; NE]	7.6411 [2.9305; 26.1174] <.0001	
Prior Taxane Use In The Non-Metastatic Setting						0.2924
Yes	118 / 177 (66.7)	0.3 [0.1; 0.9]	42 / 172 (24.4)	NE [NE; NE]	3.8432 [2.7205; 5.5359] <.0001	
No	185 / 257 (72.0)	0.2 [0.1; 0.3]	84 / 245 (34.3)	NE [NE; NE]	3.1829 [2.4647; 4.1445] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0216
1	53 / 65 (81.5)	0.1 [0.1; 0.2]	22 / 79 (27.8)	NE [NE; NE]	5.6259 [3.4349; 9.5236] <.0001	
2	203 / 293 (69.3)	0.2 [0.1; 0.3]	82 / 281 (29.2)	NE [NE; NE]	3.4011 [2.6397; 4.4246] <.0001	
>=3	46 / 75 (61.3)	0.8 [0.2; 3.9]	22 / 56 (39.3)	14.0 [1.8; NE]	1.9980 [1.2160; 3.3853] 0.0067	
ER/PR status I						0.6188
ER+, PR+	172 / 252 (68.3)	0.2 [0.1; 0.3]	71 / 234 (30.3)	NE [NE; NE]	3.2859 [2.5006; 4.3650] <.0001	
ER+, PR-	118 / 166 (71.1)	0.2 [0.1; 0.8]	50 / 171 (29.2)	NE [NE; NE]	3.6178 [2.6112; 5.0862] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5797
ER <=10%	12 / 21 (57.1)	1.0 [0.1; NE]	5 / 14 (35.7)	NE [0.3; NE]	1.9171 [0.7093; 6.0405] 0.2280	
ER >10%	250 / 362 (69.1)	0.2 [0.2; 0.3]	96 / 343 (28.0)	NE [NE; NE]	3.6070 [2.8587; 4.5914] <.0001	
Positive	41 / 51 (80.4)	0.1 [0.1; 0.1]	25 / 60 (41.7)	NE [3.9; NE]	3.5019 [2.1216; 5.8935] <.0001	
Endocrine Resistance						0.7965
Primary	91 / 127 (71.7)	0.1 [0.1; 0.2]	44 / 137 (32.1)	NE [11.8; NE]	3.4272 [2.3985; 4.9713] <.0001	
Secondary	212 / 307 (69.1)	0.2 [0.2; 0.6]	82 / 279 (29.4)	NE [NE; NE]	3.4070 [2.6500; 4.4261] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1894
Capecitabine	192 / 265 (72.5)	0.2 [0.1; 0.3]	87 / 249 (34.9)	NE [NE; NE]	2.9938 [2.3292; 3.8793] <.0001	
Nab-Paclitaxel	60 / 103 (58.3)	1.0 [0.1; NE]	19 / 101 (18.8)	NE [NE; NE]	4.2849 [2.6008; 7.3897] <.0001	
Paclitaxel	51 / 66 (77.3)	0.1 [0.1; 0.3]	20 / 67 (29.9)	NE [6.7; NE]	4.5514 [2.7409; 7.8546] <.0001	
Prior anthracycline use						0.8221
Yes	134 / 197 (68.0)	0.3 [0.2; 0.8]	54 / 198 (27.3)	NE [NE; NE]	3.4787 [2.5486; 4.8169] <.0001	
No	169 / 237 (71.3)	0.1 [0.1; 0.2]	72 / 219 (32.9)	NE [NE; NE]	3.3472 [2.5474; 4.4434] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.8342
Yes	208 / 294 (70.7)	0.2 [0.1; 0.3]	84 / 275 (30.5)	NE [NE; NE]	3.4212 [2.6631; 4.4367] <.0001	
No	95 / 140 (67.9)	0.2 [0.1; 0.8]	42 / 142 (29.6)	NE [NE; NE]	3.3501 [2.3419; 4.8739] <.0001	
ECOG						0.9725
0	176 / 251 (70.1)	0.2 [0.1; 0.3]	76 / 246 (30.9)	NE [NE; NE]	3.4797 [2.6658; 4.5854] <.0001	
>=1	124 / 178 (69.7)	0.2 [0.1; 0.6]	46 / 163 (28.2)	NE [NE; NE]	3.4726 [2.4907; 4.9266] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Vomiting						
Age at randomization						0.2248
<65 years of age	114 / 301 (37.9)	NE [NE; NE]	34 / 285 (11.9)	NE [NE; NE]	3.4286 [2.3636; 5.1063] <.0001	
>=65 years of age	32 / 133 (24.1)	NE [NE; NE]	15 / 132 (11.4)	NE [23.6; NE]	2.1593 [1.1886; 4.1062] 0.0119	
Race						0.0922
Asian	51 / 153 (33.3)	NE [NE; NE]	10 / 147 (6.8)	NE [23.6; NE]	5.4884 [2.9110; 11.4833] <.0001	
White	80 / 231 (34.6)	NE [NE; NE]	33 / 223 (14.8)	NE [NE; NE]	2.4176 [1.6264; 3.6764] <.0001	
Other	15 / 50 (30.0)	NE [NE; NE]	6 / 47 (12.8)	NE [NE; NE]	2.4374 [0.9886; 6.8448] 0.0588	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0439
Asia	48 / 148 (32.4)	NE [NE; NE]	8 / 144 (5.6)	NE [23.6; NE]	6.4820 [3.2460; 14.8275] <.0001	
Europe	73 / 227 (32.2)	NE [NE; NE]	29 / 206 (14.1)	NE [NE; NE]	2.3914 [1.5725; 3.7349] <.0001	
Rest of the World	25 / 59 (42.4)	18.6 [6.2; NE]	12 / 67 (17.9)	NE [NE; NE]	2.3710 [1.2113; 4.9047] 0.0119	
HER2 IHC expression						0.8741
IHC 1+	74 / 239 (31.0)	NE [NE; NE]	24 / 226 (10.6)	NE [23.6; NE]	3.1518 [2.0191; 5.1006] <.0001	
IHC 2+/ISH-	45 / 116 (38.8)	NE [14.9; NE]	17 / 115 (14.8)	NE [NE; NE]	2.7182 [1.5843; 4.8876] 0.0003	
IHC >0 <1+	27 / 76 (35.5)	NE [15.2; NE]	8 / 74 (10.8)	NE [NE; NE]	3.4433 [1.6350; 8.1257] 0.0011	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9681
Yes	132 / 393 (33.6)	NE [NE; NE]	44 / 377 (11.7)	NE [NE; NE]	3.0478 [2.1846; 4.3354] <.0001	
No	14 / 41 (34.1)	NE [8.5; NE]	5 / 40 (12.5)	NE [NE; NE]	3.0759 [1.1764; 9.5200] 0.0230	
Prior Taxane Use In The Non-Metastatic Setting						0.4815
Yes	52 / 177 (29.4)	NE [NE; NE]	20 / 172 (11.6)	NE [23.6; NE]	2.6164 [1.5860; 4.4893] 0.0002	
No	94 / 257 (36.6)	NE [NE; NE]	29 / 245 (11.8)	NE [NE; NE]	3.3668 [2.2500; 5.1946] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3608
1	22 / 65 (33.8)	NE [18.6; NE]	9 / 79 (11.4)	NE [NE; NE]	3.3931 [1.6090; 7.7876] 0.0011	
2	101 / 293 (34.5)	NE [NE; NE]	30 / 281 (10.7)	NE [23.6; NE]	3.3721 [2.2726; 5.1561] <.0001	
>=3	23 / 75 (30.7)	NE [NE; NE]	10 / 56 (17.9)	NE [NE; NE]	1.8133 [0.8848; 3.9973] 0.1131	
ER/PR status I						0.2773
ER+, PR+	79 / 252 (31.3)	NE [NE; NE]	20 / 234 (8.5)	NE [23.6; NE]	3.8771 [2.4230; 6.5088] <.0001	
ER+, PR-	61 / 166 (36.7)	NE [NE; NE]	25 / 171 (14.6)	NE [NE; NE]	2.7363 [1.7388; 4.4382] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1741
ER <=10%	8 / 21 (38.1)	NE [0.2; NE]	4 / 14 (28.6)	NE [0.4; NE]	1.4206 [0.4466; 5.3306] 0.5877	
ER >10%	122 / 362 (33.7)	NE [NE; NE]	35 / 343 (10.2)	NE [NE; NE]	3.5610 [2.4732; 5.2628] <.0001	
Positive	16 / 51 (31.4)	NE [7.4; NE]	10 / 60 (16.7)	23.6 [23.6; NE]	1.9391 [0.8910; 4.4308] 0.0948	
Endocrine Resistance						0.9896
Primary	39 / 127 (30.7)	NE [NE; NE]	15 / 137 (10.9)	NE [NE; NE]	3.0871 [1.7365; 5.7843] 0.0001	
Secondary	107 / 307 (34.9)	NE [NE; NE]	34 / 279 (12.2)	NE [23.6; NE]	3.0143 [2.0720; 4.4992] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1280
Capecitabine	87 / 265 (32.8)	NE [NE; NE]	35 / 249 (14.1)	NE [NE; NE]	2.4343 [1.6592; 3.6503] <.0001	
Nab-Paclitaxel	36 / 103 (35.0)	NE [NE; NE]	7 / 101 (6.9)	NE [NE; NE]	5.7464 [2.7193; 14.1049] <.0001	
Paclitaxel	23 / 66 (34.8)	NE [NE; NE]	7 / 67 (10.4)	NE [NE; NE]	3.5470 [1.6005; 8.9458] 0.0017	
Prior anthracycline use						0.1939
Yes	56 / 197 (28.4)	NE [NE; NE]	24 / 198 (12.1)	NE [23.6; NE]	2.3748 [1.4893; 3.9064] 0.0003	
No	90 / 237 (38.0)	NE [NE; NE]	25 / 219 (11.4)	NE [NE; NE]	3.6884 [2.4066; 5.8668] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5895
Yes	94 / 294 (32.0)	NE [NE; NE]	32 / 275 (11.6)	NE [NE; NE]	2.8530 [1.9312; 4.3275] <.0001	
No	52 / 140 (37.1)	NE [NE; NE]	17 / 142 (12.0)	NE [23.6; NE]	3.4860 [2.0591; 6.2099] <.0001	
ECOG						0.0628
0	88 / 251 (35.1)	NE [NE; NE]	23 / 246 (9.3)	NE [NE; NE]	4.0762 [2.6220; 6.6036] <.0001	
>=1	58 / 178 (32.6)	NE [NE; NE]	25 / 163 (15.3)	23.6 [23.6; NE]	2.2109 [1.3996; 3.5984] 0.0007	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Constipation						
Age at randomization						0.4687
<65 years of age	101 / 301 (33.6)	NE [NE; NE]	41 / 285 (14.4)	NE [NE; NE]	2.2381 [1.5668; 3.2562] <.0001	
>=65 years of age	36 / 133 (27.1)	NE [NE; NE]	21 / 132 (15.9)	NE [NE; NE]	1.7485 [1.0300; 3.0452] 0.0400	
Race						0.3641
Asian	53 / 153 (34.6)	NE [NE; NE]	19 / 147 (12.9)	NE [NE; NE]	2.8565 [1.7222; 4.9484] <.0001	
White	71 / 231 (30.7)	NE [NE; NE]	37 / 223 (16.6)	NE [NE; NE]	1.7707 [1.1966; 2.6641] 0.0045	
Other	13 / 50 (26.0)	NE [23.5; NE]	6 / 47 (12.8)	NE [NE; NE]	1.5118 [0.5712; 4.4210] 0.4177	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7770
Asia	47 / 148 (31.8)	NE [NE; NE]	20 / 144 (13.9)	NE [NE; NE]	2.3718 [1.4271; 4.0939] 0.0009	
Europe	69 / 227 (30.4)	NE [NE; NE]	28 / 206 (13.6)	NE [NE; NE]	2.1125 [1.3754; 3.3367] 0.0007	
Rest of the World	21 / 59 (35.6)	23.5 [9.7; NE]	14 / 67 (20.9)	NE [11.0; NE]	1.6804 [0.8577; 3.3926] 0.1339	
HER2 IHC expression						0.1892
IHC 1+	71 / 239 (29.7)	NE [NE; NE]	29 / 226 (12.8)	NE [NE; NE]	2.2799 [1.4955; 3.5676] 0.0001	
IHC 2+/ISH-	43 / 116 (37.1)	NE [13.9; NE]	16 / 115 (13.9)	NE [NE; NE]	2.6577 [1.5247; 4.8705] 0.0006	
IHC >0 <1+	23 / 76 (30.3)	NE [23.5; NE]	17 / 74 (23.0)	NE [11.9; NE]	1.2678 [0.6792; 2.4132] 0.4618	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5217
Yes	124 / 393 (31.6)	NE [NE; NE]	54 / 377 (14.3)	NE [NE; NE]	2.1616 [1.5784; 3.0021] <.0001	
No	13 / 41 (31.7)	NE [9.6; NE]	8 / 40 (20.0)	NE [NE; NE]	1.5446 [0.6503; 3.9056] 0.3282	
Prior Taxane Use In The Non-Metastatic Setting						0.0236
Yes	55 / 177 (31.1)	NE [NE; NE]	35 / 172 (20.3)	NE [NE; NE]	1.4729 [0.9662; 2.2746] 0.0741	
No	82 / 257 (31.9)	NE [23.5; NE]	27 / 245 (11.0)	NE [NE; NE]	2.8627 [1.8776; 4.5056] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.8411
1	21 / 65 (32.3)	NE [11.1; NE]	14 / 79 (17.7)	NE [NE; NE]	1.8883 [0.9624; 3.8146] 0.0644	
2	93 / 293 (31.7)	NE [NE; NE]	38 / 281 (13.5)	NE [NE; NE]	2.2273 [1.5382; 3.2897] <.0001	
>=3	23 / 75 (30.7)	NE [NE; NE]	10 / 56 (17.9)	NE [NE; NE]	1.7927 [0.8772; 3.9442] 0.1188	
ER/PR status I						0.8982
ER+, PR+	75 / 252 (29.8)	NE [NE; NE]	30 / 234 (12.8)	NE [NE; NE]	2.2338 [1.4775; 3.4647] 0.0001	
ER+, PR-	57 / 166 (34.3)	NE [23.5; NE]	28 / 171 (16.4)	NE [NE; NE]	2.0818 [1.3335; 3.3261] 0.0013	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7183
ER <=10%	4 / 21 (19.0)	NE [13.6; NE]	2 / 14 (14.3)	NE [2.6; NE]	0.8973 [0.1675; 6.6246] 0.9025	
ER >10%	112 / 362 (30.9)	NE [NE; NE]	47 / 343 (13.7)	NE [NE; NE]	2.1765 [1.5577; 3.0922] <.0001	
Positive	21 / 51 (41.2)	NE [0.9; NE]	13 / 60 (21.7)	NE [NE; NE]	2.1728 [1.1000; 4.4576] 0.0253	
Endocrine Resistance						0.9929
Primary	44 / 127 (34.6)	NE [NE; NE]	23 / 137 (16.8)	NE [NE; NE]	2.1439 [1.3063; 3.6137] 0.0026	
Secondary	93 / 307 (30.3)	NE [NE; NE]	39 / 279 (14.0)	NE [NE; NE]	2.0742 [1.4379; 3.0519] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0726
Capecitabine	99 / 265 (37.4)	NE [23.5; NE]	41 / 249 (16.5)	NE [NE; NE]	2.3378 [1.6366; 3.4010] <.0001	
Nab-Paclitaxel	21 / 103 (20.4)	NE [NE; NE]	17 / 101 (16.8)	NE [NE; NE]	1.0999 [0.5797; 2.1181] 0.7693	
Paclitaxel	17 / 66 (25.8)	NE [NE; NE]	4 / 67 (6.0)	NE [NE; NE]	4.1511 [1.5205; 14.5068] 0.0060	
Prior anthracycline use						0.0335
Yes	61 / 197 (31.0)	NE [NE; NE]	38 / 198 (19.2)	NE [NE; NE]	1.5628 [1.0452; 2.3661] 0.0306	
No	76 / 237 (32.1)	NE [23.5; NE]	24 / 219 (11.0)	NE [NE; NE]	2.9155 [1.8707; 4.7130] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.3008
Yes	93 / 294 (31.6)	NE [NE; NE]	45 / 275 (16.4)	NE [NE; NE]	1.8622 [1.3107; 2.6852] 0.0006	
No	44 / 140 (31.4)	NE [NE; NE]	17 / 142 (12.0)	NE [NE; NE]	2.6201 [1.5244; 4.7170] 0.0005	
ECOG						0.1458
0	86 / 251 (34.3)	NE [NE; NE]	34 / 246 (13.8)	NE [NE; NE]	2.5463 [1.7276; 3.8393] <.0001	
>=1	50 / 178 (28.1)	NE [NE; NE]	27 / 163 (16.6)	NE [NE; NE]	1.5278 [0.9615; 2.4802] 0.0766	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Dyspepsia						
Age at randomization						0.4821
<65 years of age	33 / 301 (11.0)	NE [NE; NE]	14 / 285 (4.9)	NE [NE; NE]	1.8383 [0.9989; 3.5650] 0.0549	
>=65 years of age	17 / 133 (12.8)	NE [NE; NE]	6 / 132 (4.5)	NE [20.6; NE]	2.7143 [1.1263; 7.5286] 0.0288	
Race						0.0171
Asian	7 / 153 (4.6)	NE [NE; NE]	9 / 147 (6.1)	NE [NE; NE]	0.6639 [0.2366; 1.7865] 0.4144	
White	41 / 231 (17.7)	NE [NE; NE]	10 / 223 (4.5)	NE [NE; NE]	3.5711 [1.8604; 7.5562] 0.0001	
Other	2 / 50 (4.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	1.2054 [0.1036; 27.2290] 0.8832	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1167
Asia	8 / 148 (5.4)	NE [NE; NE]	8 / 144 (5.6)	NE [NE; NE]	0.8419 [0.3082; 2.2987] 0.7318	
Europe	33 / 227 (14.5)	NE [NE; NE]	9 / 206 (4.4)	NE [NE; NE]	2.8939 [1.4411; 6.4475] 0.0032	
Rest of the World	9 / 59 (15.3)	NE [NE; NE]	3 / 67 (4.5)	NE [20.6; NE]	2.8367 [0.8330; 12.9017] 0.1066	
HER2 IHC expression						0.6552
IHC 1+	24 / 239 (10.0)	NE [NE; NE]	12 / 226 (5.3)	NE [NE; NE]	1.6648 [0.8457; 3.4565] 0.1478	
IHC 2+/ISH-	17 / 116 (14.7)	NE [NE; NE]	5 / 115 (4.3)	NE [NE; NE]	2.7697 [1.0858; 8.4741] 0.0385	
IHC >0 <1+	9 / 76 (11.8)	NE [NE; NE]	3 / 74 (4.1)	NE [NE; NE]	2.6068 [0.7760; 11.7642] 0.1360	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0240
Yes	50 / 393 (12.7)	NE [NE; NE]	18 / 377 (4.8)	NE [NE; NE]	2.3021 [1.3656; 4.0608] 0.0019	
No	0 / 41 (0.0)	NE [NE; NE]	2 / 40 (5.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.5199
Yes	19 / 177 (10.7)	NE [NE; NE]	6 / 172 (3.5)	NE [NE; NE]	2.5997 [1.0912; 7.1717] 0.0356	
No	31 / 257 (12.1)	NE [NE; NE]	14 / 245 (5.7)	NE [NE; NE]	1.8511 [1.0019; 3.5970] 0.0532	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1131
1	3 / 65 (4.6)	NE [NE; NE]	5 / 79 (6.3)	NE [NE; NE]	0.6190 [0.1264; 2.5365] 0.5090	
2	38 / 293 (13.0)	NE [NE; NE]	14 / 281 (5.0)	NE [NE; NE]	2.2211 [1.2284; 4.2540] 0.0092	
>=3	9 / 75 (12.0)	NE [NE; NE]	1 / 56 (1.8)	NE [NE; NE]	6.3174 [1.1833; 116.5747] 0.0448	
ER/PR status I						0.0632
ER+, PR+	25 / 252 (9.9)	NE [NE; NE]	5 / 234 (2.1)	NE [NE; NE]	3.8379 [1.5918; 11.3968] 0.0032	
ER+, PR-	21 / 166 (12.7)	NE [NE; NE]	14 / 171 (8.2)	NE [NE; NE]	1.3708 [0.6998; 2.7672] 0.3631	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3199
ER <=10%	2 / 21 (9.5)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	43 / 362 (11.9)	NE [NE; NE]	15 / 343 (4.4)	NE [NE; NE]	2.3204 [1.3153; 4.3266] 0.0041	
Positive	5 / 51 (9.8)	NE [NE; NE]	5 / 60 (8.3)	NE [NE; NE]	1.1042 [0.3064; 3.9774] 0.8759	
Endocrine Resistance						0.8150
Primary	10 / 127 (7.9)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	1.8151 [0.6384; 5.8699] 0.2736	
Secondary	40 / 307 (13.0)	NE [NE; NE]	15 / 279 (5.4)	NE [NE; NE]	2.1282 [1.1993; 3.9834] 0.0110	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3553
Capecitabine	34 / 265 (12.8)	NE [NE; NE]	10 / 249 (4.0)	NE [NE; NE]	2.8020 [1.4343; 5.9949] 0.0029	
Nab-Paclitaxel	9 / 103 (8.7)	NE [NE; NE]	6 / 101 (5.9)	NE [NE; NE]	1.4492 [0.5224; 4.3241] 0.4798	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	4 / 67 (6.0)	NE [NE; NE]	1.4831 [0.4399; 5.7282] 0.5328	
Prior anthracycline use						0.7124
Yes	24 / 197 (12.2)	NE [NE; NE]	9 / 198 (4.5)	NE [NE; NE]	2.3377 [1.1203; 5.3319] 0.0262	
No	26 / 237 (11.0)	NE [NE; NE]	11 / 219 (5.0)	NE [NE; NE]	1.8925 [0.9571; 4.0049] 0.0727	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5168
Yes	35 / 294 (11.9)	NE [NE; NE]	15 / 275 (5.5)	NE [NE; NE]	1.8250 [1.0126; 3.4541] 0.0494	
No	15 / 140 (10.7)	NE [NE; NE]	5 / 142 (3.5)	NE [NE; NE]	2.8006 [1.0814; 8.6294] 0.0379	
ECOG						0.5221
0	34 / 251 (13.5)	NE [NE; NE]	15 / 246 (6.1)	NE [NE; NE]	1.9705 [1.0917; 3.7327] 0.0264	
>=1	15 / 178 (8.4)	NE [NE; NE]	4 / 163 (2.5)	NE [NE; NE]	2.8861 [1.0385; 10.1764] 0.0504	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Age at randomization						0.3120
<65 years of age	13 / 301 (4.3)	NE [NE; NE]	1 / 285 (0.4)	NE [NE; NE]	9.5471 [1.8873; 173.7806] 0.0081	
>=65 years of age	2 / 133 (1.5)	NE [NE; NE]	1 / 132 (0.8)	NE [NE; NE]	1.6870 [0.1613; 36.3269] 0.6661	
Race						0.8910
Asian	6 / 153 (3.9)	NE [NE; NE]	1 / 147 (0.7)	NE [NE; NE]	5.0906 [0.8662; 96.3197] 0.0939	
White	8 / 231 (3.5)	NE [NE; NE]	1 / 223 (0.4)	NE [NE; NE]	5.8833 [1.0724; 109.3627] 0.0587	
Other	1 / 50 (2.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4737
Asia	7 / 148 (4.7)	NE [NE; NE]	1 / 144 (0.7)	NE [NE; NE]	6.1252 [1.0863; 114.6151] 0.0532	
Europe	5 / 227 (2.2)	NE [NE; NE]	0 / 206 (0.0)	NE [NE; NE]	NE [NE; NE]	
Rest of the World	3 / 59 (5.1)	NE [NE; NE]	1 / 67 (1.5)	NE [NE; NE]	2.6242 [0.3348; 53.1244] 0.3861	
HER2 IHC expression						0.3202
IHC 1+	8 / 239 (3.3)	NE [NE; NE]	2 / 226 (0.9)	NE [NE; NE]	3.1746 [0.7929; 21.0683] 0.1235	
IHC 2+/ISH-	3 / 116 (2.6)	NE [NE; NE]	0 / 115 (0.0)	NE [NE; NE]	NE [NE; NE]	
IHC >0 <1+	4 / 76 (5.3)	NE [NE; NE]	0 / 74 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2913
Yes	13 / 393 (3.3)	NE [NE; NE]	1 / 377 (0.3)	NE [NE; NE]	9.8832 [1.9565; 179.8234] 0.0068	
No	2 / 41 (4.9)	NE [NE; NE]	1 / 40 (2.5)	NE [NE; NE]	1.7237 [0.1650; 37.0936] 0.6528	
Prior Taxane Use In The Non-Metastatic Setting						0.7851
Yes	6 / 177 (3.4)	NE [NE; NE]	1 / 172 (0.6)	NE [NE; NE]	4.7620 [0.8043; 90.3074] 0.1125	
No	9 / 257 (3.5)	NE [NE; NE]	1 / 245 (0.4)	NE [NE; NE]	6.7561 [1.2630; 124.7587] 0.0363	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3939
1	4 / 65 (6.2)	NE [NE; NE]	0 / 79 (0.0)	NE [NE; NE]	NE [NE; NE]	
2	10 / 293 (3.4)	NE [NE; NE]	2 / 281 (0.7)	NE [NE; NE]	3.6041 [0.9428; 23.5379] 0.0782	
>=3	1 / 75 (1.3)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.8605
ER+, PR+	9 / 252 (3.6)	NE [NE; NE]	1 / 234 (0.4)	NE [NE; NE]	6.4082 [1.2006; 118.2475] 0.0431	
ER+, PR-	6 / 166 (3.6)	NE [NE; NE]	1 / 171 (0.6)	NE [NE; NE]	4.8713 [0.8184; 92.5771] 0.1076	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7153
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	13 / 362 (3.6)	NE [NE; NE]	2 / 343 (0.6)	NE [NE; NE]	5.0027 [1.3762; 32.0821] 0.0189	
Positive	2 / 51 (3.9)	NE [NE; NE]	0 / 60 (0.0)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						0.0772
Primary	8 / 127 (6.3)	NE [NE; NE]	0 / 137 (0.0)	NE [NE; NE]	NE [NE; NE]	
Secondary	7 / 307 (2.3)	NE [NE; NE]	2 / 279 (0.7)	NE [NE; NE]	2.5013 [0.6018; 16.8267] 0.2378	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.4750
Capecitabine	10 / 265 (3.8)	NE [NE; NE]	1 / 249 (0.4)	NE [NE; NE]	7.3891 [1.4091; 135.7415] 0.0255	
Nab-Paclitaxel	2 / 103 (1.9)	NE [NE; NE]	1 / 101 (1.0)	NE [NE; NE]	1.9286 [0.1848; 41.4756] 0.5850	
Paclitaxel	3 / 66 (4.5)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.6739
Yes	5 / 197 (2.5)	NE [NE; NE]	1 / 198 (0.5)	NE [NE; NE]	4.0396 [0.6429; 77.7314] 0.1701	
No	10 / 237 (4.2)	NE [NE; NE]	1 / 219 (0.5)	NE [NE; NE]	7.3093 [1.3930; 134.3019] 0.0266	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.2581
Yes	11 / 294 (3.7)	NE [NE; NE]	2 / 275 (0.7)	NE [NE; NE]	4.0548 [1.0803; 26.3065] 0.0498	
No	4 / 140 (2.9)	NE [NE; NE]	0 / 142 (0.0)	NE [NE; NE]	NE [NE; NE]	
ECOG						0.7483
0	9 / 251 (3.6)	NE [NE; NE]	1 / 246 (0.4)	NE [NE; NE]	7.3082 [1.3657; 134.9655] 0.0275	
>=1	6 / 178 (3.4)	NE [NE; NE]	1 / 163 (0.6)	NE [NE; NE]	4.0630 [0.6861; 77.0637] 0.1618	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: All (any PT)						
Age at randomization						0.1010
<65 years of age	208 / 301 (69.1)	2.8 [2.1; 4.9]	100 / 285 (35.1)	23.5 [16.8; NE]	2.0777 [1.6398; 2.6513] <.0001	
>=65 years of age	73 / 133 (54.9)	7.4 [4.2; 15.0]	51 / 132 (38.6)	23.3 [9.6; NE]	1.4412 [1.0088; 2.0740] 0.0454	
Race						0.0559
Asian	125 / 153 (81.7)	0.7 [0.5; 1.4]	81 / 147 (55.1)	3.7 [1.8; 11.0]	1.7022 [1.2886; 2.2608] 0.0002	
White	130 / 231 (56.3)	6.5 [4.9; 10.4]	65 / 223 (29.1)	23.3 [16.8; NE]	1.9285 [1.4368; 2.6149] <.0001	
Other	26 / 50 (52.0)	9.9 [2.6; NE]	5 / 47 (10.6)	NE [NE; NE]	5.4295 [2.2559; 16.1096] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0895
Asia	121 / 148 (81.8)	0.7 [0.5; 2.1]	81 / 144 (56.3)	3.7 [1.8; 11.0]	1.6627 [1.2563; 2.2120] 0.0004	
Europe	133 / 227 (58.6)	5.5 [4.5; 9.6]	49 / 206 (23.8)	NE [16.8; NE]	2.4889 [1.8064; 3.4863] <.0001	
Rest of the World	27 / 59 (45.8)	12.4 [5.6; NE]	21 / 67 (31.3)	23.3 [9.2; NE]	1.5086 [0.8482; 2.7291] 0.1635	
HER2 IHC expression						0.1823
IHC 1+	157 / 239 (65.7)	3.6 [2.3; 5.5]	92 / 226 (40.7)	13.1 [7.3; NE]	1.6517 [1.2793; 2.1449] 0.0001	
IHC 2+/ISH-	69 / 116 (59.5)	6.4 [2.8; 11.2]	36 / 115 (31.3)	NE [11.3; NE]	1.8244 [1.2263; 2.7609] 0.0033	
IHC >0 <1+	53 / 76 (69.7)	2.8 [0.7; 5.6]	23 / 74 (31.1)	23.3 [16.8; NE]	3.0855 [1.8736; 5.2886] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3095
Yes	252 / 393 (64.1)	4.5 [2.8; 5.5]	130 / 377 (34.5)	23.5 [14.0; NE]	1.9331 [1.5672; 2.3962] <.0001	
No	29 / 41 (70.7)	2.8 [0.8; 12.4]	21 / 40 (52.5)	9.2 [0.6; NE]	1.4790 [0.8403; 2.6556] 0.1724	
Prior Taxane Use In The Non-Metastatic Setting						0.4138
Yes	120 / 177 (67.8)	2.6 [1.3; 4.4]	63 / 172 (36.6)	NE [9.3; NE]	2.0726 [1.5338; 2.8282] <.0001	
No	161 / 257 (62.6)	5.2 [3.5; 6.9]	88 / 245 (35.9)	23.3 [11.3; 23.7]	1.7284 [1.3360; 2.2510] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.9919
1	42 / 65 (64.6)	2.6 [0.8; 5.5]	31 / 79 (39.2)	NE [4.8; NE]	1.8967 [1.1935; 3.0463] 0.0063	
2	185 / 293 (63.1)	4.9 [2.8; 7.4]	98 / 281 (34.9)	23.3 [11.3; 26.2]	1.8376 [1.4416; 2.3572] <.0001	
>=3	53 / 75 (70.7)	3.3 [2.1; 5.7]	22 / 56 (39.3)	23.5 [5.5; NE]	1.9158 [1.1794; 3.2208] 0.0089	
ER/PR status I						0.9314
ER+, PR+	161 / 252 (63.9)	4.8 [2.8; 5.7]	82 / 234 (35.0)	23.3 [23.3; 26.2]	1.8689 [1.4371; 2.4497] <.0001	
ER+, PR-	113 / 166 (68.1)	2.8 [1.4; 4.9]	68 / 171 (39.8)	11.3 [8.3; NE]	1.8190 [1.3465; 2.4749] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2298
ER <=10%	12 / 21 (57.1)	5.5 [0.5; NE]	5 / 14 (35.7)	NE [0.4; NE]	1.4196 [0.5197; 4.5005] 0.5143	
ER >10%	238 / 362 (65.7)	3.7 [2.7; 5.2]	119 / 343 (34.7)	23.3 [14.0; 26.2]	2.0158 [1.6211; 2.5206] <.0001	
Positive	31 / 51 (60.8)	5.1 [2.1; 12.4]	27 / 60 (45.0)	9.3 [2.6; NE]	1.2490 [0.7449; 2.1066] 0.3961	
Endocrine Resistance						0.3134
Primary	81 / 127 (63.8)	2.8 [0.8; 5.7]	55 / 137 (40.1)	NE [5.3; NE]	1.6473 [1.1718; 2.3329] 0.0040	
Secondary	200 / 307 (65.1)	4.8 [2.8; 5.6]	96 / 279 (34.4)	23.3 [13.1; 26.2]	1.9943 [1.5680; 2.5547] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0109
Capecitabine	174 / 265 (65.7)	4.2 [2.7; 5.5]	77 / 249 (30.9)	23.3 [14.0; 26.2]	2.4287 [1.8647; 3.1944] <.0001	
Nab-Paclitaxel	72 / 103 (69.9)	2.6 [0.6; 4.9]	50 / 101 (49.5)	7.7 [0.9; NE]	1.4526 [1.0144; 2.0962] 0.0412	
Paclitaxel	35 / 66 (53.0)	7.6 [5.1; NE]	24 / 67 (35.8)	NE [3.6; NE]	1.0801 [0.6347; 1.8639] 0.7751	
Prior anthracycline use						0.5420
Yes	126 / 197 (64.0)	3.1 [2.0; 5.7]	75 / 198 (37.9)	16.8 [8.3; NE]	1.7676 [1.3313; 2.3632] 0.0001	
No	155 / 237 (65.4)	4.9 [2.8; 5.6]	76 / 219 (34.7)	23.3 [13.1; 26.2]	1.9742 [1.5052; 2.6121] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.1942
Yes	190 / 294 (64.6)	3.7 [2.7; 5.5]	93 / 275 (33.8)	26.2 [11.3; NE]	2.0524 [1.6061; 2.6420] <.0001	
No	91 / 140 (65.0)	4.9 [2.3; 8.3]	58 / 142 (40.8)	23.3 [7.6; 23.7]	1.5562 [1.1216; 2.1761] 0.0078	
ECOG						0.2589
0	161 / 251 (64.1)	3.7 [2.3; 6.9]	84 / 246 (34.1)	23.3 [14.0; 26.2]	2.0302 [1.5634; 2.6557] <.0001	
>=1	116 / 178 (65.2)	4.2 [2.7; 5.5]	65 / 163 (39.9)	NE [5.6; NE]	1.6030 [1.1872; 2.1834] 0.0022	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Age at randomization						0.7703
<65 years of age	90 / 301 (29.9)	NE [27.7; NE]	34 / 285 (11.9)	NE [NE; NE]	2.3101 [1.5695; 3.4798] <.0001	
>=65 years of age	27 / 133 (20.3)	NE [22.6; NE]	10 / 132 (7.6)	NE [NE; NE]	2.5299 [1.2634; 5.4954] 0.0095	
Race						0.0065
Asian	54 / 153 (35.3)	NE [NE; NE]	28 / 147 (19.0)	NE [NE; NE]	1.8618 [1.1897; 2.9791] 0.0068	
White	49 / 231 (21.2)	NE [22.6; NE]	16 / 223 (7.2)	NE [NE; NE]	2.5781 [1.4948; 4.6900] 0.0007	
Other	14 / 50 (28.0)	NE [19.8; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0108
Asia	52 / 148 (35.1)	NE [NE; NE]	27 / 144 (18.8)	NE [NE; NE]	1.8799 [1.1915; 3.0352] 0.0069	
Europe	60 / 227 (26.4)	27.7 [22.6; NE]	11 / 206 (5.3)	NE [NE; NE]	4.3955 [2.4010; 8.8517] <.0001	
Rest of the World	5 / 59 (8.5)	NE [20.5; NE]	6 / 67 (9.0)	NE [NE; NE]	0.8187 [0.2348; 2.7310] 0.7419	
HER2 IHC expression						0.3783
IHC 1+	66 / 239 (27.6)	NE [22.6; NE]	30 / 226 (13.3)	NE [NE; NE]	1.9504 [1.2777; 3.0484] 0.0021	
IHC 2+/ISH-	28 / 116 (24.1)	NE [27.7; NE]	9 / 115 (7.8)	NE [NE; NE]	2.6626 [1.2980; 6.0111] 0.0086	
IHC >0 <1+	21 / 76 (27.6)	NE [NE; NE]	5 / 74 (6.8)	NE [NE; NE]	4.0409 [1.6451; 12.1132] 0.0024	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3876
Yes	105 / 393 (26.7)	NE [27.7; NE]	37 / 377 (9.8)	NE [NE; NE]	2.5040 [1.7361; 3.6926] <.0001	
No	12 / 41 (29.3)	NE [20.5; NE]	7 / 40 (17.5)	NE [NE; NE]	1.6422 [0.6583; 4.4240] 0.2924	
Prior Taxane Use In The Non-Metastatic Setting						0.8526
Yes	58 / 177 (32.8)	NE [19.8; NE]	23 / 172 (13.4)	NE [NE; NE]	2.2891 [1.4301; 3.7890] 0.0006	
No	59 / 257 (23.0)	NE [27.7; NE]	21 / 245 (8.6)	NE [NE; NE]	2.4841 [1.5320; 4.1881] 0.0002	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.7940
1	18 / 65 (27.7)	NE [19.8; NE]	11 / 79 (13.9)	NE [NE; NE]	2.0590 [0.9846; 4.5063] 0.0549	
2	86 / 293 (29.4)	27.7 [22.6; NE]	30 / 281 (10.7)	NE [NE; NE]	2.5147 [1.6774; 3.8757] <.0001	
>=3	12 / 75 (16.0)	NE [NE; NE]	3 / 56 (5.4)	NE [NE; NE]	2.8486 [0.9041; 12.5069] 0.0903	
ER/PR status I						0.2725
ER+, PR+	63 / 252 (25.0)	27.7 [22.6; NE]	26 / 234 (11.1)	NE [NE; NE]	1.9325 [1.2367; 3.1102] 0.0042	
ER+, PR-	53 / 166 (31.9)	NE [NE; NE]	18 / 171 (10.5)	NE [NE; NE]	3.1838 [1.9021; 5.5867] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5522
ER <=10%	5 / 21 (23.8)	NE [NE; NE]	2 / 14 (14.3)	NE [NE; NE]	1.3623 [0.2925; 9.5333] 0.7112	
ER >10%	105 / 362 (29.0)	NE [27.7; NE]	37 / 343 (10.8)	NE [NE; NE]	2.4962 [1.7303; 3.6820] <.0001	
Positive	7 / 51 (13.7)	NE [NE; NE]	5 / 60 (8.3)	NE [NE; NE]	1.6037 [0.5119; 5.4184] 0.4143	
Endocrine Resistance						0.0719
Primary	36 / 127 (28.3)	NE [NE; NE]	22 / 137 (16.1)	NE [NE; NE]	1.7476 [1.0349; 3.0183] 0.0375	
Secondary	81 / 307 (26.4)	NE [27.7; NE]	22 / 279 (7.9)	NE [NE; NE]	3.0648 [1.9469; 5.0335] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.2156
Capecitabine	65 / 265 (24.5)	NE [NE; NE]	18 / 249 (7.2)	NE [NE; NE]	3.2204 [1.9526; 5.5928] <.0001	
Nab-Paclitaxel	36 / 103 (35.0)	NE [12.3; NE]	21 / 101 (20.8)	NE [NE; NE]	1.6477 [0.9688; 2.8739] 0.0667	
Paclitaxel	16 / 66 (24.2)	27.7 [19.8; NE]	5 / 67 (7.5)	NE [NE; NE]	2.3930 [0.9021; 7.4692] 0.0873	
Prior anthracycline use						0.6371
Yes	57 / 197 (28.9)	NE [20.5; NE]	24 / 198 (12.1)	NE [NE; NE]	2.1532 [1.3513; 3.5409] 0.0013	
No	60 / 237 (25.3)	NE [27.7; NE]	20 / 219 (9.1)	NE [NE; NE]	2.6314 [1.6131; 4.4791] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.4636
Yes	82 / 294 (27.9)	NE [27.7; NE]	27 / 275 (9.8)	NE [NE; NE]	2.5545 [1.6730; 4.0251] <.0001	
No	35 / 140 (25.0)	NE [22.6; NE]	17 / 142 (12.0)	NE [NE; NE]	2.0529 [1.1666; 3.7569] 0.0131	
ECOG						0.9663
0	66 / 251 (26.3)	NE [22.6; NE]	26 / 246 (10.6)	NE [NE; NE]	2.3809 [1.5303; 3.8166] 0.0001	
>=1	49 / 178 (27.5)	NE [27.7; NE]	17 / 163 (10.4)	NE [NE; NE]	2.3925 [1.4033; 4.2835] 0.0015	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Alanine aminotransferase increased						
Age at randomization						0.7970
<65 years of age	77 / 301 (25.6)	NE [NE; NE]	40 / 285 (14.0)	NE [NE; NE]	1.7157 [1.1769; 2.5399] 0.0053	
>=65 years of age	16 / 133 (12.0)	NE [NE; NE]	8 / 132 (6.1)	NE [NE; NE]	1.9020 [0.8358; 4.6955] 0.1315	
Race						0.0077
Asian	50 / 153 (32.7)	NE [NE; NE]	34 / 147 (23.1)	NE [NE; NE]	1.3981 [0.9077; 2.1793] 0.1307	
White	33 / 231 (14.3)	NE [NE; NE]	14 / 223 (6.3)	NE [NE; NE]	2.0648 [1.1268; 3.9916] 0.0206	
Other	10 / 50 (20.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1339
Asia	48 / 148 (32.4)	NE [NE; NE]	33 / 144 (22.9)	NE [NE; NE]	1.4047 [0.9051; 2.2065] 0.1316	
Europe	37 / 227 (16.3)	NE [NE; NE]	10 / 206 (4.9)	NE [NE; NE]	3.0431 [1.5690; 6.4816] 0.0011	
Rest of the World	8 / 59 (13.6)	NE [NE; NE]	5 / 67 (7.5)	NE [NE; NE]	1.7171 [0.5725; 5.6854] 0.3389	
HER2 IHC expression						0.1461
IHC 1+	50 / 239 (20.9)	NE [NE; NE]	33 / 226 (14.6)	NE [NE; NE]	1.3879 [0.8978; 2.1741] 0.1434	
IHC 2+/ISH-	24 / 116 (20.7)	NE [NE; NE]	10 / 115 (8.7)	NE [NE; NE]	2.0969 [1.0280; 4.6123] 0.0454	
IHC >0 <1+	19 / 76 (25.0)	NE [NE; NE]	5 / 74 (6.8)	NE [NE; NE]	3.6448 [1.4643; 11.0008] 0.0060	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8523
Yes	83 / 393 (21.1)	NE [NE; NE]	42 / 377 (11.1)	NE [NE; NE]	1.7845 [1.2379; 2.6118] 0.0020	
No	10 / 41 (24.4)	NE [NE; NE]	6 / 40 (15.0)	NE [NE; NE]	1.6258 [0.6032; 4.7818] 0.3415	
Prior Taxane Use In The Non-Metastatic Setting						0.6066
Yes	46 / 177 (26.0)	NE [NE; NE]	26 / 172 (15.1)	NE [NE; NE]	1.5955 [0.9927; 2.6196] 0.0553	
No	47 / 257 (18.3)	NE [NE; NE]	22 / 245 (9.0)	NE [NE; NE]	1.9769 [1.2060; 3.3439] 0.0073	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1204
1	12 / 65 (18.5)	NE [NE; NE]	12 / 79 (15.2)	NE [NE; NE]	1.1868 [0.5255; 2.6792] 0.6771	
2	71 / 293 (24.2)	NE [NE; NE]	29 / 281 (10.3)	NE [NE; NE]	2.2929 [1.5043; 3.5874] 0.0001	
>=3	9 / 75 (12.0)	NE [NE; NE]	7 / 56 (12.5)	NE [NE; NE]	0.8591 [0.3199; 2.4051] 0.7685	
ER/PR status I						0.1715
ER+, PR+	49 / 252 (19.4)	NE [NE; NE]	29 / 234 (12.4)	NE [NE; NE]	1.4250 [0.9053; 2.2837] 0.1311	
ER+, PR-	43 / 166 (25.9)	NE [NE; NE]	19 / 171 (11.1)	NE [NE; NE]	2.3622 [1.3969; 4.1505] 0.0013	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4161
ER <=10%	4 / 21 (19.0)	NE [NE; NE]	2 / 14 (14.3)	NE [5.6; NE]	1.1152 [0.2161; 8.0816] 0.9002	
ER >10%	83 / 362 (22.9)	NE [NE; NE]	39 / 343 (11.4)	NE [NE; NE]	1.9386 [1.3340; 2.8677] 0.0005	
Positive	6 / 51 (11.8)	NE [NE; NE]	7 / 60 (11.7)	NE [NE; NE]	0.9385 [0.3017; 2.8284] 0.9079	
Endocrine Resistance						0.0236
Primary	26 / 127 (20.5)	NE [NE; NE]	24 / 137 (17.5)	NE [NE; NE]	1.0620 [0.6069; 1.8658] 0.8310	
Secondary	67 / 307 (21.8)	NE [NE; NE]	24 / 279 (8.6)	NE [NE; NE]	2.4660 [1.5692; 4.0106] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0899
Capecitabine	54 / 265 (20.4)	NE [NE; NE]	19 / 249 (7.6)	NE [NE; NE]	2.6026 [1.5708; 4.5052] 0.0002	
Nab-Paclitaxel	29 / 103 (28.2)	NE [20.3; NE]	24 / 101 (23.8)	NE [NE; NE]	1.1229 [0.6533; 1.9487] 0.6677	
Paclitaxel	10 / 66 (15.2)	NE [NE; NE]	5 / 67 (7.5)	NE [NE; NE]	1.8347 [0.6457; 5.9258] 0.2603	
Prior anthracycline use						0.4246
Yes	43 / 197 (21.8)	NE [NE; NE]	26 / 198 (13.1)	NE [NE; NE]	1.5140 [0.9351; 2.4992] 0.0940	
No	50 / 237 (21.1)	NE [NE; NE]	22 / 219 (10.0)	NE [NE; NE]	2.0682 [1.2694; 3.4841] 0.0038	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.2475
Yes	65 / 294 (22.1)	NE [NE; NE]	28 / 275 (10.2)	NE [NE; NE]	2.0134 [1.3055; 3.1888] 0.0017	
No	28 / 140 (20.0)	NE [NE; NE]	20 / 142 (14.1)	NE [NE; NE]	1.4029 [0.7943; 2.5239] 0.2444	
ECOG						0.8763
0	57 / 251 (22.7)	NE [NE; NE]	30 / 246 (12.2)	NE [NE; NE]	1.8148 [1.1752; 2.8601] 0.0076	
>=1	36 / 178 (20.2)	NE [NE; NE]	18 / 163 (11.0)	NE [NE; NE]	1.6856 [0.9686; 3.0399] 0.0682	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Platelet count decreased						
Age at randomization						0.8910
<65 years of age	49 / 301 (16.3)	NE [NE; NE]	12 / 285 (4.2)	NE [26.2; NE]	3.3571 [1.8404; 6.6345] 0.0001	
>=65 years of age	12 / 133 (9.0)	NE [NE; NE]	3 / 132 (2.3)	NE [NE; NE]	3.6382 [1.1511; 16.0022] 0.0332	
Race						0.1073
Asian	48 / 153 (31.4)	NE [21.5; NE]	9 / 147 (6.1)	NE [NE; NE]	5.3154 [2.7391; 11.5968] <.0001	
White	11 / 231 (4.8)	NE [NE; NE]	6 / 223 (2.7)	NE [26.2; NE]	1.3218 [0.4957; 3.8798] 0.5875	
Other	2 / 50 (4.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2593
Asia	49 / 148 (33.1)	NE [21.5; NE]	10 / 144 (6.9)	NE [26.2; NE]	4.9596 [2.6224; 10.3968] <.0001	
Europe	10 / 227 (4.4)	NE [NE; NE]	3 / 206 (1.5)	NE [NE; NE]	2.3313 [0.7025; 10.4902] 0.1906	
Rest of the World	2 / 59 (3.4)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	0.6766 [0.0776; 5.8844] 0.7025	
HER2 IHC expression						0.4485
IHC 1+	35 / 239 (14.6)	NE [NE; NE]	7 / 226 (3.1)	NE [NE; NE]	4.2377 [1.9952; 10.4334] 0.0002	
IHC 2+/ISH-	15 / 116 (12.9)	NE [NE; NE]	6 / 115 (5.2)	NE [NE; NE]	2.2024 [0.8878; 6.2102] 0.0982	
IHC >0 <1+	11 / 76 (14.5)	NE [21.5; NE]	2 / 74 (2.7)	26.2 [26.2; NE]	4.9715 [1.3288; 32.2046] 0.0211	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4399
Yes	49 / 393 (12.5)	NE [NE; NE]	13 / 377 (3.4)	NE [26.2; NE]	3.1995 [1.7853; 6.1634] 0.0001	
No	12 / 41 (29.3)	NE [17.1; NE]	2 / 40 (5.0)	NE [NE; NE]	5.4040 [1.4601; 34.8868] 0.0140	
Prior Taxane Use In The Non-Metastatic Setting						0.7807
Yes	34 / 177 (19.2)	NE [NE; NE]	8 / 172 (4.7)	NE [NE; NE]	3.8896 [1.8898; 9.0558] 0.0002	
No	27 / 257 (10.5)	NE [NE; NE]	7 / 245 (2.9)	NE [26.2; NE]	3.0707 [1.4053; 7.6867] 0.0057	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.7748
1	5 / 65 (7.7)	NE [NE; NE]	2 / 79 (2.5)	NE [NE; NE]	3.0490 [0.6571; 21.2839] 0.1613	
2	45 / 293 (15.4)	NE [NE; NE]	10 / 281 (3.6)	NE [26.2; NE]	3.7182 [1.9485; 7.8398] 0.0001	
>=3	10 / 75 (13.3)	NE [NE; NE]	3 / 56 (5.4)	NE [NE; NE]	2.2787 [0.6942; 10.1861] 0.1997	
ER/PR status I						0.5155
ER+, PR+	29 / 252 (11.5)	NE [NE; NE]	8 / 234 (3.4)	NE [26.2; NE]	2.8596 [1.3643; 6.7322] 0.0064	
ER+, PR-	32 / 166 (19.3)	NE [NE; NE]	7 / 171 (4.1)	NE [NE; NE]	4.4786 [2.0923; 11.0752] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4122
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	1 / 14 (7.1)	NE [NE; NE]	0.6325 [0.0250; 15.9887] 0.7439	
ER >10%	53 / 362 (14.6)	NE [NE; NE]	12 / 343 (3.5)	NE [26.2; NE]	3.6591 [2.0193; 7.1999] <.0001	
Positive	7 / 51 (13.7)	NE [NE; NE]	2 / 60 (3.3)	NE [NE; NE]	3.8472 [0.9279; 25.8458] 0.0715	
Endocrine Resistance						0.6349
Primary	18 / 127 (14.2)	NE [NE; NE]	6 / 137 (4.4)	NE [NE; NE]	2.9788 [1.2436; 8.2390] 0.0157	
Secondary	43 / 307 (14.0)	NE [NE; NE]	9 / 279 (3.2)	NE [26.2; NE]	3.8081 [1.9412; 8.3641] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3743
Capecitabine	27 / 265 (10.2)	NE [NE; NE]	8 / 249 (3.2)	NE [26.2; NE]	2.8255 [1.3396; 6.6756] 0.0076	
Nab-Paclitaxel	30 / 103 (29.1)	NE [17.5; NE]	7 / 101 (6.9)	NE [NE; NE]	4.1784 [1.9402; 10.3686] 0.0002	
Paclitaxel	4 / 66 (6.1)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.9032
Yes	34 / 197 (17.3)	NE [NE; NE]	9 / 198 (4.5)	NE [NE; NE]	3.4807 [1.7376; 7.7434] 0.0004	
No	27 / 237 (11.4)	NE [NE; NE]	6 / 219 (2.7)	NE [26.2; NE]	3.5538 [1.5632; 9.5524] 0.0029	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.2037
Yes	44 / 294 (15.0)	NE [NE; NE]	8 / 275 (2.9)	NE [26.2; NE]	4.7963 [2.3814; 11.0251] <.0001	
No	17 / 140 (12.1)	NE [NE; NE]	7 / 142 (4.9)	NE [NE; NE]	1.9602 [0.8413; 5.0934] 0.1291	
ECOG						0.9435
0	30 / 251 (12.0)	NE [NE; NE]	7 / 246 (2.8)	NE [26.2; NE]	3.7965 [1.7618; 9.4248] 0.0007	
>=1	31 / 178 (17.4)	NE [NE; NE]	7 / 163 (4.3)	NE [NE; NE]	3.4887 [1.6191; 8.6626] 0.0016	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Blood alkaline phosphatase increased						
Age at randomization						0.2958
<65 years of age	33 / 301 (11.0)	NE [NE; NE]	13 / 285 (4.6)	NE [NE; NE]	1.7031 [0.9105; 3.3793] 0.1045	
>=65 years of age	15 / 133 (11.3)	NE [NE; NE]	4 / 132 (3.0)	NE [NE; NE]	3.3494 [1.2129; 11.7659] 0.0228	
Race						0.3611
Asian	20 / 153 (13.1)	NE [NE; NE]	6 / 147 (4.1)	NE [NE; NE]	2.6048 [1.1036; 7.1477] 0.0337	
White	25 / 231 (10.8)	NE [NE; NE]	11 / 223 (4.9)	NE [NE; NE]	1.7052 [0.8560; 3.6261] 0.1384	
Other	3 / 50 (6.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0824
Asia	19 / 148 (12.8)	NE [NE; NE]	6 / 144 (4.2)	NE [NE; NE]	2.5455 [1.0714; 7.0097] 0.0395	
Europe	26 / 227 (11.5)	NE [NE; NE]	6 / 206 (2.9)	NE [NE; NE]	2.8750 [1.2557; 7.7611] 0.0156	
Rest of the World	3 / 59 (5.1)	NE [NE; NE]	5 / 67 (7.5)	NE [NE; NE]	0.5073 [0.1021; 2.1113] 0.3513	
HER2 IHC expression						0.7112
IHC 1+	30 / 239 (12.6)	NE [NE; NE]	10 / 226 (4.4)	NE [NE; NE]	2.3076 [1.1614; 4.9908] 0.0194	
IHC 2+/ISH-	10 / 116 (8.6)	NE [NE; NE]	5 / 115 (4.3)	NE [NE; NE]	1.2422 [0.4343; 4.0387] 0.6957	
IHC >0 <1+	7 / 76 (9.2)	NE [22.0; NE]	2 / 74 (2.7)	NE [NE; NE]	2.9315 [0.7017; 19.7754] 0.1619	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5291
Yes	43 / 393 (10.9)	NE [NE; NE]	14 / 377 (3.7)	NE [NE; NE]	2.2859 [1.2780; 4.3471] 0.0061	
No	5 / 41 (12.2)	NE [NE; NE]	3 / 40 (7.5)	NE [NE; NE]	1.1897 [0.2872; 5.8700] 0.8138	
Prior Taxane Use In The Non-Metastatic Setting						0.2850
Yes	19 / 177 (10.7)	NE [NE; NE]	9 / 172 (5.2)	NE [NE; NE]	1.4444 [0.6635; 3.3839] 0.3677	
No	29 / 257 (11.3)	NE [NE; NE]	8 / 245 (3.3)	NE [NE; NE]	2.7776 [1.3261; 6.5360] 0.0079	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0841
1	7 / 65 (10.8)	NE [NE; NE]	5 / 79 (6.3)	NE [NE; NE]	1.4267 [0.4522; 4.8480] 0.5440	
2	33 / 293 (11.3)	NE [NE; NE]	12 / 281 (4.3)	NE [NE; NE]	1.9132 [1.0105; 3.8752] 0.0521	
>=3	8 / 75 (10.7)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.0894
ER+, PR+	31 / 252 (12.3)	NE [NE; NE]	7 / 234 (3.0)	NE [NE; NE]	3.2267 [1.5007; 8.0018] 0.0032	
ER+, PR-	16 / 166 (9.6)	NE [NE; NE]	10 / 171 (5.8)	NE [NE; NE]	1.2141 [0.5489; 2.8072] 0.6368	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4279
ER <=10%	2 / 21 (9.5)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	41 / 362 (11.3)	NE [NE; NE]	16 / 343 (4.7)	NE [NE; NE]	1.8063 [1.0289; 3.3298] 0.0438	
Positive	5 / 51 (9.8)	NE [NE; NE]	1 / 60 (1.7)	NE [NE; NE]	5.5067 [0.8867; 105.5406] 0.0799	
Endocrine Resistance						0.0156
Primary	14 / 127 (11.0)	NE [25.2; NE]	11 / 137 (8.0)	NE [NE; NE]	0.9850 [0.4363; 2.2627] 0.9700	
Secondary	34 / 307 (11.1)	NE [NE; NE]	6 / 279 (2.2)	NE [NE; NE]	4.0164 [1.8088; 10.6566] 0.0007	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.5134
Capecitabine	30 / 265 (11.3)	NE [NE; NE]	8 / 249 (3.2)	NE [NE; NE]	2.9473 [1.4142; 6.9136] 0.0045	
Nab-Paclitaxel	13 / 103 (12.6)	NE [25.2; NE]	7 / 101 (6.9)	NE [NE; NE]	1.3283 [0.5302; 3.5915] 0.5524	
Paclitaxel	5 / 66 (7.6)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	1.6334 [0.3386; 11.6625] 0.5620	
Prior anthracycline use						0.0120
Yes	20 / 197 (10.2)	NE [NE; NE]	13 / 198 (6.6)	NE [NE; NE]	1.1883 [0.5917; 2.4668] 0.6326	
No	28 / 237 (11.8)	NE [NE; NE]	4 / 219 (1.8)	NE [NE; NE]	4.9691 [1.9413; 16.8222] 0.0009	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5121
Yes	34 / 294 (11.6)	NE [NE; NE]	13 / 275 (4.7)	NE [NE; NE]	1.8348 [0.9867; 3.6261] 0.0612	
No	14 / 140 (10.0)	NE [NE; NE]	4 / 142 (2.8)	NE [NE; NE]	2.7349 [0.9729; 9.6987] 0.0664	
ECOG						0.0836
0	27 / 251 (10.8)	NE [NE; NE]	6 / 246 (2.4)	NE [NE; NE]	3.2190 [1.4148; 8.6580] 0.0065	
>=1	20 / 178 (11.2)	NE [NE; NE]	11 / 163 (6.7)	NE [NE; NE]	1.3789 [0.6694; 2.9925] 0.3928	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Gamma-glutamyltransferase increased						
Age at randomization						0.1304
<65 years of age	28 / 301 (9.3)	NE [NE; NE]	8 / 285 (2.8)	NE [NE; NE]	2.3872 [1.1277; 5.6576] 0.0273	
>=65 years of age	12 / 133 (9.0)	NE [NE; NE]	1 / 132 (0.8)	NE [NE; NE]	10.7079 [2.1069; 195.0862] 0.0044	
Race						0.3428
Asian	19 / 153 (12.4)	NE [NE; NE]	5 / 147 (3.4)	NE [NE; NE]	2.8014 [1.1180; 8.4917] 0.0337	
White	15 / 231 (6.5)	NE [NE; NE]	4 / 223 (1.8)	NE [NE; NE]	2.8688 [1.0335; 10.1106] 0.0516	
Other	6 / 50 (12.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7163
Asia	18 / 148 (12.2)	NE [NE; NE]	5 / 144 (3.5)	NE [NE; NE]	2.7467 [1.0887; 8.3551] 0.0384	
Europe	20 / 227 (8.8)	NE [NE; NE]	3 / 206 (1.5)	NE [NE; NE]	4.8567 [1.6542; 20.7044] 0.0050	
Rest of the World	2 / 59 (3.4)	NE [NE; NE]	1 / 67 (1.5)	NE [NE; NE]	1.6026 [0.1487; 35.0863] 0.7015	
HER2 IHC expression						0.1474
IHC 1+	24 / 239 (10.0)	NE [NE; NE]	7 / 226 (3.1)	NE [NE; NE]	2.5637 [1.1541; 6.4793] 0.0244	
IHC 2+/ISH-	8 / 116 (6.9)	NE [NE; NE]	2 / 115 (1.7)	NE [NE; NE]	2.9325 [0.7209; 19.6183] 0.1586	
IHC >0 <1+	8 / 76 (10.5)	NE [20.0; NE]	0 / 74 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3414
Yes	38 / 393 (9.7)	NE [NE; NE]	9 / 377 (2.4)	NE [NE; NE]	3.1002 [1.5606; 6.8639] 0.0014	
No	2 / 41 (4.9)	NE [NE; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.0420
Yes	17 / 177 (9.6)	NE [NE; NE]	7 / 172 (4.1)	NE [NE; NE]	1.7047 [0.7245; 4.4581] 0.2369	
No	23 / 257 (8.9)	NE [NE; NE]	2 / 245 (0.8)	NE [NE; NE]	8.8506 [2.6081; 55.2448] 0.0004	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.7100
1	7 / 65 (10.8)	NE [NE; NE]	1 / 79 (1.3)	NE [NE; NE]	7.2303 [1.2646; 135.8966] 0.0322	
2	28 / 293 (9.6)	NE [NE; NE]	7 / 281 (2.5)	NE [NE; NE]	2.8343 [1.3004; 7.0866] 0.0107	
>=3	5 / 75 (6.7)	NE [NE; NE]	1 / 56 (1.8)	NE [NE; NE]	3.3450 [0.5386; 64.1050] 0.2422	
ER/PR status I						0.0510
ER+, PR+	23 / 252 (9.1)	NE [NE; NE]	2 / 234 (0.9)	NE [NE; NE]	8.6928 [2.5612; 54.2631] 0.0004	
ER+, PR-	16 / 166 (9.6)	NE [NE; NE]	7 / 171 (4.1)	NE [NE; NE]	1.6691 [0.7002; 4.3978] 0.2616	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3981
ER <=10%	3 / 21 (14.3)	NE [12.7; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	35 / 362 (9.7)	NE [NE; NE]	9 / 343 (2.6)	NE [NE; NE]	2.8901 [1.4433; 6.4300] 0.0032	
Positive	2 / 51 (3.9)	NE [NE; NE]	0 / 60 (0.0)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						0.5081
Primary	12 / 127 (9.4)	NE [25.2; NE]	4 / 137 (2.9)	NE [NE; NE]	2.2553 [0.7610; 8.2102] 0.1573	
Secondary	28 / 307 (9.1)	NE [NE; NE]	5 / 279 (1.8)	NE [NE; NE]	4.0597 [1.7020; 11.9897] 0.0019	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0394
Capecitabine	19 / 265 (7.2)	NE [NE; NE]	1 / 249 (0.4)	NE [NE; NE]	14.7995 [3.0642; 266.0065] 0.0005	
Nab-Paclitaxel	17 / 103 (16.5)	NE [25.2; NE]	8 / 101 (7.9)	NE [NE; NE]	1.6133 [0.7035; 4.0063] 0.2697	
Paclitaxel	4 / 66 (6.1)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.0127
Yes	18 / 197 (9.1)	NE [NE; NE]	8 / 198 (4.0)	NE [NE; NE]	1.7691 [0.7853; 4.3496] 0.1797	
No	22 / 237 (9.3)	NE [NE; NE]	1 / 219 (0.5)	NE [NE; NE]	15.6066 [3.2679; 279.6789] 0.0003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.4936
Yes	23 / 294 (7.8)	NE [NE; NE]	6 / 275 (2.2)	NE [NE; NE]	2.7158 [1.1657; 7.4040] 0.0249	
No	17 / 140 (12.1)	NE [NE; NE]	3 / 142 (2.1)	NE [NE; NE]	4.6230 [1.5456; 19.8591] 0.0075	
ECOG						0.5371
0	21 / 251 (8.4)	NE [NE; NE]	6 / 246 (2.4)	NE [NE; NE]	2.5862 [1.1008; 7.0821] 0.0347	
>=1	18 / 178 (10.1)	NE [NE; NE]	3 / 163 (1.8)	NE [NE; NE]	4.6228 [1.5580; 19.7894] 0.0071	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Ejection fraction decreased						
Age at randomization						0.6571
<65 years of age	25 / 301 (8.3)	NE [NE; NE]	7 / 285 (2.5)	NE [NE; NE]	2.2599 [1.0229; 5.6948] 0.0522	
>=65 years of age	10 / 133 (7.5)	NE [NE; NE]	5 / 132 (3.8)	NE [NE; NE]	1.6220 [0.5754; 5.2138] 0.3730	
Race						0.5264
Asian	11 / 153 (7.2)	NE [NE; NE]	3 / 147 (2.0)	NE [NE; NE]	2.7918 [0.8688; 12.3666] 0.1006	
White	21 / 231 (9.1)	NE [NE; NE]	7 / 223 (3.1)	NE [NE; NE]	1.9942 [0.8843; 5.0835] 0.1088	
Other	3 / 50 (6.0)	NE [NE; NE]	2 / 47 (4.3)	NE [8.0; NE]	0.8607 [0.1330; 6.8557] 0.8742	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4868
Asia	11 / 148 (7.4)	NE [NE; NE]	3 / 144 (2.1)	NE [NE; NE]	2.8313 [0.8812; 12.5407] 0.0956	
Europe	19 / 227 (8.4)	NE [NE; NE]	5 / 206 (2.4)	NE [NE; NE]	2.3114 [0.9215; 7.0116] 0.0890	
Rest of the World	5 / 59 (8.5)	NE [22.9; NE]	4 / 67 (6.0)	NE [14.0; NE]	0.9793 [0.2552; 4.0037] 0.9754	
HER2 IHC expression						0.2554
IHC 1+	21 / 239 (8.8)	NE [NE; NE]	5 / 226 (2.2)	NE [NE; NE]	3.1216 [1.2683; 9.3692] 0.0162	
IHC 2+/ISH-	9 / 116 (7.8)	NE [22.9; NE]	6 / 115 (5.2)	NE [NE; NE]	0.8155 [0.2867; 2.4861] 0.7035	
IHC >0 <1+	4 / 76 (5.3)	NE [NE; NE]	1 / 74 (1.4)	NE [16.8; NE]	2.7162 [0.3996; 53.2232] 0.3529	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8360
Yes	32 / 393 (8.1)	NE [NE; NE]	11 / 377 (2.9)	NE [NE; NE]	1.9179 [0.9923; 3.9998] 0.0599	
No	3 / 41 (7.3)	NE [NE; NE]	1 / 40 (2.5)	NE [NE; NE]	2.6198 [0.3344; 53.0214] 0.3869	
Prior Taxane Use In The Non-Metastatic Setting						0.2938
Yes	12 / 177 (6.8)	NE [NE; NE]	6 / 172 (3.5)	NE [NE; NE]	1.4407 [0.5539; 4.1688] 0.4673	
No	23 / 257 (8.9)	NE [NE; NE]	6 / 245 (2.4)	NE [NE; NE]	2.5820 [1.1164; 7.0061] 0.0324	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5367
1	5 / 65 (7.7)	NE [NE; NE]	3 / 79 (3.8)	NE [NE; NE]	1.7333 [0.4235; 8.4755] 0.4464	
2	27 / 293 (9.2)	NE [NE; NE]	7 / 281 (2.5)	NE [NE; NE]	2.4861 [1.1383; 6.2222] 0.0273	
>=3	3 / 75 (4.0)	NE [NE; NE]	2 / 56 (3.6)	NE [NE; NE]	0.9044 [0.1492; 6.8909] 0.9126	
ER/PR status I						0.7902
ER+, PR+	19 / 252 (7.5)	NE [NE; NE]	6 / 234 (2.6)	NE [NE; NE]	2.0338 [0.8560; 5.6016] 0.1231	
ER+, PR-	14 / 166 (8.4)	NE [NE; NE]	6 / 171 (3.5)	NE [NE; NE]	1.6880 [0.6674; 4.8167] 0.2845	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2551
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	31 / 362 (8.6)	NE [NE; NE]	8 / 343 (2.3)	NE [NE; NE]	2.5902 [1.2439; 6.0746] 0.0134	
Positive	3 / 51 (5.9)	NE [NE; NE]	4 / 60 (6.7)	NE [NE; NE]	0.6614 [0.1301; 3.0070] 0.5863	
Endocrine Resistance						0.6910
Primary	10 / 127 (7.9)	NE [NE; NE]	3 / 137 (2.2)	NE [NE; NE]	2.6107 [0.7930; 11.6918] 0.1319	
Secondary	25 / 307 (8.1)	NE [NE; NE]	9 / 279 (3.2)	NE [NE; NE]	1.7733 [0.8545; 4.0353] 0.1373	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.4059
Capecitabine	20 / 265 (7.5)	NE [NE; NE]	9 / 249 (3.6)	NE [NE; NE]	1.5009 [0.7013; 3.4765] 0.3101	
Nab-Paclitaxel	11 / 103 (10.7)	NE [NE; NE]	2 / 101 (2.0)	NE [NE; NE]	4.8331 [1.2897; 31.3328] 0.0241	
Paclitaxel	4 / 66 (6.1)	NE [21.9; NE]	1 / 67 (1.5)	NE [NE; NE]	1.7316 [0.2151; 35.4436] 0.6336	
Prior anthracycline use						0.1646
Yes	18 / 197 (9.1)	NE [NE; NE]	9 / 198 (4.5)	NE [NE; NE]	1.5091 [0.6908; 3.5391] 0.3142	
No	17 / 237 (7.2)	NE [NE; NE]	3 / 219 (1.4)	NE [NE; NE]	3.4711 [1.1612; 14.9037] 0.0348	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9965
Yes	22 / 294 (7.5)	NE [NE; NE]	7 / 275 (2.5)	NE [NE; NE]	1.8786 [0.8354; 4.7832] 0.1436	
No	13 / 140 (9.3)	NE [NE; NE]	5 / 142 (3.5)	NE [NE; NE]	2.1144 [0.7949; 6.6053] 0.1466	
ECOG						0.3075
0	21 / 251 (8.4)	NE [NE; NE]	6 / 246 (2.4)	NE [NE; NE]	2.4536 [1.0463; 6.7099] 0.0463	
>=1	12 / 178 (6.7)	NE [NE; NE]	6 / 163 (3.7)	NE [NE; NE]	1.3082 [0.5033; 3.7825] 0.5934	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Weight decreased						
Age at randomization						0.1247
<65 years of age	26 / 301 (8.6)	NE [NE; NE]	4 / 285 (1.4)	NE [NE; NE]	4.4754 [1.7335; 15.2279] 0.0024	
>=65 years of age	6 / 133 (4.5)	NE [NE; NE]	4 / 132 (3.0)	NE [23.7; NE]	1.2099 [0.3382; 4.7938] 0.7706	
Race						0.5510
Asian	16 / 153 (10.5)	NE [NE; NE]	4 / 147 (2.7)	NE [NE; NE]	2.9726 [1.0786; 10.4377] 0.0426	
White	13 / 231 (5.6)	NE [NE; NE]	4 / 223 (1.8)	NE [23.7; NE]	2.4384 [0.8604; 8.6739] 0.1081	
Other	3 / 50 (6.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7913
Asia	16 / 148 (10.8)	NE [NE; NE]	4 / 144 (2.8)	NE [NE; NE]	3.0349 [1.1033; 10.6463] 0.0382	
Europe	12 / 227 (5.3)	NE [NE; NE]	2 / 206 (1.0)	NE [NE; NE]	4.4395 [1.2061; 28.5912] 0.0331	
Rest of the World	4 / 59 (6.8)	NE [NE; NE]	2 / 67 (3.0)	NE [23.7; NE]	1.6443 [0.3180; 11.9266] 0.5638	
HER2 IHC expression						0.2379
IHC 1+	22 / 239 (9.2)	NE [NE; NE]	3 / 226 (1.3)	NE [23.7; NE]	5.4677 [1.8798; 23.1854] 0.0021	
IHC 2+/ISH-	6 / 116 (5.2)	NE [NE; NE]	3 / 115 (2.6)	NE [NE; NE]	1.3577 [0.3550; 6.4761] 0.6657	
IHC >0 <1+	4 / 76 (5.3)	NE [NE; NE]	2 / 74 (2.7)	NE [NE; NE]	1.5951 [0.3108; 11.5173] 0.5867	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0446
Yes	25 / 393 (6.4)	NE [NE; NE]	8 / 377 (2.1)	NE [23.7; NE]	2.3042 [1.0805; 5.4802] 0.0356	
No	7 / 41 (17.1)	NE [24.4; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.0935
Yes	18 / 177 (10.2)	NE [NE; NE]	2 / 172 (1.2)	NE [NE; NE]	7.3709 [2.1223; 46.4096] 0.0017	
No	14 / 257 (5.4)	NE [NE; NE]	6 / 245 (2.4)	NE [23.7; NE]	1.5452 [0.6119; 4.4028] 0.3746	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3673
1	6 / 65 (9.2)	NE [NE; NE]	1 / 79 (1.3)	NE [NE; NE]	6.7757 [1.1570; 128.0471] 0.0400	
2	23 / 293 (7.8)	NE [NE; NE]	7 / 281 (2.5)	NE [23.7; NE]	2.2588 [1.0117; 5.7260] 0.0546	
>=3	3 / 75 (4.0)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.1921
ER+, PR+	21 / 252 (8.3)	NE [NE; NE]	3 / 234 (1.3)	NE [23.7; NE]	4.6440 [1.5958; 19.6956] 0.0063	
ER+, PR-	11 / 166 (6.6)	NE [NE; NE]	5 / 171 (2.9)	NE [NE; NE]	1.9543 [0.7005; 6.2534] 0.2106	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7301
ER <=10%	2 / 21 (9.5)	NE [12.4; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	28 / 362 (7.7)	NE [NE; NE]	7 / 343 (2.0)	NE [23.7; NE]	2.9383 [1.3496; 7.3390] 0.0079	
Positive	2 / 51 (3.9)	NE [NE; NE]	1 / 60 (1.7)	NE [NE; NE]	1.8496 [0.1759; 39.9723] 0.6113	
Endocrine Resistance						0.0061
Primary	12 / 127 (9.4)	NE [NE; NE]	0 / 137 (0.0)	NE [NE; NE]	NE [NE; NE]	
Secondary	20 / 307 (6.5)	NE [NE; NE]	8 / 279 (2.9)	NE [23.7; NE]	1.7131 [0.7767; 4.1586] 0.1965	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1379
Capecitabine	15 / 265 (5.7)	NE [NE; NE]	5 / 249 (2.0)	NE [23.7; NE]	2.2540 [0.8690; 6.9530] 0.1076	
Nab-Paclitaxel	13 / 103 (12.6)	NE [24.4; NE]	1 / 101 (1.0)	NE [NE; NE]	10.9387 [2.1401; 199.6119] 0.0041	
Paclitaxel	4 / 66 (6.1)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	1.1218 [0.2105; 8.2975] 0.8966	
Prior anthracycline use						0.0549
Yes	19 / 197 (9.6)	NE [NE; NE]	2 / 198 (1.0)	NE [NE; NE]	8.1301 [2.3551; 51.0723] 0.0008	
No	13 / 237 (5.5)	NE [NE; NE]	6 / 219 (2.7)	NE [23.7; NE]	1.3612 [0.5315; 3.9077] 0.5354	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9920
Yes	21 / 294 (7.1)	NE [NE; NE]	5 / 275 (1.8)	NE [NE; NE]	3.0620 [1.2439; 9.1913] 0.0183	
No	11 / 140 (7.9)	NE [NE; NE]	3 / 142 (2.1)	NE [23.7; NE]	2.7185 [0.8355; 12.1220] 0.1138	
ECOG						0.9172
0	15 / 251 (6.0)	NE [NE; NE]	4 / 246 (1.6)	NE [23.7; NE]	2.6894 [0.9650; 9.4976] 0.0700	
>=1	17 / 178 (9.6)	NE [NE; NE]	4 / 163 (2.5)	NE [NE; NE]	3.1171 [1.1491; 10.8584] 0.0316	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)						
Age at randomization						0.0156
<65 years of age	182 / 301 (60.5)	2.2 [1.4; 3.8]	183 / 285 (64.2)	2.1 [1.4; 2.8]	0.8241 [0.6701; 1.0133] 0.0625	
>=65 years of age	68 / 133 (51.1)	6.3 [3.3; NE]	95 / 132 (72.0)	1.4 [1.2; 2.1]	0.4920 [0.3573; 0.6737] <.0001	
Race						0.3231
Asian	86 / 153 (56.2)	2.8 [1.4; 11.0]	100 / 147 (68.0)	1.4 [1.1; 2.5]	0.6902 [0.5157; 0.9219] 0.0113	
White	130 / 231 (56.3)	3.8 [2.2; 8.5]	150 / 223 (67.3)	2.0 [1.5; 2.5]	0.6666 [0.5251; 0.8450] 0.0007	
Other	34 / 50 (68.0)	2.0 [1.4; 6.2]	28 / 47 (59.6)	2.4 [1.1; 7.4]	0.9678 [0.5835; 1.6170] 0.8914	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.6697
Asia	79 / 148 (53.4)	3.4 [1.4; NE]	95 / 144 (66.0)	1.4 [1.1; 2.8]	0.6754 [0.4992; 0.9112] 0.0094	
Europe	133 / 227 (58.6)	3.5 [2.0; 5.9]	138 / 206 (67.0)	2.1 [1.4; 2.7]	0.7043 [0.5531; 0.8965] 0.0040	
Rest of the World	38 / 59 (64.4)	3.0 [0.9; 6.4]	45 / 67 (67.2)	1.8 [1.1; 2.8]	0.8127 [0.5239; 1.2530] 0.3463	
HER2 IHC expression						0.4657
IHC 1+	131 / 239 (54.8)	3.8 [2.1; 9.5]	150 / 226 (66.4)	1.6 [1.3; 2.4]	0.6671 [0.5262; 0.8446] 0.0007	
IHC 2+/ISH-	74 / 116 (63.8)	2.2 [1.4; 4.4]	82 / 115 (71.3)	1.4 [1.1; 2.1]	0.6668 [0.4843; 0.9164] 0.0116	
IHC >0 <1+	43 / 76 (56.6)	3.7 [0.9; NE]	45 / 74 (60.8)	2.8 [1.9; 4.8]	0.8722 [0.5702; 1.3321] 0.5225	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0864
Yes	226 / 393 (57.5)	3.3 [2.2; 5.5]	255 / 377 (67.6)	1.8 [1.4; 2.1]	0.6701 [0.5588; 0.8031] <.0001	
No	24 / 41 (58.5)	3.5 [0.8; NE]	23 / 40 (57.5)	5.6 [1.4; NE]	1.0669 [0.5997; 1.9024] 0.8401	
Prior Taxane Use In The Non-Metastatic Setting						0.9534
Yes	102 / 177 (57.6)	3.3 [1.6; 7.8]	112 / 172 (65.1)	1.8 [1.4; 2.5]	0.7224 [0.5501; 0.9474] 0.0177	
No	148 / 257 (57.6)	3.3 [2.1; 5.9]	166 / 245 (67.8)	2.0 [1.4; 2.7]	0.6995 [0.5592; 0.8742] 0.0015	

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4815
1	43 / 65 (66.2)	1.0 [0.8; 2.7]	59 / 79 (74.7)	1.4 [1.1; 2.5]	0.9075 [0.6077; 1.3440] 0.6141	
2	163 / 293 (55.6)	4.3 [2.6; 9.5]	178 / 281 (63.3)	2.0 [1.4; 2.8]	0.6862 [0.5531; 0.8508] 0.0005	
>=3	43 / 75 (57.3)	3.2 [1.6; 7.8]	40 / 56 (71.4)	1.8 [1.0; 2.8]	0.6667 [0.4328; 1.0293] 0.0632	
ER/PR status I						0.4928
ER+, PR+	138 / 252 (54.8)	5.0 [2.7; 9.5]	151 / 234 (64.5)	2.1 [1.4; 2.5]	0.6505 [0.5145; 0.8216] 0.0003	
ER+, PR-	100 / 166 (60.2)	2.4 [1.4; 4.3]	118 / 171 (69.0)	1.4 [1.2; 2.7]	0.7609 [0.5814; 0.9941] 0.0434	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6874
ER <=10%	10 / 21 (47.6)	8.8 [1.0; NE]	7 / 14 (50.0)	4.8 [0.6; NE]	0.7204 [0.2668; 2.0257] 0.5173	
ER >10%	209 / 362 (57.7)	3.4 [2.1; 5.6]	224 / 343 (65.3)	2.1 [1.4; 2.8]	0.7341 [0.6069; 0.8876] 0.0012	
Positive	31 / 51 (60.8)	2.1 [0.8; 8.5]	47 / 60 (78.3)	1.2 [1.0; 1.8]	0.6046 [0.3773; 0.9548] 0.0312	
Endocrine Resistance						0.9158
Primary	69 / 127 (54.3)	2.1 [1.4; NE]	91 / 137 (66.4)	1.8 [1.1; 2.8]	0.7273 [0.5293; 0.9950] 0.0438	
Secondary	181 / 307 (59.0)	3.5 [2.3; 5.5]	187 / 279 (67.0)	1.9 [1.4; 2.4]	0.6977 [0.5674; 0.8575] 0.0006	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3880
Capecitabine	163 / 265 (61.5)	2.4 [1.4; 4.0]	172 / 249 (69.1)	2.0 [1.4; 2.5]	0.7460 [0.6001; 0.9269] 0.0075	
Nab-Paclitaxel	45 / 103 (43.7)	NE [3.8; NE]	59 / 101 (58.4)	3.2 [1.1; 8.6]	0.6345 [0.4282; 0.9339] 0.0206	
Paclitaxel	42 / 66 (63.6)	2.0 [1.4; 7.7]	47 / 67 (70.1)	1.0 [0.7; 1.9]	0.5699 [0.3688; 0.8757] 0.0097	
Prior anthracycline use						0.3107
Yes	116 / 197 (58.9)	2.6 [1.5; 7.7]	126 / 198 (63.6)	2.0 [1.4; 2.8]	0.7816 [0.6054; 1.0080] 0.0540	
No	134 / 237 (56.5)	3.7 [2.0; 6.3]	152 / 219 (69.4)	1.8 [1.2; 2.4]	0.6489 [0.5128; 0.8201] 0.0003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5976
Yes	170 / 294 (57.8)	3.2 [1.9; 4.4]	185 / 275 (67.3)	1.6 [1.2; 2.1]	0.6883 [0.5575; 0.8492] 0.0004	
No	80 / 140 (57.1)	3.6 [1.7; 11.0]	93 / 142 (65.5)	2.1 [1.4; 3.5]	0.7403 [0.5465; 1.0003] 0.0490	
ECOG						0.4064
0	144 / 251 (57.4)	3.7 [2.1; 6.4]	170 / 246 (69.1)	1.9 [1.4; 2.4]	0.6674 [0.5328; 0.8348] 0.0004	
>=1	103 / 178 (57.9)	2.6 [1.6; 8.5]	102 / 163 (62.6)	1.9 [1.2; 2.9]	0.7798 [0.5917; 1.0278] 0.0719	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia						
Age at randomization						0.4954
<65 years of age	155 / 301 (51.5)	5.5 [2.2; NE]	61 / 285 (21.4)	NE [NE; NE]	2.6537 [1.9841; 3.5948] <.0001	
>=65 years of age	55 / 133 (41.4)	NE [5.5; NE]	26 / 132 (19.7)	NE [NE; NE]	2.2065 [1.3991; 3.5731] 0.0006	
Race						0.4588
Asian	76 / 153 (49.7)	6.4 [2.1; NE]	35 / 147 (23.8)	NE [NE; NE]	2.2059 [1.4905; 3.3314] 0.0001	
White	108 / 231 (46.8)	NE [4.1; NE]	45 / 223 (20.2)	NE [NE; NE]	2.5257 [1.7976; 3.6119] <.0001	
Other	26 / 50 (52.0)	5.5 [1.4; NE]	7 / 47 (14.9)	NE [NE; NE]	4.0004 [1.8292; 10.0150] 0.0005	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0423
Asia	70 / 148 (47.3)	NE [2.3; NE]	33 / 144 (22.9)	NE [NE; NE]	2.1777 [1.4521; 3.3350] 0.0002	
Europe	109 / 227 (48.0)	9.7 [3.5; NE]	47 / 206 (22.8)	NE [NE; NE]	2.2457 [1.6065; 3.1908] <.0001	
Rest of the World	31 / 59 (52.5)	4.4 [1.0; NE]	7 / 67 (10.4)	NE [NE; NE]	6.1432 [2.8631; 15.2121] <.0001	
HER2 IHC expression						0.4306
IHC 1+	104 / 239 (43.5)	NE [5.5; NE]	48 / 226 (21.2)	NE [NE; NE]	2.2038 [1.5755; 3.1288] <.0001	
IHC 2+/ISH-	64 / 116 (55.2)	2.8 [1.5; NE]	26 / 115 (22.6)	NE [NE; NE]	2.6130 [1.6766; 4.1938] <.0001	
IHC >0 <1+	40 / 76 (52.6)	5.5 [1.0; NE]	13 / 74 (17.6)	NE [NE; NE]	3.4908 [1.9184; 6.7916] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5217
Yes	189 / 393 (48.1)	9.7 [4.1; NE]	79 / 377 (21.0)	NE [NE; NE]	2.4703 [1.9087; 3.2308] <.0001	
No	21 / 41 (51.2)	3.8 [0.8; NE]	8 / 40 (20.0)	NE [NE; NE]	2.9528 [1.3565; 7.1058] 0.0063	
Prior Taxane Use In The Non-Metastatic Setting						0.9131
Yes	87 / 177 (49.2)	7.7 [2.3; NE]	37 / 172 (21.5)	NE [NE; NE]	2.4737 [1.6986; 3.6781] <.0001	
No	123 / 257 (47.9)	11.7 [2.8; NE]	50 / 245 (20.4)	NE [NE; NE]	2.5538 [1.8504; 3.5785] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3060
1	40 / 65 (61.5)	1.4 [0.9; 6.3]	19 / 79 (24.1)	NE [NE; NE]	3.1931 [1.8701; 5.6483] <.0001	
2	131 / 293 (44.7)	NE [6.4; NE]	58 / 281 (20.6)	NE [NE; NE]	2.2490 [1.6604; 3.0860] <.0001	
>=3	38 / 75 (50.7)	4.3 [2.0; NE]	9 / 56 (16.1)	NE [NE; NE]	3.6757 [1.8600; 8.1075] 0.0002	
ER/PR status I						0.6847
ER+, PR+	112 / 252 (44.4)	NE [6.3; NE]	45 / 234 (19.2)	NE [NE; NE]	2.4292 [1.7317; 3.4663] <.0001	
ER+, PR-	87 / 166 (52.4)	3.8 [1.7; NE]	38 / 171 (22.2)	NE [NE; NE]	2.6894 [1.8520; 3.9825] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1737
ER <=10%	8 / 21 (38.1)	NE [1.0; NE]	4 / 14 (28.6)	NE [0.6; NE]	1.1275 [0.3546; 4.2290] 0.8425	
ER >10%	175 / 362 (48.3)	9.7 [3.6; NE]	74 / 343 (21.6)	NE [NE; NE]	2.4350 [1.8645; 3.2150] <.0001	
Positive	27 / 51 (52.9)	4.3 [1.2; NE]	9 / 60 (15.0)	NE [NE; NE]	4.1917 [2.0462; 9.4513] 0.0001	
Endocrine Resistance						0.6141
Primary	63 / 127 (49.6)	5.6 [1.4; NE]	33 / 137 (24.1)	NE [NE; NE]	2.2820 [1.5081; 3.5177] 0.0001	
Secondary	147 / 307 (47.9)	9.7 [4.1; NE]	54 / 279 (19.4)	NE [NE; NE]	2.6705 [1.9681; 3.6784] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						<.0001
Capecitabine	135 / 265 (50.9)	5.5 [2.2; NE]	7 / 249 (2.8)	NE [NE; NE]	23.1606 [11.6856; 54.7105] <.0001	
Nab-Paclitaxel	41 / 103 (39.8)	NE [5.4; NE]	46 / 101 (45.5)	NE [1.1; NE]	0.7691 [0.5031; 1.1717] 0.2220	
Paclitaxel	34 / 66 (51.5)	7.4 [1.4; NE]	34 / 67 (50.7)	2.3 [1.0; NE]	0.7746 [0.4780; 1.2544] 0.2986	
Prior anthracycline use						0.9334
Yes	98 / 197 (49.7)	8.5 [2.2; NE]	42 / 198 (21.2)	NE [NE; NE]	2.5496 [1.7900; 3.6984] <.0001	
No	112 / 237 (47.3)	NE [3.7; NE]	45 / 219 (20.5)	NE [NE; NE]	2.5011 [1.7828; 3.5691] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.4508
Yes	145 / 294 (49.3)	7.7 [2.6; NE]	62 / 275 (22.5)	NE [NE; NE]	2.3639 [1.7655; 3.2056] <.0001	
No	65 / 140 (46.4)	NE [2.8; NE]	25 / 142 (17.6)	NE [NE; NE]	2.9057 [1.8566; 4.6939] <.0001	
ECOG						0.0019
0	122 / 251 (48.6)	11.7 [2.8; NE]	38 / 246 (15.4)	NE [NE; NE]	3.5678 [2.5042; 5.2026] <.0001	
>=1	85 / 178 (47.8)	9.7 [2.6; NE]	49 / 163 (30.1)	NE [NE; NE]	1.6018 [1.1321; 2.2916] 0.0081	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Rash						
Age at randomization						0.6426
<65 years of age	16 / 301 (5.3)	NE [NE; NE]	19 / 285 (6.7)	NE [NE; NE]	0.4839 [0.2425; 0.9531] 0.0325	
>=65 years of age	10 / 133 (7.5)	NE [NE; NE]	12 / 132 (9.1)	NE [NE; NE]	0.7327 [0.3088; 1.7016] 0.4672	
Race						0.1167
Asian	6 / 153 (3.9)	NE [NE; NE]	15 / 147 (10.2)	NE [NE; NE]	0.3219 [0.1145; 0.7937] 0.0137	
White	16 / 231 (6.9)	NE [NE; NE]	15 / 223 (6.7)	NE [NE; NE]	0.7317 [0.3573; 1.5061] 0.3883	
Other	4 / 50 (8.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	1.3393 [0.1878; 26.9718] 0.7978	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1492
Asia	6 / 148 (4.1)	NE [NE; NE]	15 / 144 (10.4)	NE [NE; NE]	0.3264 [0.1161; 0.8048] 0.0150	
Europe	15 / 227 (6.6)	NE [NE; NE]	13 / 206 (6.3)	NE [NE; NE]	0.6737 [0.3153; 1.4576] 0.3041	
Rest of the World	5 / 59 (8.5)	NE [24.4; NE]	3 / 67 (4.5)	NE [NE; NE]	1.4334 [0.3486; 7.0352] 0.6224	
HER2 IHC expression						0.4647
IHC 1+	12 / 239 (5.0)	NE [NE; NE]	20 / 226 (8.8)	NE [NE; NE]	0.4295 [0.2022; 0.8741] 0.0188	
IHC 2+/ISH-	10 / 116 (8.6)	NE [24.4; NE]	9 / 115 (7.8)	NE [NE; NE]	0.6493 [0.2576; 1.6588] 0.3535	
IHC >0 <1+	3 / 76 (3.9)	NE [NE; NE]	2 / 74 (2.7)	NE [NE; NE]	1.2222 [0.2010; 9.3306] 0.8265	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1394
Yes	25 / 393 (6.4)	NE [NE; NE]	26 / 377 (6.9)	NE [NE; NE]	0.6557 [0.3743; 1.1460] 0.1344	
No	1 / 41 (2.4)	NE [NE; NE]	5 / 40 (12.5)	NE [NE; NE]	0.1538 [0.0080; 0.9612] 0.0503	
Prior Taxane Use In The Non-Metastatic Setting						0.5678
Yes	10 / 177 (5.6)	NE [NE; NE]	14 / 172 (8.1)	NE [NE; NE]	0.5095 [0.2173; 1.1509] 0.1020	
No	16 / 257 (6.2)	NE [NE; NE]	17 / 245 (6.9)	NE [NE; NE]	0.6350 [0.3158; 1.2709] 0.1936	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5639
1	2 / 65 (3.1)	NE [NE; NE]	4 / 79 (5.1)	NE [NE; NE]	0.4607 [0.0629; 2.4046] 0.3653	
2	23 / 293 (7.8)	NE [NE; NE]	24 / 281 (8.5)	NE [NE; NE]	0.6493 [0.3619; 1.1619] 0.1413	
>=3	1 / 75 (1.3)	NE [NE; NE]	3 / 56 (5.4)	NE [NE; NE]	0.1941 [0.0096; 1.5163] 0.1133	
ER/PR status I						0.1286
ER+, PR+	16 / 252 (6.3)	NE [NE; NE]	14 / 234 (6.0)	NE [NE; NE]	0.7440 [0.3603; 1.5540] 0.4218	
ER+, PR-	8 / 166 (4.8)	NE [NE; NE]	17 / 171 (9.9)	NE [NE; NE]	0.3514 [0.1401; 0.8059] 0.0133	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1670
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	2 / 14 (14.3)	NE [2.6; NE]	0.1353 [0.0055; 1.6774] 0.0950	
ER >10%	18 / 362 (5.0)	NE [NE; NE]	24 / 343 (7.0)	NE [NE; NE]	0.5015 [0.2662; 0.9281] 0.0263	
Positive	7 / 51 (13.7)	NE [NE; NE]	5 / 60 (8.3)	NE [NE; NE]	1.3358 [0.4250; 4.5263] 0.6208	
Endocrine Resistance						0.3539
Primary	5 / 127 (3.9)	NE [NE; NE]	10 / 137 (7.3)	NE [NE; NE]	0.3821 [0.1174; 1.0924] 0.0733	
Secondary	21 / 307 (6.8)	NE [NE; NE]	21 / 279 (7.5)	NE [NE; NE]	0.6561 [0.3545; 1.2140] 0.1734	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0064
Capecitabine	18 / 265 (6.8)	NE [NE; NE]	10 / 249 (4.0)	NE [NE; NE]	1.2475 [0.5842; 2.8207] 0.5765	
Nab-Paclitaxel	3 / 103 (2.9)	NE [NE; NE]	11 / 101 (10.9)	NE [NE; NE]	0.2212 [0.0496; 0.7161] 0.0121	
Paclitaxel	5 / 66 (7.6)	NE [NE; NE]	10 / 67 (14.9)	NE [7.9; NE]	0.1693 [0.0403; 0.5765] 0.0038	
Prior anthracycline use						0.8346
Yes	14 / 197 (7.1)	NE [NE; NE]	16 / 198 (8.1)	NE [NE; NE]	0.6131 [0.2926; 1.2698] 0.1830	
No	12 / 237 (5.1)	NE [NE; NE]	15 / 219 (6.8)	NE [NE; NE]	0.5454 [0.2484; 1.1720] 0.1163	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.6116
Yes	17 / 294 (5.8)	NE [NE; NE]	17 / 275 (6.2)	NE [NE; NE]	0.6207 [0.3104; 1.2393] 0.1695	
No	9 / 140 (6.4)	NE [NE; NE]	14 / 142 (9.9)	NE [NE; NE]	0.5027 [0.2082; 1.1533] 0.1038	
ECOG						0.4473
0	18 / 251 (7.2)	NE [NE; NE]	19 / 246 (7.7)	NE [NE; NE]	0.6486 [0.3355; 1.2489] 0.1900	
>=1	8 / 178 (4.5)	NE [NE; NE]	12 / 163 (7.4)	NE [NE; NE]	0.4573 [0.1775; 1.1159] 0.0826	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome						
Age at randomization						0.6504
<65 years of age	3 / 301 (1.0)	NE [NE; NE]	92 / 285 (32.3)	NE [NE; NE]	0.0209 [0.0051; 0.0558] <.0001	
>=65 years of age	1 / 133 (0.8)	NE [NE; NE]	54 / 132 (40.9)	9.5 [5.5; NE]	0.0118 [0.0007; 0.0541] <.0001	
Race						0.0528
Asian	0 / 153 (0.0)	NE [NE; NE]	53 / 147 (36.1)	NE [9.5; NE]	NE [NE; NE]	
White	2 / 231 (0.9)	NE [NE; NE]	79 / 223 (35.4)	NE [9.5; NE]	0.0161 [0.0026; 0.0513] <.0001	
Other	2 / 50 (4.0)	NE [NE; NE]	14 / 47 (29.8)	NE [6.9; NE]	0.0545 [0.0078; 0.2211] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0404
Asia	0 / 148 (0.0)	NE [NE; NE]	52 / 144 (36.1)	NE [9.5; NE]	NE [NE; NE]	
Europe	4 / 227 (1.8)	NE [NE; NE]	62 / 206 (30.1)	NE [12.5; NE]	0.0369 [0.0111; 0.0902] <.0001	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	32 / 67 (47.8)	5.2 [2.1; NE]	NE [NE; NE]	
HER2 IHC expression						0.6124
IHC 1+	2 / 239 (0.8)	NE [NE; NE]	79 / 226 (35.0)	NE [12.5; NE]	0.0164 [0.0027; 0.0523] <.0001	
IHC 2+/ISH-	1 / 116 (0.9)	NE [NE; NE]	43 / 115 (37.4)	NE [4.8; NE]	0.0145 [0.0008; 0.0673] <.0001	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	23 / 74 (31.1)	NE [6.3; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4828
Yes	4 / 393 (1.0)	NE [NE; NE]	135 / 377 (35.8)	NE [12.5; NE]	0.0184 [0.0056; 0.0437] <.0001	
No	0 / 41 (0.0)	NE [NE; NE]	11 / 40 (27.5)	NE [9.5; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.6947
Yes	1 / 177 (0.6)	NE [NE; NE]	52 / 172 (30.2)	NE [NE; NE]	0.0145 [0.0008; 0.0659] <.0001	
No	3 / 257 (1.2)	NE [NE; NE]	94 / 245 (38.4)	NE [6.3; NE]	0.0187 [0.0046; 0.0500] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4631
1	1 / 65 (1.5)	NE [NE; NE]	29 / 79 (36.7)	NE [5.6; NE]	0.0278 [0.0016; 0.1320] <.0001	
2	3 / 293 (1.0)	NE [NE; NE]	97 / 281 (34.5)	NE [9.5; NE]	0.0190 [0.0047; 0.0508] <.0001	
>=3	0 / 75 (0.0)	NE [NE; NE]	20 / 56 (35.7)	NE [3.5; NE]	NE [NE; NE]	
ER/PR status I						0.1344
ER+, PR+	1 / 252 (0.4)	NE [NE; NE]	84 / 234 (35.9)	NE [7.4; NE]	0.0070 [0.0004; 0.0318] <.0001	
ER+, PR-	3 / 166 (1.8)	NE [NE; NE]	59 / 171 (34.5)	NE [12.5; NE]	0.0358 [0.0087; 0.0975] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4548
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	2 / 14 (14.3)	NE [2.1; NE]	NE [NE; NE]	
ER >10%	2 / 362 (0.6)	NE [NE; NE]	112 / 343 (32.7)	NE [NE; NE]	0.0116 [0.0019; 0.0364] <.0001	
Positive	2 / 51 (3.9)	NE [NE; NE]	32 / 60 (53.3)	2.8 [1.4; NE]	0.0377 [0.0060; 0.1283] <.0001	
Endocrine Resistance						0.1300
Primary	0 / 127 (0.0)	NE [NE; NE]	44 / 137 (32.1)	NE [12.5; NE]	NE [NE; NE]	
Secondary	4 / 307 (1.3)	NE [NE; NE]	102 / 279 (36.6)	NE [8.3; NE]	0.0227 [0.0069; 0.0545] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1045
Capecitabine	3 / 265 (1.1)	NE [NE; NE]	143 / 249 (57.4)	2.8 [2.1; 3.9]	0.0098 [0.0024; 0.0259] <.0001	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	1 / 101 (1.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	1 / 66 (1.5)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	0.1570 [0.0054; 2.3854] 0.1889	
Prior anthracycline use						0.5829
Yes	2 / 197 (1.0)	NE [NE; NE]	59 / 198 (29.8)	NE [NE; NE]	0.0238 [0.0039; 0.0766] <.0001	
No	2 / 237 (0.8)	NE [NE; NE]	87 / 219 (39.7)	12.5 [5.5; NE]	0.0133 [0.0022; 0.0423] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.3702
Yes	2 / 294 (0.7)	NE [NE; NE]	99 / 275 (36.0)	NE [9.5; NE]	0.0118 [0.0019; 0.0375] <.0001	
No	2 / 140 (1.4)	NE [NE; NE]	47 / 142 (33.1)	NE [9.5; NE]	0.0310 [0.0050; 0.1003] <.0001	
ECOG						0.9462
0	3 / 251 (1.2)	NE [NE; NE]	104 / 246 (42.3)	9.5 [5.5; NE]	0.0173 [0.0042; 0.0461] <.0001	
>=1	1 / 178 (0.6)	NE [NE; NE]	40 / 163 (24.5)	NE [NE; NE]	0.0174 [0.0010; 0.0801] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Nail discolouration						
Age at randomization						0.8838
<65 years of age	1 / 301 (0.3)	NE [NE; NE]	5 / 285 (1.8)	NE [NE; NE]	0.1356 [0.0071; 0.8424] 0.0324	
>=65 years of age	1 / 133 (0.8)	NE [NE; NE]	5 / 132 (3.8)	NE [NE; NE]	0.1751 [0.0091; 1.0884] 0.0724	
Race						0.8377
Asian	1 / 153 (0.7)	NE [NE; NE]	3 / 147 (2.0)	NE [NE; NE]	0.2683 [0.0133; 2.0960] 0.2214	
White	1 / 231 (0.4)	NE [NE; NE]	7 / 223 (3.1)	NE [NE; NE]	0.1050 [0.0056; 0.5941] 0.0103	
Other	0 / 50 (0.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1596
Asia	0 / 148 (0.0)	NE [NE; NE]	2 / 144 (1.4)	NE [NE; NE]	NE [NE; NE]	
Europe	0 / 227 (0.0)	NE [NE; NE]	4 / 206 (1.9)	NE [NE; NE]	NE [NE; NE]	
Rest of the World	2 / 59 (3.4)	NE [NE; NE]	4 / 67 (6.0)	NE [NE; NE]	0.4727 [0.0654; 2.4279] 0.3766	
HER2 IHC expression						0.5251
IHC 1+	1 / 239 (0.4)	NE [NE; NE]	2 / 226 (0.9)	NE [NE; NE]	0.3994 [0.0185; 4.1848] 0.4387	
IHC 2+/ISH-	1 / 116 (0.9)	NE [NE; NE]	6 / 115 (5.2)	NE [NE; NE]	0.1254 [0.0066; 0.7347] 0.0223	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	2 / 74 (2.7)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5685
Yes	2 / 393 (0.5)	NE [NE; NE]	9 / 377 (2.4)	NE [NE; NE]	0.1606 [0.0244; 0.6265] 0.0077	
No	0 / 41 (0.0)	NE [NE; NE]	1 / 40 (2.5)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.1179
Yes	0 / 177 (0.0)	NE [NE; NE]	5 / 172 (2.9)	NE [NE; NE]	NE [NE; NE]	
No	2 / 257 (0.8)	NE [NE; NE]	5 / 245 (2.0)	NE [NE; NE]	0.3163 [0.0452; 1.4691] 0.1465	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5385
1	0 / 65 (0.0)	NE [NE; NE]	1 / 79 (1.3)	NE [NE; NE]	NE [NE; NE]	
2	2 / 293 (0.7)	NE [NE; NE]	7 / 281 (2.5)	NE [NE; NE]	0.2013 [0.0298; 0.8395] 0.0276	
>=3	0 / 75 (0.0)	NE [NE; NE]	2 / 56 (3.6)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.8909
ER+, PR+	1 / 252 (0.4)	NE [NE; NE]	4 / 234 (1.7)	NE [NE; NE]	0.1610 [0.0082; 1.0990] 0.0634	
ER+, PR-	1 / 166 (0.6)	NE [NE; NE]	6 / 171 (3.5)	NE [NE; NE]	0.1528 [0.0081; 0.8942] 0.0447	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7142
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	2 / 362 (0.6)	NE [NE; NE]	8 / 343 (2.3)	NE [NE; NE]	0.1811 [0.0272; 0.7270] 0.0155	
Positive	0 / 51 (0.0)	NE [NE; NE]	2 / 60 (3.3)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						0.4026
Primary	0 / 127 (0.0)	NE [NE; NE]	2 / 137 (1.5)	NE [NE; NE]	NE [NE; NE]	
Secondary	2 / 307 (0.7)	NE [NE; NE]	8 / 279 (2.9)	NE [NE; NE]	0.1841 [0.0278; 0.7356] 0.0163	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3009
Capecitabine	2 / 265 (0.8)	NE [NE; NE]	5 / 249 (2.0)	NE [NE; NE]	0.3030 [0.0433; 1.4083] 0.1307	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	3 / 101 (3.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.8318
Yes	1 / 197 (0.5)	NE [NE; NE]	6 / 198 (3.0)	NE [NE; NE]	0.1230 [0.0065; 0.7282] 0.0219	
No	1 / 237 (0.4)	NE [NE; NE]	4 / 219 (1.8)	NE [NE; NE]	0.1898 [0.0097; 1.2871] 0.0970	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0881
Yes	2 / 294 (0.7)	NE [NE; NE]	4 / 275 (1.5)	NE [NE; NE]	0.3801 [0.0526; 1.9538] 0.2468	
No	0 / 140 (0.0)	NE [NE; NE]	6 / 142 (4.2)	NE [NE; NE]	NE [NE; NE]	
ECOG						0.9546
0	1 / 251 (0.4)	NE [NE; NE]	5 / 246 (2.0)	NE [NE; NE]	0.1428 [0.0074; 0.8927] 0.0397	
>=1	1 / 178 (0.6)	NE [NE; NE]	5 / 163 (3.1)	NE [NE; NE]	0.1510 [0.0079; 0.9366] 0.0461	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: All (any PT)						
Age at randomization						0.4047
<65 years of age	135 / 301 (44.9)	16.3 [10.6; NE]	65 / 285 (22.8)	NE [NE; NE]	1.8557 [1.3838; 2.5141] <.0001	
>=65 years of age	62 / 133 (46.6)	14.0 [5.3; NE]	42 / 132 (31.8)	NE [20.8; NE]	1.5171 [1.0286; 2.2596] 0.0365	
Race						0.0797
Asian	86 / 153 (56.2)	5.3 [3.1; 14.6]	38 / 147 (25.9)	NE [NE; NE]	2.4087 [1.6568; 3.5704] <.0001	
White	92 / 231 (39.8)	20.3 [13.7; NE]	56 / 223 (25.1)	NE [20.8; NE]	1.4610 [1.0502; 2.0505] 0.0249	
Other	19 / 50 (38.0)	NE [9.6; NE]	13 / 47 (27.7)	NE [NE; NE]	1.1733 [0.5716; 2.4699] 0.6683	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0161
Asia	84 / 148 (56.8)	5.6 [4.0; 14.6]	37 / 144 (25.7)	NE [NE; NE]	2.3775 [1.6277; 3.5428] <.0001	
Europe	80 / 227 (35.2)	NE [20.3; NE]	53 / 206 (25.7)	NE [NE; NE]	1.2126 [0.8573; 1.7288] 0.2786	
Rest of the World	33 / 59 (55.9)	5.7 [1.4; NE]	17 / 67 (25.4)	20.8 [20.8; NE]	2.4511 [1.3810; 4.5116] 0.0020	
HER2 IHC expression						0.0331
IHC 1+	103 / 239 (43.1)	19.1 [12.1; NE]	54 / 226 (23.9)	NE [NE; NE]	1.7690 [1.2766; 2.4789] 0.0006	
IHC 2+/ISH-	61 / 116 (52.6)	9.0 [4.4; NE]	25 / 115 (21.7)	NE [NE; NE]	2.4474 [1.5532; 3.9739] 0.0001	
IHC >0 <1+	32 / 76 (42.1)	18.9 [6.2; NE]	28 / 74 (37.8)	20.8 [4.1; NE]	1.0169 [0.6115; 1.7009] 0.9451	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3701
Yes	171 / 393 (43.5)	16.3 [12.1; NE]	94 / 377 (24.9)	NE [NE; NE]	1.6733 [1.3028; 2.1623] 0.0001	
No	26 / 41 (63.4)	4.4 [1.3; 19.1]	13 / 40 (32.5)	20.8 [9.7; NE]	2.3261 [1.2148; 4.6800] 0.0111	
Prior Taxane Use In The Non-Metastatic Setting						0.6213
Yes	79 / 177 (44.6)	14.6 [9.8; NE]	40 / 172 (23.3)	NE [NE; NE]	1.8574 [1.2759; 2.7468] 0.0013	
No	118 / 257 (45.9)	14.8 [9.7; NE]	67 / 245 (27.3)	NE [20.8; NE]	1.6391 [1.2170; 2.2257] 0.0012	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3150
1	24 / 65 (36.9)	14.2 [10.0; NE]	24 / 79 (30.4)	NE [9.7; NE]	1.1103 [0.6244; 1.9723] 0.7206	
2	138 / 293 (47.1)	14.8 [8.7; NE]	69 / 281 (24.6)	NE [20.8; NE]	1.8679 [1.4031; 2.5101] <.0001	
>=3	35 / 75 (46.7)	12.1 [4.4; NE]	14 / 56 (25.0)	NE [NE; NE]	1.9807 [1.0896; 3.8054] 0.0274	
ER/PR status I						0.4808
ER+, PR+	110 / 252 (43.7)	20.3 [12.1; NE]	54 / 234 (23.1)	NE [NE; NE]	1.9113 [1.3859; 2.6681] 0.0001	
ER+, PR-	80 / 166 (48.2)	12.0 [7.9; NE]	49 / 171 (28.7)	NE [NE; NE]	1.5510 [1.0886; 2.2316] 0.0154	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6048
ER <=10%	9 / 21 (42.9)	NE [4.2; NE]	2 / 14 (14.3)	NE [NE; NE]	2.3758 [0.6009; 15.7105] 0.2581	
ER >10%	165 / 362 (45.6)	14.8 [11.1; NE]	84 / 343 (24.5)	NE [NE; NE]	1.8220 [1.4042; 2.3820] <.0001	
Positive	23 / 51 (45.1)	13.7 [4.4; NE]	21 / 60 (35.0)	NE [4.4; NE]	1.3308 [0.7336; 2.4273] 0.3470	
Endocrine Resistance						0.0174
Primary	51 / 127 (40.2)	14.6 [11.1; NE]	44 / 137 (32.1)	NE [9.8; NE]	1.1070 [0.7375; 1.6684] 0.6221	
Secondary	146 / 307 (47.6)	14.0 [7.9; NE]	63 / 279 (22.6)	NE [NE; NE]	2.1385 [1.5989; 2.8955] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.7839
Capecitabine	122 / 265 (46.0)	14.6 [9.8; NE]	68 / 249 (27.3)	NE [20.8; NE]	1.6348 [1.2183; 2.2120] 0.0011	
Nab-Paclitaxel	46 / 103 (44.7)	14.8 [7.9; NE]	23 / 101 (22.8)	NE [NE; NE]	1.9878 [1.2171; 3.3388] 0.0061	
Paclitaxel	29 / 66 (43.9)	NE [4.4; NE]	16 / 67 (23.9)	NE [NE; NE]	1.7762 [0.9692; 3.3677] 0.0661	
Prior anthracycline use						0.7210
Yes	86 / 197 (43.7)	18.9 [10.4; NE]	50 / 198 (25.3)	NE [NE; NE]	1.6633 [1.1766; 2.3762] 0.0040	
No	111 / 237 (46.8)	14.6 [8.7; NE]	57 / 219 (26.0)	NE [20.8; NE]	1.7747 [1.2943; 2.4604] 0.0004	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0498
Yes	127 / 294 (43.2)	18.9 [13.1; NE]	76 / 275 (27.6)	NE [NE; NE]	1.4631 [1.1021; 1.9553] 0.0088	
No	70 / 140 (50.0)	10.0 [5.6; NE]	31 / 142 (21.8)	NE [20.8; NE]	2.3942 [1.5833; 3.7070] <.0001	
ECOG						0.0562
0	99 / 251 (39.4)	20.3 [14.6; NE]	44 / 246 (17.9)	NE [NE; NE]	2.1102 [1.4883; 3.0422] <.0001	
>=1	95 / 178 (53.4)	7.9 [3.1; 14.6]	61 / 163 (37.4)	NE [NE; NE]	1.3895 [1.0085; 1.9285] 0.0456	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Age at randomization						0.2350
<65 years of age	75 / 301 (24.9)	NE [NE; NE]	26 / 285 (9.1)	NE [NE; NE]	2.7175 [1.7619; 4.3280] <.0001	
>=65 years of age	39 / 133 (29.3)	NE [NE; NE]	22 / 132 (16.7)	NE [NE; NE]	1.7760 [1.0631; 3.0439] 0.0290	
Race						0.0239
Asian	50 / 153 (32.7)	NE [NE; NE]	12 / 147 (8.2)	NE [NE; NE]	4.3076 [2.3742; 8.4810] <.0001	
White	54 / 231 (23.4)	NE [NE; NE]	29 / 223 (13.0)	NE [NE; NE]	1.7301 [1.1098; 2.7530] 0.0161	
Other	10 / 50 (20.0)	NE [NE; NE]	7 / 47 (14.9)	NE [NE; NE]	1.2134 [0.4566; 3.3873] 0.7017	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0009
Asia	46 / 148 (31.1)	NE [NE; NE]	11 / 144 (7.6)	NE [NE; NE]	4.3148 [2.3198; 8.7752] <.0001	
Europe	47 / 227 (20.7)	NE [NE; NE]	32 / 206 (15.5)	NE [NE; NE]	1.2558 [0.8033; 1.9879] 0.3212	
Rest of the World	21 / 59 (35.6)	NE [10.3; NE]	5 / 67 (7.5)	NE [NE; NE]	5.0305 [2.0464; 15.0863] 0.0003	
HER2 IHC expression						0.4702
IHC 1+	56 / 239 (23.4)	NE [NE; NE]	24 / 226 (10.6)	NE [NE; NE]	2.1654 [1.3583; 3.5615] 0.0012	
IHC 2+/ISH-	39 / 116 (33.6)	NE [NE; NE]	13 / 115 (11.3)	NE [NE; NE]	3.0101 [1.6487; 5.8696] 0.0003	
IHC >0 <1+	19 / 76 (25.0)	NE [NE; NE]	11 / 74 (14.9)	NE [NE; NE]	1.6995 [0.8217; 3.6944] 0.1575	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1188
Yes	102 / 393 (26.0)	NE [NE; NE]	46 / 377 (12.2)	NE [NE; NE]	2.0998 [1.4914; 3.0033] <.0001	
No	12 / 41 (29.3)	NE [19.1; NE]	2 / 40 (5.0)	NE [NE; NE]	6.2772 [1.7090; 40.3897] 0.0059	
Prior Taxane Use In The Non-Metastatic Setting						0.9870
Yes	43 / 177 (24.3)	NE [NE; NE]	18 / 172 (10.5)	NE [NE; NE]	2.2200 [1.3010; 3.9517] 0.0036	
No	71 / 257 (27.6)	NE [NE; NE]	30 / 245 (12.2)	NE [NE; NE]	2.2984 [1.5150; 3.5769] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5373
1	12 / 65 (18.5)	NE [NE; NE]	10 / 79 (12.7)	NE [NE; NE]	1.3807 [0.5932; 3.2825] 0.4523	
2	82 / 293 (28.0)	NE [NE; NE]	32 / 281 (11.4)	NE [NE; NE]	2.4377 [1.6358; 3.7221] <.0001	
>=3	20 / 75 (26.7)	NE [NE; NE]	6 / 56 (10.7)	NE [NE; NE]	2.6741 [1.1388; 7.3130] 0.0277	
ER/PR status I						0.2440
ER+, PR+	66 / 252 (26.2)	NE [NE; NE]	22 / 234 (9.4)	NE [NE; NE]	2.8450 [1.7847; 4.7149] <.0001	
ER+, PR-	43 / 166 (25.9)	NE [NE; NE]	23 / 171 (13.5)	NE [NE; NE]	1.8138 [1.1013; 3.0648] 0.0200	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1150
ER <=10%	2 / 21 (9.5)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	95 / 362 (26.2)	NE [NE; NE]	32 / 343 (9.3)	NE [NE; NE]	2.8024 [1.8978; 4.2490] <.0001	
Positive	17 / 51 (33.3)	NE [9.0; NE]	16 / 60 (26.7)	NE [NE; NE]	1.3207 [0.6640; 2.6392] 0.4266	
Endocrine Resistance						0.0930
Primary	23 / 127 (18.1)	NE [NE; NE]	17 / 137 (12.4)	NE [NE; NE]	1.3939 [0.7465; 2.6541] 0.2999	
Secondary	91 / 307 (29.6)	NE [NE; NE]	31 / 279 (11.1)	NE [NE; NE]	2.7034 [1.8188; 4.1289] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1062
Capecitabine	71 / 265 (26.8)	NE [NE; NE]	36 / 249 (14.5)	NE [NE; NE]	1.8324 [1.2353; 2.7668] 0.0027	
Nab-Paclitaxel	22 / 103 (21.4)	NE [NE; NE]	4 / 101 (4.0)	NE [NE; NE]	5.4692 [2.0900; 18.7220] 0.0004	
Paclitaxel	21 / 66 (31.8)	NE [NE; NE]	8 / 67 (11.9)	NE [NE; NE]	2.6914 [1.2317; 6.4921] 0.0140	
Prior anthracycline use						0.8382
Yes	48 / 197 (24.4)	NE [NE; NE]	20 / 198 (10.1)	NE [NE; NE]	2.3485 [1.4148; 4.0509] 0.0010	
No	66 / 237 (27.8)	NE [NE; NE]	28 / 219 (12.8)	NE [NE; NE]	2.2013 [1.4299; 3.4822] 0.0003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0006
Yes	64 / 294 (21.8)	NE [NE; NE]	38 / 275 (13.8)	NE [NE; NE]	1.5024 [1.0096; 2.2663] 0.0465	
No	50 / 140 (35.7)	NE [NE; NE]	10 / 142 (7.0)	NE [NE; NE]	5.5005 [2.9143; 11.5160] <.0001	
ECOG						0.9617
0	63 / 251 (25.1)	NE [NE; NE]	27 / 246 (11.0)	NE [NE; NE]	2.2303 [1.4362; 3.5612] 0.0004	
>=1	50 / 178 (28.1)	NE [NE; NE]	20 / 163 (12.3)	NE [NE; NE]	2.3324 [1.4102; 4.0092] 0.0010	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: Hypokalaemia						
Age at randomization						0.8809
<65 years of age	31 / 301 (10.3)	NE [NE; NE]	7 / 285 (2.5)	NE [NE; NE]	2.8176 [1.3010; 7.0213] 0.0108	
>=65 years of age	25 / 133 (18.8)	NE [NE; NE]	8 / 132 (6.1)	NE [NE; NE]	2.9941 [1.4102; 7.0991] 0.0046	
Race						0.2468
Asian	30 / 153 (19.6)	NE [NE; NE]	5 / 147 (3.4)	NE [NE; NE]	4.9804 [2.1026; 14.6569] 0.0002	
White	20 / 231 (8.7)	NE [NE; NE]	8 / 223 (3.6)	NE [NE; NE]	1.8743 [0.8504; 4.5497] 0.1300	
Other	6 / 50 (12.0)	NE [NE; NE]	2 / 47 (4.3)	NE [NE; NE]	1.7690 [0.3819; 12.4631] 0.4894	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0933
Asia	33 / 148 (22.3)	NE [25.8; NE]	5 / 144 (3.5)	NE [NE; NE]	5.5520 [2.3650; 16.2500] 0.0001	
Europe	17 / 227 (7.5)	NE [NE; NE]	8 / 206 (3.9)	NE [NE; NE]	1.5121 [0.6665; 3.7311] 0.3351	
Rest of the World	6 / 59 (10.2)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	2.5890 [0.5839; 17.8622] 0.2321	
HER2 IHC expression						0.9771
IHC 1+	31 / 239 (13.0)	NE [NE; NE]	9 / 226 (4.0)	NE [NE; NE]	2.5114 [1.2376; 5.6336] 0.0126	
IHC 2+/ISH-	13 / 116 (11.2)	NE [NE; NE]	3 / 115 (2.6)	NE [NE; NE]	3.2055 [1.0215; 14.0652] 0.0567	
IHC >0 <1+	11 / 76 (14.5)	NE [18.9; NE]	3 / 74 (4.1)	NE [NE; NE]	3.3338 [1.0398; 14.7479] 0.0501	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2302
Yes	47 / 393 (12.0)	NE [NE; NE]	14 / 377 (3.7)	NE [NE; NE]	2.5442 [1.4333; 4.8134] 0.0016	
No	9 / 41 (22.0)	NE [25.8; NE]	1 / 40 (2.5)	NE [NE; NE]	7.1657 [1.3070; 133.1515] 0.0305	
Prior Taxane Use In The Non-Metastatic Setting						0.9629
Yes	30 / 177 (16.9)	NE [NE; NE]	8 / 172 (4.7)	NE [NE; NE]	2.8872 [1.3755; 6.8060] 0.0059	
No	26 / 257 (10.1)	NE [NE; NE]	7 / 245 (2.9)	NE [NE; NE]	2.7696 [1.2640; 6.9427] 0.0130	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6506
1	7 / 65 (10.8)	NE [NE; NE]	3 / 79 (3.8)	NE [NE; NE]	2.2573 [0.6175; 10.5912] 0.2309	
2	39 / 293 (13.3)	NE [NE; NE]	11 / 281 (3.9)	NE [NE; NE]	2.7042 [1.4280; 5.5657] 0.0026	
>=3	10 / 75 (13.3)	NE [18.6; NE]	1 / 56 (1.8)	NE [NE; NE]	5.9898 [1.1386; 110.1379] 0.0529	
ER/PR status I						0.3436
ER+, PR+	34 / 252 (13.5)	NE [NE; NE]	6 / 234 (2.6)	NE [NE; NE]	4.3072 [1.9384; 11.4336] 0.0003	
ER+, PR-	20 / 166 (12.0)	NE [NE; NE]	7 / 171 (4.1)	NE [NE; NE]	2.1432 [0.9363; 5.5134] 0.0798	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5803
ER <=10%	3 / 21 (14.3)	NE [10.6; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	47 / 362 (13.0)	NE [NE; NE]	12 / 343 (3.5)	NE [NE; NE]	2.9492 [1.6100; 5.8451] 0.0005	
Positive	6 / 51 (11.8)	NE [NE; NE]	3 / 60 (5.0)	NE [NE; NE]	1.9010 [0.4998; 9.0323] 0.3546	
Endocrine Resistance						0.4752
Primary	15 / 127 (11.8)	NE [NE; NE]	6 / 137 (4.4)	NE [NE; NE]	2.0147 [0.8093; 5.7030] 0.1438	
Secondary	41 / 307 (13.4)	NE [NE; NE]	9 / 279 (3.2)	NE [NE; NE]	3.3681 [1.7097; 7.4168] 0.0005	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1357
Capecitabine	34 / 265 (12.8)	NE [NE; NE]	10 / 249 (4.0)	NE [NE; NE]	2.6328 [1.3474; 5.6335] 0.0053	
Nab-Paclitaxel	20 / 103 (19.4)	NE [25.8; NE]	3 / 101 (3.0)	NE [NE; NE]	5.5471 [1.8770; 23.7145] 0.0021	
Paclitaxel	2 / 66 (3.0)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	0.2401 [0.0106; 2.7018] 0.2294	
Prior anthracycline use						0.7508
Yes	30 / 197 (15.2)	NE [NE; NE]	9 / 198 (4.5)	NE [NE; NE]	2.6099 [1.2798; 5.8734] 0.0096	
No	26 / 237 (11.0)	NE [NE; NE]	6 / 219 (2.7)	NE [NE; NE]	3.2079 [1.4062; 8.6390] 0.0068	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5706
Yes	36 / 294 (12.2)	NE [NE; NE]	8 / 275 (2.9)	NE [NE; NE]	3.3247 [1.6196; 7.7305] 0.0012	
No	20 / 140 (14.3)	NE [NE; NE]	7 / 142 (4.9)	NE [NE; NE]	2.3248 [1.0215; 5.9577] 0.0499	
ECOG						0.2331
0	26 / 251 (10.4)	NE [NE; NE]	5 / 246 (2.0)	NE [NE; NE]	4.0102 [1.6689; 11.8882] 0.0022	
>=1	28 / 178 (15.7)	NE [NE; NE]	10 / 163 (6.1)	NE [NE; NE]	2.0313 [1.0105; 4.4276] 0.0526	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)						
Age at randomization						0.3641
<65 years of age	148 / 301 (49.2)	12.2 [8.8; 15.4]	67 / 285 (23.5)	NE [20.4; NE]	1.6781 [1.2611; 2.2567] 0.0004	
>=65 years of age	61 / 133 (45.9)	13.1 [8.3; NE]	39 / 132 (29.5)	NE [16.1; NE]	1.3374 [0.8982; 2.0151] 0.1555	
Race						0.2066
Asian	69 / 153 (45.1)	15.0 [9.9; 26.8]	28 / 147 (19.0)	NE [16.3; NE]	2.0878 [1.3605; 3.2921] 0.0008	
White	116 / 231 (50.2)	10.4 [7.4; 15.4]	66 / 223 (29.6)	NE [21.3; NE]	1.4177 [1.0500; 1.9300] 0.0235	
Other	24 / 50 (48.0)	14.0 [8.2; NE]	12 / 47 (25.5)	NE [5.6; NE]	1.0298 [0.5100; 2.1806] 0.9298	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1058
Asia	65 / 148 (43.9)	15.3 [11.4; 26.8]	25 / 144 (17.4)	NE [16.3; NE]	2.2442 [1.4333; 3.6266] 0.0004	
Europe	107 / 227 (47.1)	12.2 [8.6; 21.2]	59 / 206 (28.6)	21.3 [21.3; NE]	1.2785 [0.9317; 1.7711] 0.1318	
Rest of the World	37 / 59 (62.7)	7.6 [3.8; 12.1]	22 / 67 (32.8)	NE [5.5; NE]	1.6134 [0.9534; 2.7916] 0.0769	
HER2 IHC expression						0.0537
IHC 1+	114 / 239 (47.7)	12.9 [8.7; 19.0]	54 / 226 (23.9)	NE [21.3; NE]	1.6826 [1.2225; 2.3453] 0.0015	
IHC 2+/ISH-	57 / 116 (49.1)	12.2 [8.3; 23.5]	39 / 115 (33.9)	20.4 [8.1; NE]	1.0436 [0.6926; 1.5876] 0.8397	
IHC >0 <1+	37 / 76 (48.7)	11.8 [7.4; 19.2]	13 / 74 (17.6)	NE [16.3; NE]	2.5401 [1.3846; 4.9690] 0.0028	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3715
Yes	193 / 393 (49.1)	12.1 [8.9; 15.2]	100 / 377 (26.5)	NE [20.4; NE]	1.5069 [1.1855; 1.9272] 0.0008	
No	16 / 41 (39.0)	NE [8.1; NE]	6 / 40 (15.0)	NE [15.5; NE]	2.3205 [0.9532; 6.4719] 0.0711	
Prior Taxane Use In The Non-Metastatic Setting						0.2431
Yes	81 / 177 (45.8)	15.3 [8.9; 21.4]	46 / 172 (26.7)	NE [21.3; NE]	1.3583 [0.9477; 1.9698] 0.0984	
No	128 / 257 (49.8)	11.0 [8.3; 14.9]	60 / 245 (24.5)	NE [16.3; NE]	1.7303 [1.2787; 2.3685] 0.0004	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6926
1	37 / 65 (56.9)	5.2 [3.8; 15.3]	23 / 79 (29.1)	NE [13.7; NE]	2.0645 [1.2346; 3.5255] 0.0054	
2	134 / 293 (45.7)	14.9 [11.8; 19.2]	66 / 281 (23.5)	NE [21.3; NE]	1.5173 [1.1331; 2.0519] 0.0055	
>=3	38 / 75 (50.7)	9.7 [7.2; 23.5]	16 / 56 (28.6)	20.4 [20.4; NE]	1.5499 [0.8791; 2.8625] 0.1391	
ER/PR status I						0.3741
ER+, PR+	114 / 252 (45.2)	13.2 [9.9; 21.4]	52 / 234 (22.2)	NE [NE; NE]	1.6828 [1.2182; 2.3564] 0.0017	
ER+, PR-	82 / 166 (49.4)	12.4 [8.3; 18.2]	52 / 171 (30.4)	20.4 [16.1; NE]	1.2902 [0.9110; 1.8427] 0.1538	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.0618
ER <=10%	9 / 21 (42.9)	19.0 [4.2; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	171 / 362 (47.2)	13.2 [10.0; 15.9]	90 / 343 (26.2)	NE [21.3; NE]	1.4616 [1.1340; 1.8965] 0.0036	
Positive	29 / 51 (56.9)	7.2 [5.4; 14.9]	16 / 60 (26.7)	20.4 [16.3; NE]	2.1141 [1.1608; 3.9920] 0.0143	
Endocrine Resistance						0.5036
Primary	65 / 127 (51.2)	8.9 [5.4; 18.2]	35 / 137 (25.5)	NE [NE; NE]	1.8424 [1.2286; 2.8100] 0.0032	
Secondary	144 / 307 (46.9)	14.0 [10.6; 15.9]	71 / 279 (25.4)	NE [20.4; NE]	1.4583 [1.1007; 1.9497] 0.0091	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0013
Capecitabine	138 / 265 (52.1)	11.8 [8.2; 14.9]	65 / 249 (26.1)	NE [20.4; NE]	1.7127 [1.2805; 2.3152] 0.0003	
Nab-Paclitaxel	46 / 103 (44.7)	15.4 [8.1; 23.5]	17 / 101 (16.8)	NE [NE; NE]	2.3245 [1.3537; 4.1824] 0.0024	
Paclitaxel	25 / 66 (37.9)	NE [10.5; NE]	24 / 67 (35.8)	NE [3.9; NE]	0.6564 [0.3670; 1.1730] 0.1511	
Prior anthracycline use						0.3273
Yes	96 / 197 (48.7)	14.0 [8.1; 18.2]	55 / 198 (27.8)	NE [21.3; NE]	1.4045 [1.0103; 1.9718] 0.0448	
No	113 / 237 (47.7)	11.9 [8.8; 19.2]	51 / 219 (23.3)	NE [16.3; NE]	1.7179 [1.2403; 2.4128] 0.0012	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.8642
Yes	134 / 294 (45.6)	12.2 [9.7; 18.2]	67 / 275 (24.4)	NE [20.4; NE]	1.5380 [1.1501; 2.0765] 0.0039	
No	75 / 140 (53.6)	12.9 [8.1; 15.4]	39 / 142 (27.5)	NE [15.5; NE]	1.5919 [1.0868; 2.3690] 0.0179	
ECOG						0.5857
0	120 / 251 (47.8)	13.1 [8.7; 21.2]	66 / 246 (26.8)	NE [21.3; NE]	1.4968 [1.1113; 2.0335] 0.0083	
>=1	85 / 178 (47.8)	12.2 [8.9; 15.3]	37 / 163 (22.7)	20.4 [15.5; NE]	1.6884 [1.1542; 2.5186] 0.0076	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Age at randomization						0.7921
<65 years of age	33 / 301 (11.0)	NE [NE; NE]	11 / 285 (3.9)	NE [NE; NE]	1.9098 [0.9875; 3.9865] 0.0621	
>=65 years of age	11 / 133 (8.3)	NE [26.8; NE]	4 / 132 (3.0)	NE [NE; NE]	2.3251 [0.7886; 8.4302] 0.1393	
Race						0.8227
Asian	8 / 153 (5.2)	NE [NE; NE]	2 / 147 (1.4)	NE [NE; NE]	2.3874 [0.5878; 15.9656] 0.2612	
White	31 / 231 (13.4)	NE [NE; NE]	12 / 223 (5.4)	NE [NE; NE]	1.9767 [1.0386; 4.0162] 0.0422	
Other	5 / 50 (10.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	2.1147 [0.3213; 41.5472] 0.4949	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.6501
Asia	8 / 148 (5.4)	NE [NE; NE]	2 / 144 (1.4)	NE [NE; NE]	2.5049 [0.6197; 16.7114] 0.2329	
Europe	26 / 227 (11.5)	NE [NE; NE]	10 / 206 (4.9)	NE [NE; NE]	1.6986 [0.8396; 3.7185] 0.1533	
Rest of the World	10 / 59 (16.9)	NE [NE; NE]	3 / 67 (4.5)	NE [NE; NE]	3.0939 [0.9383; 13.8681] 0.0727	
HER2 IHC expression						0.4598
IHC 1+	24 / 239 (10.0)	NE [NE; NE]	6 / 226 (2.7)	NE [NE; NE]	2.9021 [1.2568; 7.8697] 0.0153	
IHC 2+/ISH-	14 / 116 (12.1)	NE [NE; NE]	5 / 115 (4.3)	NE [NE; NE]	1.8795 [0.7104; 5.8660] 0.2235	
IHC >0 <1+	6 / 76 (7.9)	NE [NE; NE]	4 / 74 (5.4)	NE [NE; NE]	1.1116 [0.3155; 4.3706] 0.8704	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2540
Yes	42 / 393 (10.7)	NE [NE; NE]	15 / 377 (4.0)	NE [NE; NE]	1.9769 [1.1160; 3.6973] 0.0221	
No	2 / 41 (4.9)	NE [NE; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.7460
Yes	14 / 177 (7.9)	NE [NE; NE]	4 / 172 (2.3)	NE [NE; NE]	2.5166 [0.8923; 8.9423] 0.0952	
No	30 / 257 (11.7)	NE [NE; NE]	11 / 245 (4.5)	NE [NE; NE]	1.9590 [1.0070; 4.1020] 0.0534	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0371
1	4 / 65 (6.2)	NE [NE; NE]	4 / 79 (5.1)	NE [NE; NE]	1.1023 [0.2602; 4.6687] 0.8907	
2	36 / 293 (12.3)	NE [NE; NE]	7 / 281 (2.5)	NE [NE; NE]	3.5439 [1.6697; 8.7240] 0.0012	
>=3	4 / 75 (5.3)	NE [26.8; NE]	4 / 56 (7.1)	NE [NE; NE]	0.5605 [0.1281; 2.4263] 0.4173	
ER/PR status I						0.6746
ER+, PR+	26 / 252 (10.3)	NE [NE; NE]	10 / 234 (4.3)	NE [NE; NE]	1.7818 [0.8825; 3.8953] 0.1177	
ER+, PR-	15 / 166 (9.0)	NE [NE; NE]	5 / 171 (2.9)	NE [NE; NE]	2.3211 [0.8848; 7.2093] 0.0982	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9558
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	36 / 362 (9.9)	NE [NE; NE]	12 / 343 (3.5)	NE [NE; NE]	2.0967 [1.1169; 4.2234] 0.0244	
Positive	8 / 51 (15.7)	NE [NE; NE]	3 / 60 (5.0)	NE [16.3; NE]	2.6257 [0.7574; 12.0087] 0.1398	
Endocrine Resistance						0.6869
Primary	11 / 127 (8.7)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	1.8078 [0.6513; 5.7792] 0.2695	
Secondary	33 / 307 (10.7)	NE [NE; NE]	10 / 279 (3.6)	NE [NE; NE]	2.2205 [1.1297; 4.7706] 0.0243	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1598
Capecitabine	31 / 265 (11.7)	NE [NE; NE]	7 / 249 (2.8)	NE [NE; NE]	3.2716 [1.5225; 8.1097] 0.0028	
Nab-Paclitaxel	7 / 103 (6.8)	NE [NE; NE]	4 / 101 (4.0)	NE [NE; NE]	1.3249 [0.3920; 5.1273] 0.6572	
Paclitaxel	6 / 66 (9.1)	NE [NE; NE]	4 / 67 (6.0)	NE [NE; NE]	0.6972 [0.1887; 2.8471] 0.5900	
Prior anthracycline use						0.1134
Yes	21 / 197 (10.7)	NE [NE; NE]	4 / 198 (2.0)	NE [NE; NE]	4.0377 [1.5258; 13.9032] 0.0060	
No	23 / 237 (9.7)	NE [NE; NE]	11 / 219 (5.0)	NE [NE; NE]	1.4041 [0.6959; 3.0099] 0.3561	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.6916
Yes	30 / 294 (10.2)	NE [NE; NE]	9 / 275 (3.3)	NE [NE; NE]	2.3106 [1.1364; 5.1893] 0.0244	
No	14 / 140 (10.0)	NE [26.8; NE]	6 / 142 (4.2)	NE [NE; NE]	1.7478 [0.6948; 4.9698] 0.2508	
ECOG						0.8568
0	29 / 251 (11.6)	NE [NE; NE]	10 / 246 (4.1)	NE [NE; NE]	2.2484 [1.1296; 4.8677] 0.0240	
>=1	15 / 178 (8.4)	NE [NE; NE]	5 / 163 (3.1)	NE [NE; NE]	1.7600 [0.6702; 5.4757] 0.2748	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Age at randomization						0.7745
<65 years of age	20 / 301 (6.6)	NE [NE; NE]	1 / 285 (0.4)	NE [NE; NE]	12.1052 [2.4968; 218.0680] 0.0020	
>=65 years of age	10 / 133 (7.5)	NE [NE; NE]	1 / 132 (0.8)	NE [NE; NE]	8.7185 [1.6678; 159.9924] 0.0128	
Race						0.2689
Asian	14 / 153 (9.2)	NE [NE; NE]	2 / 147 (1.4)	NE [NE; NE]	5.6730 [1.5801; 36.1693] 0.0097	
White	11 / 231 (4.8)	NE [NE; NE]	0 / 223 (0.0)	NE [NE; NE]	NE [NE; NE]	
Other	5 / 50 (10.0)	NE [23.5; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2764
Asia	14 / 148 (9.5)	NE [NE; NE]	2 / 144 (1.4)	NE [NE; NE]	5.7249 [1.5951; 36.4953] 0.0092	
Europe	15 / 227 (6.6)	NE [27.2; NE]	0 / 206 (0.0)	NE [NE; NE]	NE [NE; NE]	
Rest of the World	1 / 59 (1.7)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
HER2 IHC expression						0.2400
IHC 1+	14 / 239 (5.9)	NE [NE; NE]	2 / 226 (0.9)	NE [NE; NE]	4.7867 [1.3207; 30.6382] 0.0232	
IHC 2+/ISH-	9 / 116 (7.8)	NE [NE; NE]	0 / 115 (0.0)	NE [NE; NE]	NE [NE; NE]	
IHC >0 <1+	7 / 76 (9.2)	NE [NE; NE]	0 / 74 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.7013
Yes	29 / 393 (7.4)	NE [NE; NE]	2 / 377 (0.5)	NE [NE; NE]	9.6909 [2.9059; 60.0935] 0.0001	
No	1 / 41 (2.4)	NE [NE; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.0573
Yes	12 / 177 (6.8)	NE [NE; NE]	2 / 172 (1.2)	NE [NE; NE]	4.0821 [1.1002; 26.3780] 0.0477	
No	18 / 257 (7.0)	NE [NE; NE]	0 / 245 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3416
1	6 / 65 (9.2)	NE [NE; NE]	0 / 79 (0.0)	NE [NE; NE]	NE [NE; NE]	
2	19 / 293 (6.5)	NE [NE; NE]	1 / 281 (0.4)	NE [NE; NE]	11.9715 [2.4699; 215.6380] 0.0021	
>=3	5 / 75 (6.7)	NE [23.5; NE]	1 / 56 (1.8)	NE [NE; NE]	2.7192 [0.4233; 52.6254] 0.3467	
ER/PR status I						0.1121
ER+, PR+	15 / 252 (6.0)	NE [NE; NE]	2 / 234 (0.9)	NE [NE; NE]	4.6026 [1.2816; 29.3632] 0.0271	
ER+, PR-	12 / 166 (7.2)	NE [NE; NE]	0 / 171 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5642
ER <=10%	2 / 21 (9.5)	NE [15.1; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	23 / 362 (6.4)	NE [NE; NE]	2 / 343 (0.6)	NE [NE; NE]	7.8157 [2.2944; 48.8548] 0.0010	
Positive	5 / 51 (9.8)	NE [NE; NE]	0 / 60 (0.0)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						0.3231
Primary	6 / 127 (4.7)	NE [NE; NE]	0 / 137 (0.0)	NE [NE; NE]	NE [NE; NE]	
Secondary	24 / 307 (7.8)	NE [NE; NE]	2 / 279 (0.7)	NE [NE; NE]	7.6921 [2.2706; 47.9803] 0.0011	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3439
Capecitabine	19 / 265 (7.2)	NE [NE; NE]	1 / 249 (0.4)	NE [NE; NE]	12.8725 [2.6627; 231.7268] 0.0013	
Nab-Paclitaxel	6 / 103 (5.8)	NE [NE; NE]	0 / 101 (0.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	5 / 66 (7.6)	NE [NE; NE]	1 / 67 (1.5)	NE [NE; NE]	2.8312 [0.4261; 55.1927] 0.3294	
Prior anthracycline use						0.1325
Yes	13 / 197 (6.6)	NE [NE; NE]	0 / 198 (0.0)	NE [NE; NE]	NE [NE; NE]	
No	17 / 237 (7.2)	NE [NE; NE]	2 / 219 (0.9)	NE [NE; NE]	5.8709 [1.6701; 37.1379] 0.0075	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.1399
Yes	18 / 294 (6.1)	NE [NE; NE]	2 / 275 (0.7)	NE [NE; NE]	5.9920 [1.7120; 37.8405] 0.0065	
No	12 / 140 (8.6)	NE [NE; NE]	0 / 142 (0.0)	NE [NE; NE]	NE [NE; NE]	
ECOG						0.1764
0	18 / 251 (7.2)	NE [NE; NE]	2 / 246 (0.8)	NE [NE; NE]	6.2987 [1.8012; 39.7708] 0.0049	
>=1	12 / 178 (6.7)	NE [NE; NE]	0 / 163 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Age at randomization						0.9999
<65 years of age	22 / 301 (7.3)	NE [29.3; NE]	0 / 285 (0.0)	NE [NE; NE]	NE [NE; NE]	
>=65 years of age	8 / 133 (6.0)	NE [NE; NE]	0 / 132 (0.0)	NE [NE; NE]	NE [NE; NE]	
Race						1.0000
Asian	12 / 153 (7.8)	NE [NE; NE]	0 / 147 (0.0)	NE [NE; NE]	NE [NE; NE]	
White	16 / 231 (6.9)	NE [29.3; NE]	0 / 223 (0.0)	NE [NE; NE]	NE [NE; NE]	
Other	2 / 50 (4.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						1.0000
Asia	12 / 148 (8.1)	NE [NE; NE]	0 / 144 (0.0)	NE [NE; NE]	NE [NE; NE]	
Europe	14 / 227 (6.2)	NE [NE; NE]	0 / 206 (0.0)	NE [NE; NE]	NE [NE; NE]	
Rest of the World	4 / 59 (6.8)	29.3 [21.4; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
HER2 IHC expression						1.0000
IHC 1+	16 / 239 (6.7)	NE [NE; NE]	0 / 226 (0.0)	NE [NE; NE]	NE [NE; NE]	
IHC 2+/ISH-	11 / 116 (9.5)	NE [29.3; NE]	0 / 115 (0.0)	NE [NE; NE]	NE [NE; NE]	
IHC >0 <1+	3 / 76 (3.9)	NE [NE; NE]	0 / 74 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9996
Yes	24 / 393 (6.1)	NE [NE; NE]	0 / 377 (0.0)	NE [NE; NE]	NE [NE; NE]	
No	6 / 41 (14.6)	NE [NE; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.9998
Yes	10 / 177 (5.6)	NE [NE; NE]	0 / 172 (0.0)	NE [NE; NE]	NE [NE; NE]	
No	20 / 257 (7.8)	NE [29.3; NE]	0 / 245 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						1.0000
1	1 / 65 (1.5)	NE [NE; NE]	0 / 79 (0.0)	NE [NE; NE]	NE [NE; NE]	
2	23 / 293 (7.8)	NE [29.3; NE]	0 / 281 (0.0)	NE [NE; NE]	NE [NE; NE]	
>=3	6 / 75 (8.0)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.9997
ER+, PR+	14 / 252 (5.6)	NE [NE; NE]	0 / 234 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER+, PR-	15 / 166 (9.0)	NE [29.3; NE]	0 / 171 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						1.0000
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	27 / 362 (7.5)	NE [NE; NE]	0 / 343 (0.0)	NE [NE; NE]	NE [NE; NE]	
Positive	2 / 51 (3.9)	NE [NE; NE]	0 / 60 (0.0)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						1.0000
Primary	8 / 127 (6.3)	NE [NE; NE]	0 / 137 (0.0)	NE [NE; NE]	NE [NE; NE]	
Secondary	22 / 307 (7.2)	NE [NE; NE]	0 / 279 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						1.0000
Capecitabine	19 / 265 (7.2)	NE [29.3; NE]	0 / 249 (0.0)	NE [NE; NE]	NE [NE; NE]	
Nab-Paclitaxel	9 / 103 (8.7)	NE [NE; NE]	0 / 101 (0.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	2 / 66 (3.0)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						1.0000
Yes	14 / 197 (7.1)	NE [NE; NE]	0 / 198 (0.0)	NE [NE; NE]	NE [NE; NE]	
No	16 / 237 (6.8)	NE [29.3; NE]	0 / 219 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9999
Yes	18 / 294 (6.1)	NE [29.3; NE]	0 / 275 (0.0)	NE [NE; NE]	NE [NE; NE]	
No	12 / 140 (8.6)	NE [NE; NE]	0 / 142 (0.0)	NE [NE; NE]	NE [NE; NE]	
ECOG						0.9997
0	14 / 251 (5.6)	NE [29.3; NE]	0 / 246 (0.0)	NE [NE; NE]	NE [NE; NE]	
>=1	14 / 178 (7.9)	NE [NE; NE]	0 / 163 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea						
Age at randomization						0.8536
<65 years of age	17 / 301 (5.6)	NE [NE; NE]	25 / 285 (8.8)	NE [NE; NE]	0.5038 [0.2651; 0.9343] 0.0286	
>=65 years of age	10 / 133 (7.5)	NE [NE; NE]	16 / 132 (12.1)	NE [NE; NE]	0.5625 [0.2463; 1.2237] 0.1484	
Race						0.1830
Asian	8 / 153 (5.2)	NE [NE; NE]	6 / 147 (4.1)	NE [NE; NE]	1.0354 [0.3568; 3.1696] 0.9489	
White	15 / 231 (6.5)	NE [NE; NE]	31 / 223 (13.9)	NE [NE; NE]	0.3801 [0.1990; 0.6949] 0.0015	
Other	4 / 50 (8.0)	NE [NE; NE]	4 / 47 (8.5)	NE [NE; NE]	0.7741 [0.1802; 3.3139] 0.7195	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2594
Asia	7 / 148 (4.7)	NE [NE; NE]	5 / 144 (3.5)	NE [NE; NE]	1.1013 [0.3480; 3.7516] 0.8702	
Europe	16 / 227 (7.0)	NE [NE; NE]	27 / 206 (13.1)	NE [NE; NE]	0.4213 [0.2211; 0.7769] 0.0051	
Rest of the World	4 / 59 (6.8)	NE [NE; NE]	9 / 67 (13.4)	NE [NE; NE]	0.4636 [0.1254; 1.4252] 0.1903	
HER2 IHC expression						0.6298
IHC 1+	15 / 239 (6.3)	NE [NE; NE]	21 / 226 (9.3)	NE [NE; NE]	0.5785 [0.2916; 1.1195] 0.1034	
IHC 2+/ISH-	6 / 116 (5.2)	NE [NE; NE]	13 / 115 (11.3)	NE [20.4; NE]	0.3296 [0.1142; 0.8467] 0.0204	
IHC >0 <1+	6 / 76 (7.9)	NE [NE; NE]	7 / 74 (9.5)	NE [NE; NE]	0.7143 [0.2285; 2.1637] 0.5459	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8812
Yes	26 / 393 (6.6)	NE [NE; NE]	39 / 377 (10.3)	NE [NE; NE]	0.5261 [0.3156; 0.8625] 0.0105	
No	1 / 41 (2.4)	NE [NE; NE]	2 / 40 (5.0)	NE [NE; NE]	0.3891 [0.0179; 4.1226] 0.4279	
Prior Taxane Use In The Non-Metastatic Setting						0.8018
Yes	12 / 177 (6.8)	NE [NE; NE]	17 / 172 (9.9)	NE [NE; NE]	0.5863 [0.2718; 1.2242] 0.1546	
No	15 / 257 (5.8)	NE [NE; NE]	24 / 245 (9.8)	NE [NE; NE]	0.4783 [0.2441; 0.9071] 0.0232	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6891
1	6 / 65 (9.2)	NE [NE; NE]	8 / 79 (10.1)	NE [NE; NE]	0.9147 [0.3011; 2.6305] 0.8684	
2	18 / 293 (6.1)	NE [NE; NE]	27 / 281 (9.6)	NE [NE; NE]	0.4921 [0.2651; 0.8920] 0.0186	
>=3	3 / 75 (4.0)	NE [NE; NE]	5 / 56 (8.9)	NE [20.4; NE]	0.3785 [0.0766; 1.5631] 0.1719	
ER/PR status I						0.0221
ER+, PR+	18 / 252 (7.1)	NE [NE; NE]	20 / 234 (8.5)	NE [NE; NE]	0.6935 [0.3622; 1.3183] 0.2599	
ER+, PR-	4 / 166 (2.4)	NE [NE; NE]	19 / 171 (11.1)	NE [20.4; NE]	0.1642 [0.0470; 0.4438] 0.0003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4615
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	22 / 362 (6.1)	NE [NE; NE]	35 / 343 (10.2)	NE [NE; NE]	0.4892 [0.2820; 0.8308] 0.0078	
Positive	4 / 51 (7.8)	NE [NE; NE]	6 / 60 (10.0)	NE [20.4; NE]	0.7057 [0.1799; 2.4781] 0.5902	
Endocrine Resistance						0.6375
Primary	9 / 127 (7.1)	NE [NE; NE]	13 / 137 (9.5)	NE [NE; NE]	0.6675 [0.2742; 1.5541] 0.3505	
Secondary	18 / 307 (5.9)	NE [NE; NE]	28 / 279 (10.0)	NE [NE; NE]	0.4665 [0.2526; 0.8401] 0.0104	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.4251
Capecitabine	18 / 265 (6.8)	NE [NE; NE]	25 / 249 (10.0)	NE [NE; NE]	0.5473 [0.2932; 1.0014] 0.0492	
Nab-Paclitaxel	5 / 103 (4.9)	NE [NE; NE]	6 / 101 (5.9)	NE [NE; NE]	0.7520 [0.2151; 2.5129] 0.6387	
Paclitaxel	4 / 66 (6.1)	NE [NE; NE]	10 / 67 (14.9)	NE [NE; NE]	0.2798 [0.0736; 0.8677] 0.0276	
Prior anthracycline use						0.5197
Yes	12 / 197 (6.1)	NE [NE; NE]	22 / 198 (11.1)	NE [NE; NE]	0.4749 [0.2269; 0.9464] 0.0346	
No	15 / 237 (6.3)	NE [NE; NE]	19 / 219 (8.7)	NE [NE; NE]	0.5770 [0.2870; 1.1393] 0.1102	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9429
Yes	18 / 294 (6.1)	NE [NE; NE]	26 / 275 (9.5)	NE [NE; NE]	0.5194 [0.2785; 0.9475] 0.0317	
No	9 / 140 (6.4)	NE [NE; NE]	15 / 142 (10.6)	NE [NE; NE]	0.5188 [0.2171; 1.1702] 0.1150	
ECOG						0.3629
0	12 / 251 (4.8)	NE [NE; NE]	23 / 246 (9.3)	NE [NE; NE]	0.4337 [0.2082; 0.8582] 0.0163	
>=1	14 / 178 (7.9)	NE [NE; NE]	16 / 163 (9.8)	NE [20.4; NE]	0.6381 [0.3040; 1.3228] 0.2224	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: All (any PT)						
Age at randomization						0.5260
<65 years of age	122 / 301 (40.5)	NE [13.4; NE]	126 / 285 (44.2)	9.1 [5.3; 14.7]	0.7559 [0.5869; 0.9732] 0.0283	
>=65 years of age	47 / 133 (35.3)	NE [13.9; NE]	62 / 132 (47.0)	7.7 [4.0; 18.1]	0.6312 [0.4294; 0.9219] 0.0168	
Race						0.9530
Asian	49 / 153 (32.0)	NE [NE; NE]	61 / 147 (41.5)	9.2 [6.6; NE]	0.6870 [0.4688; 1.0015] 0.0499	
White	97 / 231 (42.0)	20.0 [10.5; NE]	105 / 223 (47.1)	8.3 [3.7; 14.7]	0.7122 [0.5381; 0.9416] 0.0161	
Other	23 / 50 (46.0)	13.1 [5.9; NE]	22 / 47 (46.8)	7.4 [2.0; NE]	0.7342 [0.3987; 1.3494] 0.3118	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0379
Asia	45 / 148 (30.4)	NE [NE; NE]	57 / 144 (39.6)	11.8 [7.7; NE]	0.6684 [0.4489; 0.9893] 0.0433	
Europe	88 / 227 (38.8)	22.0 [13.9; NE]	100 / 206 (48.5)	7.4 [3.4; 12.5]	0.6108 [0.4559; 0.8168] 0.0008	
Rest of the World	36 / 59 (61.0)	5.3 [2.0; 9.3]	31 / 67 (46.3)	7.2 [2.3; NE]	1.2617 [0.7776; 2.0573] 0.3506	
HER2 IHC expression						0.5886
IHC 1+	91 / 239 (38.1)	NE [14.2; NE]	105 / 226 (46.5)	8.9 [5.3; 12.5]	0.6795 [0.5109; 0.9020] 0.0072	
IHC 2+/ISH-	49 / 116 (42.2)	NE [6.5; NE]	49 / 115 (42.6)	7.4 [3.6; NE]	0.8751 [0.5861; 1.3071] 0.5058	
IHC >0 <1+	27 / 76 (35.5)	NE [10.1; NE]	34 / 74 (45.9)	8.5 [2.8; 20.9]	0.5843 [0.3474; 0.9730] 0.0369	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0707
Yes	152 / 393 (38.7)	NE [14.9; NE]	176 / 377 (46.7)	8.0 [4.9; 10.9]	0.6666 [0.5345; 0.8303] 0.0003	
No	17 / 41 (41.5)	NE [5.2; NE]	12 / 40 (30.0)	NE [5.9; NE]	1.3991 [0.6725; 3.0047] 0.3735	
Prior Taxane Use In The Non-Metastatic Setting						0.9263
Yes	68 / 177 (38.4)	NE [14.2; NE]	76 / 172 (44.2)	8.9 [5.3; 18.1]	0.7000 [0.5003; 0.9771] 0.0347	
No	101 / 257 (39.3)	NE [13.4; NE]	112 / 245 (45.7)	8.5 [3.7; 14.7]	0.7150 [0.5447; 0.9372] 0.0145	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0125
1	30 / 65 (46.2)	11.3 [3.7; NE]	33 / 79 (41.8)	8.0 [4.9; NE]	0.9975 [0.6008; 1.6481] 0.9848	
2	118 / 293 (40.3)	NE [14.5; NE]	122 / 281 (43.4)	9.5 [5.8; 20.9]	0.7932 [0.6142; 1.0240] 0.0726	
>=3	21 / 75 (28.0)	NE [14.9; NE]	32 / 56 (57.1)	4.1 [2.2; 10.9]	0.3009 [0.1680; 0.5268] <.0001	
ER/PR status I						0.9415
ER+, PR+	93 / 252 (36.9)	NE [14.9; NE]	100 / 234 (42.7)	9.5 [7.2; 20.9]	0.7136 [0.5363; 0.9486] 0.0196	
ER+, PR-	67 / 166 (40.4)	22.0 [13.1; NE]	82 / 171 (48.0)	7.6 [3.7; 14.3]	0.6794 [0.4873; 0.9433] 0.0195	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3123
ER <=10%	5 / 21 (23.8)	NE [5.5; NE]	6 / 14 (42.9)	3.7 [1.2; NE]	0.4188 [0.1174; 1.4237] 0.1476	
ER >10%	141 / 362 (39.0)	NE [14.5; NE]	155 / 343 (45.2)	9.1 [5.3; 14.3]	0.7080 [0.5617; 0.8916] 0.0031	
Positive	23 / 51 (45.1)	8.4 [3.2; NE]	27 / 60 (45.0)	8.0 [2.5; NE]	0.9231 [0.5239; 1.6128] 0.7743	
Endocrine Resistance						0.7218
Primary	47 / 127 (37.0)	NE [13.2; NE]	61 / 137 (44.5)	5.9 [3.7; NE]	0.7039 [0.4759; 1.0343] 0.0722	
Secondary	122 / 307 (39.7)	NE [13.9; NE]	127 / 279 (45.5)	9.1 [6.6; 14.3]	0.7216 [0.5613; 0.9271] 0.0101	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						<.0001
Capecitabine	125 / 265 (47.2)	13.4 [6.5; NE]	87 / 249 (34.9)	18.1 [10.9; NE]	1.2718 [0.9678; 1.6788] 0.0886	
Nab-Paclitaxel	22 / 103 (21.4)	NE [NE; NE]	51 / 101 (50.5)	6.6 [4.6; 11.9]	0.2997 [0.1763; 0.4926] <.0001	
Paclitaxel	22 / 66 (33.3)	NE [13.1; NE]	50 / 67 (74.6)	1.4 [1.0; 2.1]	0.2045 [0.1148; 0.3499] <.0001	
Prior anthracycline use						0.5691
Yes	73 / 197 (37.1)	NE [14.9; NE]	88 / 198 (44.4)	9.5 [5.3; 12.5]	0.6625 [0.4817; 0.9081] 0.0101	
No	96 / 237 (40.5)	NE [11.3; NE]	100 / 219 (45.7)	8.3 [4.6; 14.7]	0.7535 [0.5680; 0.9991] 0.0473	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.1644
Yes	112 / 294 (38.1)	NE [13.9; NE]	128 / 275 (46.5)	7.7 [4.0; 12.5]	0.6346 [0.4902; 0.8203] 0.0005	
No	57 / 140 (40.7)	NE [13.2; NE]	60 / 142 (42.3)	11.8 [7.2; NE]	0.8902 [0.6167; 1.2835] 0.5252	
ECOG						0.0020
0	107 / 251 (42.6)	22.0 [11.3; NE]	100 / 246 (40.7)	14.3 [7.7; NE]	0.9529 [0.7242; 1.2550] 0.7179	
>=1	61 / 178 (34.3)	NE [14.2; NE]	85 / 163 (52.1)	4.0 [2.8; 9.1]	0.4664 [0.3319; 0.6512] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Headache						
Age at randomization						0.5489
<65 years of age	58 / 301 (19.3)	NE [28.1; NE]	30 / 285 (10.5)	NE [NE; NE]	1.6270 [1.0508; 2.5698] 0.0310	
>=65 years of age	16 / 133 (12.0)	NE [NE; NE]	12 / 132 (9.1)	NE [NE; NE]	1.2773 [0.6069; 2.7621] 0.5219	
Race						0.4682
Asian	21 / 153 (13.7)	NE [NE; NE]	8 / 147 (5.4)	NE [NE; NE]	2.3680 [1.0854; 5.7057] 0.0333	
White	40 / 231 (17.3)	NE [NE; NE]	27 / 223 (12.1)	NE [NE; NE]	1.2914 [0.7948; 2.1304] 0.3083	
Other	13 / 50 (26.0)	28.1 [22.0; NE]	7 / 47 (14.9)	NE [NE; NE]	1.4558 [0.5760; 3.9551] 0.4382	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0990
Asia	19 / 148 (12.8)	NE [NE; NE]	5 / 144 (3.5)	NE [NE; NE]	3.4587 [1.3859; 10.4552] 0.0088	
Europe	32 / 227 (14.1)	NE [NE; NE]	23 / 206 (11.2)	NE [NE; NE]	1.1061 [0.6476; 1.9184] 0.7173	
Rest of the World	23 / 59 (39.0)	28.1 [8.1; NE]	14 / 67 (20.9)	NE [NE; NE]	1.8753 [0.9678; 3.7568] 0.0639	
HER2 IHC expression						0.2759
IHC 1+	35 / 239 (14.6)	NE [NE; NE]	19 / 226 (8.4)	NE [NE; NE]	1.5842 [0.9137; 2.8315] 0.1061	
IHC 2+/ISH-	27 / 116 (23.3)	NE [NE; NE]	12 / 115 (10.4)	NE [NE; NE]	2.1082 [1.0889; 4.3322] 0.0289	
IHC >0 <1+	11 / 76 (14.5)	NE [28.1; NE]	11 / 74 (14.9)	NE [NE; NE]	0.8039 [0.3340; 1.9120] 0.6167	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4498
Yes	67 / 393 (17.0)	NE [NE; NE]	36 / 377 (9.5)	NE [NE; NE]	1.6351 [1.0955; 2.4807] 0.0171	
No	7 / 41 (17.1)	NE [25.9; NE]	6 / 40 (15.0)	NE [NE; NE]	0.9481 [0.2961; 3.0356] 0.9266	
Prior Taxane Use In The Non-Metastatic Setting						0.2001
Yes	31 / 177 (17.5)	NE [NE; NE]	13 / 172 (7.6)	NE [NE; NE]	2.0693 [1.1019; 4.1151] 0.0260	
No	43 / 257 (16.7)	NE [28.1; NE]	29 / 245 (11.8)	NE [NE; NE]	1.2843 [0.8036; 2.0814] 0.3003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5278
1	12 / 65 (18.5)	28.1 [28.1; NE]	9 / 79 (11.4)	NE [NE; NE]	1.4548 [0.6001; 3.6190] 0.4058	
2	54 / 293 (18.4)	NE [NE; NE]	27 / 281 (9.6)	NE [NE; NE]	1.7715 [1.1249; 2.8568] 0.0145	
>=3	8 / 75 (10.7)	NE [NE; NE]	6 / 56 (10.7)	NE [NE; NE]	0.8928 [0.3100; 2.7159] 0.8357	
ER/PR status I						0.8325
ER+, PR+	41 / 252 (16.3)	NE [NE; NE]	23 / 234 (9.8)	NE [NE; NE]	1.5220 [0.9206; 2.5784] 0.1056	
ER+, PR-	29 / 166 (17.5)	NE [25.9; NE]	17 / 171 (9.9)	NE [NE; NE]	1.5253 [0.8384; 2.8566] 0.1739	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.1356
ER <=10%	3 / 21 (14.3)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	60 / 362 (16.6)	NE [NE; NE]	38 / 343 (11.1)	NE [NE; NE]	1.3357 [0.8906; 2.0272] 0.1665	
Positive	11 / 51 (21.6)	NE [NE; NE]	4 / 60 (6.7)	NE [NE; NE]	3.1654 [1.0814; 11.4284] 0.0373	
Endocrine Resistance						0.9180
Primary	21 / 127 (16.5)	NE [NE; NE]	13 / 137 (9.5)	NE [NE; NE]	1.6454 [0.8304; 3.3838] 0.1582	
Secondary	53 / 307 (17.3)	NE [28.1; NE]	29 / 279 (10.4)	NE [NE; NE]	1.5019 [0.9603; 2.3960] 0.0784	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0168
Capecitabine	56 / 265 (21.1)	NE [28.1; NE]	23 / 249 (9.2)	NE [NE; NE]	2.1809 [1.3596; 3.6186] 0.0013	
Nab-Paclitaxel	11 / 103 (10.7)	NE [25.9; NE]	8 / 101 (7.9)	NE [NE; NE]	1.1382 [0.4461; 2.9966] 0.7871	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	11 / 67 (16.4)	NE [NE; NE]	0.5067 [0.1855; 1.2940] 0.1546	
Prior anthracycline use						0.3786
Yes	33 / 197 (16.8)	NE [NE; NE]	16 / 198 (8.1)	NE [NE; NE]	1.8583 [1.0347; 3.4769] 0.0405	
No	41 / 237 (17.3)	NE [28.1; NE]	26 / 219 (11.9)	NE [NE; NE]	1.3337 [0.8188; 2.2109] 0.2538	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.3686
Yes	55 / 294 (18.7)	NE [28.1; NE]	27 / 275 (9.8)	NE [NE; NE]	1.7078 [1.0839; 2.7552] 0.0225	
No	19 / 140 (13.6)	NE [NE; NE]	15 / 142 (10.6)	NE [NE; NE]	1.1900 [0.6042; 2.3856] 0.6191	
ECOG						0.1147
0	51 / 251 (20.3)	NE [28.1; NE]	24 / 246 (9.8)	NE [NE; NE]	1.9658 [1.2215; 3.2544] 0.0057	
>=1	23 / 178 (12.9)	NE [NE; NE]	18 / 163 (11.0)	NE [NE; NE]	1.0028 [0.5395; 1.8916] 0.9944	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Dysgeusia						
Age at randomization						0.9472
<65 years of age	36 / 301 (12.0)	NE [NE; NE]	16 / 285 (5.6)	NE [NE; NE]	1.8378 [1.0348; 3.4127] 0.0408	
>=65 years of age	15 / 133 (11.3)	NE [NE; NE]	8 / 132 (6.1)	NE [NE; NE]	1.7270 [0.7497; 4.2923] 0.2069	
Race						0.0711
Asian	17 / 153 (11.1)	NE [NE; NE]	5 / 147 (3.4)	NE [NE; NE]	3.1043 [1.2262; 9.4518] 0.0191	
White	31 / 231 (13.4)	NE [NE; NE]	14 / 223 (6.3)	NE [NE; NE]	1.8239 [0.9868; 3.5457] 0.0592	
Other	3 / 50 (6.0)	NE [NE; NE]	5 / 47 (10.6)	NE [NE; NE]	0.4423 [0.0877; 1.8550] 0.2638	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0172
Asia	15 / 148 (10.1)	NE [NE; NE]	4 / 144 (2.8)	NE [NE; NE]	3.4084 [1.2350; 11.9687] 0.0207	
Europe	27 / 227 (11.9)	NE [NE; NE]	19 / 206 (9.2)	NE [NE; NE]	1.0595 [0.5898; 1.9418] 0.8473	
Rest of the World	9 / 59 (15.3)	NE [NE; NE]	1 / 67 (1.5)	NE [NE; NE]	9.5313 [1.7840; 175.9174] 0.0090	
HER2 IHC expression						0.3162
IHC 1+	29 / 239 (12.1)	NE [NE; NE]	11 / 226 (4.9)	NE [NE; NE]	2.2007 [1.1287; 4.6132] 0.0228	
IHC 2+/ISH-	16 / 116 (13.8)	NE [NE; NE]	7 / 115 (6.1)	NE [NE; NE]	2.0597 [0.8765; 5.3735] 0.1046	
IHC >0 <1+	6 / 76 (7.9)	NE [NE; NE]	6 / 74 (8.1)	NE [NE; NE]	0.8062 [0.2511; 2.5877] 0.7097	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1914
Yes	49 / 393 (12.5)	NE [NE; NE]	24 / 377 (6.4)	NE [NE; NE]	1.7057 [1.0562; 2.8306] 0.0308	
No	2 / 41 (4.9)	NE [NE; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.5934
Yes	18 / 177 (10.2)	NE [NE; NE]	10 / 172 (5.8)	NE [NE; NE]	1.4720 [0.6884; 3.3307] 0.3270	
No	33 / 257 (12.8)	NE [NE; NE]	14 / 245 (5.7)	NE [NE; NE]	2.0218 [1.1039; 3.9072] 0.0245	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6748
1	8 / 65 (12.3)	NE [NE; NE]	6 / 79 (7.6)	NE [NE; NE]	1.4901 [0.5150; 4.5473] 0.4610	
2	38 / 293 (13.0)	NE [NE; NE]	15 / 281 (5.3)	NE [NE; NE]	2.1124 [1.1840; 3.9683] 0.0125	
>=3	5 / 75 (6.7)	NE [NE; NE]	3 / 56 (5.4)	NE [NE; NE]	1.0479 [0.2539; 5.1521] 0.9460	
ER/PR status I						0.5124
ER+, PR+	30 / 252 (11.9)	NE [NE; NE]	16 / 234 (6.8)	NE [NE; NE]	1.4840 [0.8183; 2.7936] 0.2010	
ER+, PR-	18 / 166 (10.8)	NE [NE; NE]	8 / 171 (4.7)	NE [NE; NE]	2.0647 [0.9219; 5.0557] 0.0834	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.6539
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	41 / 362 (11.3)	NE [NE; NE]	20 / 343 (5.8)	NE [NE; NE]	1.6898 [1.0006; 2.9486] 0.0529	
Positive	9 / 51 (17.6)	NE [NE; NE]	4 / 60 (6.7)	NE [NE; NE]	2.5347 [0.8245; 9.3661] 0.1088	
Endocrine Resistance						0.8598
Primary	12 / 127 (9.4)	NE [NE; NE]	6 / 137 (4.4)	NE [NE; NE]	1.9042 [0.7336; 5.5012] 0.1934	
Secondary	39 / 307 (12.7)	NE [NE; NE]	18 / 279 (6.5)	NE [NE; NE]	1.7307 [1.0039; 3.1012] 0.0520	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0067
Capecitabine	40 / 265 (15.1)	NE [NE; NE]	11 / 249 (4.4)	NE [NE; NE]	3.0479 [1.6183; 6.2490] 0.0006	
Nab-Paclitaxel	4 / 103 (3.9)	NE [NE; NE]	3 / 101 (3.0)	NE [NE; NE]	1.1650 [0.2544; 5.9541] 0.8423	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	10 / 67 (14.9)	NE [NE; NE]	0.5482 [0.1958; 1.4471] 0.2240	
Prior anthracycline use						0.3459
Yes	19 / 197 (9.6)	NE [NE; NE]	12 / 198 (6.1)	NE [NE; NE]	1.3957 [0.6827; 2.9671] 0.3661	
No	32 / 237 (13.5)	NE [NE; NE]	12 / 219 (5.5)	NE [NE; NE]	2.1793 [1.1511; 4.4119] 0.0187	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0981
Yes	28 / 294 (9.5)	NE [NE; NE]	17 / 275 (6.2)	NE [NE; NE]	1.2934 [0.7127; 2.4171] 0.4042	
No	23 / 140 (16.4)	NE [NE; NE]	7 / 142 (4.9)	NE [NE; NE]	3.1484 [1.4183; 7.9494] 0.0052	
ECOG						0.4892
0	32 / 251 (12.7)	NE [NE; NE]	14 / 246 (5.7)	NE [NE; NE]	1.9937 [1.0837; 3.8638] 0.0287	
>=1	18 / 178 (10.1)	NE [NE; NE]	10 / 163 (6.1)	NE [NE; NE]	1.4596 [0.6854; 3.2920] 0.3358	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Paraesthesia						
Age at randomization						0.0182
<65 years of age	8 / 301 (2.7)	NE [NE; NE]	18 / 285 (6.3)	NE [NE; NE]	0.2981 [0.1207; 0.6738] 0.0031	
>=65 years of age	4 / 133 (3.0)	NE [29.7; NE]	1 / 132 (0.8)	NE [NE; NE]	3.0804 [0.4503; 60.5138] 0.2918	
Race						0.2315
Asian	0 / 153 (0.0)	NE [NE; NE]	3 / 147 (2.0)	NE [NE; NE]	NE [NE; NE]	
White	10 / 231 (4.3)	NE [29.7; NE]	14 / 223 (6.3)	NE [NE; NE]	0.4965 [0.2056; 1.1391] 0.0972	
Other	2 / 50 (4.0)	NE [NE; NE]	2 / 47 (4.3)	NE [NE; NE]	0.4564 [0.0494; 4.2189] 0.4548	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.3503
Asia	0 / 148 (0.0)	NE [NE; NE]	2 / 144 (1.4)	NE [NE; NE]	NE [NE; NE]	
Europe	8 / 227 (3.5)	NE [29.7; NE]	12 / 206 (5.8)	NE [NE; NE]	0.3904 [0.1435; 0.9837] 0.0438	
Rest of the World	4 / 59 (6.8)	NE [NE; NE]	5 / 67 (7.5)	NE [NE; NE]	0.7234 [0.1764; 2.7698] 0.6320	
HER2 IHC expression						0.1692
IHC 1+	8 / 239 (3.3)	NE [NE; NE]	11 / 226 (4.9)	NE [NE; NE]	0.5276 [0.2024; 1.3155] 0.1665	
IHC 2+/ISH-	1 / 116 (0.9)	NE [29.7; NE]	6 / 115 (5.2)	NE [NE; NE]	0.1139 [0.0058; 0.7198] 0.0235	
IHC >0 <1+	3 / 76 (3.9)	NE [NE; NE]	2 / 74 (2.7)	NE [NE; NE]	1.0197 [0.1669; 7.8226] 0.9830	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9997
Yes	12 / 393 (3.1)	NE [29.7; NE]	19 / 377 (5.0)	NE [NE; NE]	0.4383 [0.2046; 0.9023] 0.0238	
No	0 / 41 (0.0)	NE [NE; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.4130
Yes	4 / 177 (2.3)	NE [NE; NE]	9 / 172 (5.2)	NE [NE; NE]	0.3524 [0.0946; 1.0932] 0.0726	
No	8 / 257 (3.1)	NE [29.7; NE]	10 / 245 (4.1)	NE [NE; NE]	0.5310 [0.1991; 1.3683] 0.1835	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.2871
1	5 / 65 (7.7)	NE [NE; NE]	5 / 79 (6.3)	NE [NE; NE]	0.9080 [0.2482; 3.3174] 0.8806	
2	4 / 293 (1.4)	NE [NE; NE]	11 / 281 (3.9)	NE [NE; NE]	0.2805 [0.0772; 0.8279] 0.0214	
>=3	3 / 75 (4.0)	NE [29.7; NE]	3 / 56 (5.4)	NE [NE; NE]	0.4104 [0.0537; 2.4944] 0.3159	
ER/PR status I						0.0710
ER+, PR+	3 / 252 (1.2)	NE [NE; NE]	11 / 234 (4.7)	NE [NE; NE]	0.1989 [0.0447; 0.6425] 0.0063	
ER+, PR-	8 / 166 (4.8)	NE [29.7; NE]	8 / 171 (4.7)	NE [NE; NE]	0.6911 [0.2484; 1.9169] 0.4681	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.8300
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	1 / 14 (7.1)	NE [NE; NE]	0.6831 [0.0270; 17.2611] 0.7863	
ER >10%	10 / 362 (2.8)	NE [29.7; NE]	17 / 343 (5.0)	NE [NE; NE]	0.3860 [0.1670; 0.8446] 0.0160	
Positive	1 / 51 (2.0)	NE [NE; NE]	1 / 60 (1.7)	NE [NE; NE]	1.0180 [0.0401; 25.8445] 0.9899	
Endocrine Resistance						0.2952
Primary	2 / 127 (1.6)	NE [NE; NE]	7 / 137 (5.1)	NE [NE; NE]	0.2457 [0.0364; 1.0282] 0.0602	
Secondary	10 / 307 (3.3)	NE [29.7; NE]	12 / 279 (4.3)	NE [NE; NE]	0.5469 [0.2279; 1.2837] 0.1593	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.6029
Capecitabine	8 / 265 (3.0)	NE [29.7; NE]	10 / 249 (4.0)	NE [NE; NE]	0.5940 [0.2246; 1.5195] 0.2717	
Nab-Paclitaxel	2 / 103 (1.9)	NE [NE; NE]	4 / 101 (4.0)	NE [NE; NE]	0.4067 [0.0557; 2.1131] 0.2879	
Paclitaxel	2 / 66 (3.0)	NE [NE; NE]	5 / 67 (7.5)	NE [NE; NE]	0.1148 [0.0128; 0.7043] 0.0180	
Prior anthracycline use						0.2071
Yes	4 / 197 (2.0)	NE [NE; NE]	11 / 198 (5.6)	NE [NE; NE]	0.2844 [0.0781; 0.8410] 0.0233	
No	8 / 237 (3.4)	NE [29.7; NE]	8 / 219 (3.7)	NE [NE; NE]	0.6534 [0.2356; 1.8071] 0.4006	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9799
Yes	8 / 294 (2.7)	NE [29.7; NE]	12 / 275 (4.4)	NE [NE; NE]	0.3709 [0.1366; 0.9334] 0.0326	
No	4 / 140 (2.9)	NE [NE; NE]	7 / 142 (4.9)	NE [NE; NE]	0.5293 [0.1382; 1.7589] 0.3029	
ECOG						0.2473
0	6 / 251 (2.4)	NE [29.7; NE]	13 / 246 (5.3)	NE [NE; NE]	0.3102 [0.1067; 0.8019] 0.0148	
>=1	6 / 178 (3.4)	NE [NE; NE]	5 / 163 (3.1)	NE [NE; NE]	0.8778 [0.2599; 3.0864] 0.8318	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Age at randomization						0.6135
<65 years of age	7 / 301 (2.3)	NE [NE; NE]	31 / 285 (10.9)	NE [NE; NE]	0.1711 [0.0689; 0.3683] <.0001	
>=65 years of age	5 / 133 (3.8)	NE [NE; NE]	18 / 132 (13.6)	NE [NE; NE]	0.2419 [0.0798; 0.6069] 0.0023	
Race						0.8904
Asian	5 / 153 (3.3)	NE [NE; NE]	20 / 147 (13.6)	NE [NE; NE]	0.1977 [0.0656; 0.4896] 0.0003	
White	6 / 231 (2.6)	NE [NE; NE]	23 / 223 (10.3)	NE [NE; NE]	0.2115 [0.0779; 0.4890] 0.0002	
Other	1 / 50 (2.0)	NE [NE; NE]	6 / 47 (12.8)	NE [NE; NE]	0.1409 [0.0075; 0.8266] 0.0344	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1894
Asia	5 / 148 (3.4)	NE [NE; NE]	20 / 144 (13.9)	NE [NE; NE]	0.1994 [0.0662; 0.4938] 0.0004	
Europe	7 / 227 (3.1)	NE [NE; NE]	21 / 206 (10.2)	NE [NE; NE]	0.2493 [0.0978; 0.5620] 0.0006	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	8 / 67 (11.9)	NE [NE; NE]	NE [NE; NE]	
HER2 IHC expression						0.0658
IHC 1+	9 / 239 (3.8)	NE [NE; NE]	24 / 226 (10.6)	NE [NE; NE]	0.3100 [0.1361; 0.6452] 0.0016	
IHC 2+/ISH-	3 / 116 (2.6)	NE [NE; NE]	16 / 115 (13.9)	NE [NE; NE]	0.1355 [0.0312; 0.4126] 0.0003	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	9 / 74 (12.2)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4776
Yes	10 / 393 (2.5)	NE [NE; NE]	44 / 377 (11.7)	NE [NE; NE]	0.1820 [0.0863; 0.3474] <.0001	
No	2 / 41 (4.9)	NE [NE; NE]	5 / 40 (12.5)	NE [NE; NE]	0.3348 [0.0478; 1.5609] 0.1711	
Prior Taxane Use In The Non-Metastatic Setting						0.9029
Yes	5 / 177 (2.8)	NE [NE; NE]	20 / 172 (11.6)	NE [NE; NE]	0.2114 [0.0703; 0.5228] 0.0006	
No	7 / 257 (2.7)	NE [NE; NE]	29 / 245 (11.8)	NE [NE; NE]	0.1861 [0.0747; 0.4027] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.7897
1	1 / 65 (1.5)	NE [NE; NE]	10 / 79 (12.7)	NE [NE; NE]	0.1135 [0.0062; 0.5932] 0.0122	
2	7 / 293 (2.4)	NE [NE; NE]	28 / 281 (10.0)	NE [NE; NE]	0.1997 [0.0801; 0.4334] <.0001	
>=3	4 / 75 (5.3)	NE [NE; NE]	11 / 56 (19.6)	NE [NE; NE]	0.2041 [0.0559; 0.6055] 0.0031	
ER/PR status I						0.4847
ER+, PR+	7 / 252 (2.8)	NE [NE; NE]	23 / 234 (9.8)	NE [NE; NE]	0.2342 [0.0926; 0.5207] 0.0003	
ER+, PR-	4 / 166 (2.4)	NE [NE; NE]	24 / 171 (14.0)	NE [NE; NE]	0.1419 [0.0415; 0.3698] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.3358
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	3 / 14 (21.4)	NE [3.7; NE]	NE [NE; NE]	
ER >10%	10 / 362 (2.8)	NE [NE; NE]	38 / 343 (11.1)	NE [NE; NE]	0.2055 [0.0966; 0.3976] <.0001	
Positive	2 / 51 (3.9)	NE [NE; NE]	8 / 60 (13.3)	NE [NE; NE]	0.2586 [0.0390; 1.0351] 0.0658	
Endocrine Resistance						0.9458
Primary	4 / 127 (3.1)	NE [NE; NE]	19 / 137 (13.9)	NE [NE; NE]	0.1982 [0.0573; 0.5287] 0.0011	
Secondary	8 / 307 (2.6)	NE [NE; NE]	30 / 279 (10.8)	NE [NE; NE]	0.1952 [0.0832; 0.4071] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0057
Capecitabine	8 / 265 (3.0)	NE [NE; NE]	13 / 249 (5.2)	NE [NE; NE]	0.5122 [0.2023; 1.2181] 0.1305	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	11 / 101 (10.9)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	4 / 66 (6.1)	NE [NE; NE]	25 / 67 (37.3)	NE [2.7; NE]	0.0831 [0.0238; 0.2222] <.0001	
Prior anthracycline use						0.1626
Yes	7 / 197 (3.6)	NE [NE; NE]	19 / 198 (9.6)	NE [NE; NE]	0.3265 [0.1274; 0.7439] 0.0078	
No	5 / 237 (2.1)	NE [NE; NE]	30 / 219 (13.7)	NE [NE; NE]	0.1231 [0.0418; 0.2915] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.8495
Yes	9 / 294 (3.1)	NE [NE; NE]	34 / 275 (12.4)	NE [NE; NE]	0.2042 [0.0918; 0.4088] <.0001	
No	3 / 140 (2.1)	NE [NE; NE]	15 / 142 (10.6)	NE [NE; NE]	0.1687 [0.0390; 0.5134] 0.0015	
ECOG						0.3987
0	6 / 251 (2.4)	NE [NE; NE]	19 / 246 (7.7)	NE [NE; NE]	0.2601 [0.0945; 0.6171] 0.0020	
>=1	6 / 178 (3.4)	NE [NE; NE]	29 / 163 (17.8)	NE [NE; NE]	0.1525 [0.0570; 0.3441] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Age at randomization						0.9833
<65 years of age	5 / 301 (1.7)	NE [NE; NE]	21 / 285 (7.4)	NE [NE; NE]	0.1775 [0.0590; 0.4385] 0.0001	
>=65 years of age	3 / 133 (2.3)	NE [NE; NE]	15 / 132 (11.4)	NE [NE; NE]	0.1679 [0.0388; 0.5096] 0.0014	
Race						0.8600
Asian	1 / 153 (0.7)	NE [NE; NE]	8 / 147 (5.4)	NE [NE; NE]	0.1046 [0.0056; 0.5722] 0.0093	
White	5 / 231 (2.2)	NE [NE; NE]	20 / 223 (9.0)	NE [NE; NE]	0.1802 [0.0597; 0.4475] 0.0001	
Other	2 / 50 (4.0)	NE [NE; NE]	8 / 47 (17.0)	NE [NE; NE]	0.1794 [0.0267; 0.7310] 0.0166	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7858
Asia	2 / 148 (1.4)	NE [NE; NE]	6 / 144 (4.2)	NE [NE; NE]	0.2812 [0.0411; 1.2245] 0.0978	
Europe	5 / 227 (2.2)	NE [NE; NE]	24 / 206 (11.7)	NE [NE; NE]	0.1423 [0.0477; 0.3457] <.0001	
Rest of the World	1 / 59 (1.7)	NE [NE; NE]	6 / 67 (9.0)	NE [NE; NE]	0.1387 [0.0073; 0.8302] 0.0356	
HER2 IHC expression						0.1100
IHC 1+	4 / 239 (1.7)	NE [NE; NE]	19 / 226 (8.4)	NE [NE; NE]	0.1690 [0.0489; 0.4507] 0.0003	
IHC 2+/ISH-	4 / 116 (3.4)	NE [NE; NE]	9 / 115 (7.8)	NE [NE; NE]	0.3147 [0.0844; 0.9785] 0.0449	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	8 / 74 (10.8)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5565
Yes	8 / 393 (2.0)	NE [NE; NE]	35 / 377 (9.3)	NE [NE; NE]	0.1709 [0.0734; 0.3512] <.0001	
No	0 / 41 (0.0)	NE [NE; NE]	1 / 40 (2.5)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.4478
Yes	4 / 177 (2.3)	NE [NE; NE]	13 / 172 (7.6)	NE [NE; NE]	0.2370 [0.0664; 0.6745] 0.0066	
No	4 / 257 (1.6)	NE [NE; NE]	23 / 245 (9.4)	NE [NE; NE]	0.1321 [0.0386; 0.3445] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0153
1	4 / 65 (6.2)	NE [NE; NE]	6 / 79 (7.6)	NE [NE; NE]	0.6843 [0.1733; 2.4184] 0.5577	
2	4 / 293 (1.4)	NE [NE; NE]	22 / 281 (7.8)	NE [NE; NE]	0.1346 [0.0393; 0.3532] <.0001	
>=3	0 / 75 (0.0)	NE [NE; NE]	8 / 56 (14.3)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.2258
ER+, PR+	3 / 252 (1.2)	NE [NE; NE]	23 / 234 (9.8)	NE [NE; NE]	0.0910 [0.0215; 0.2625] <.0001	
ER+, PR-	4 / 166 (2.4)	NE [NE; NE]	13 / 171 (7.6)	NE [NE; NE]	0.2701 [0.0757; 0.7678] 0.0148	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4293
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	1 / 14 (7.1)	NE [NE; NE]	NE [NE; NE]	
ER >10%	8 / 362 (2.2)	NE [NE; NE]	32 / 343 (9.3)	NE [NE; NE]	0.1885 [0.0806; 0.3904] <.0001	
Positive	0 / 51 (0.0)	NE [NE; NE]	3 / 60 (5.0)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						0.5534
Primary	3 / 127 (2.4)	NE [NE; NE]	11 / 137 (8.0)	NE [NE; NE]	0.2304 [0.0517; 0.7458] 0.0150	
Secondary	5 / 307 (1.6)	NE [NE; NE]	25 / 279 (9.0)	NE [NE; NE]	0.1451 [0.0489; 0.3496] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0043
Capecitabine	7 / 265 (2.6)	NE [NE; NE]	11 / 249 (4.4)	NE [NE; NE]	0.4542 [0.1663; 1.1601] 0.0964	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	13 / 101 (12.9)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	1 / 66 (1.5)	NE [NE; NE]	12 / 67 (17.9)	NE [NE; NE]	0.0666 [0.0036; 0.3394] 0.0006	
Prior anthracycline use						0.0636
Yes	6 / 197 (3.0)	NE [NE; NE]	15 / 198 (7.6)	NE [NE; NE]	0.3340 [0.1187; 0.8250] 0.0177	
No	2 / 237 (0.8)	NE [NE; NE]	21 / 219 (9.6)	NE [NE; NE]	0.0678 [0.0108; 0.2320] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.2151
Yes	7 / 294 (2.4)	NE [NE; NE]	23 / 275 (8.4)	NE [NE; NE]	0.2276 [0.0899; 0.5069] 0.0002	
No	1 / 140 (0.7)	NE [NE; NE]	13 / 142 (9.2)	NE [NE; NE]	0.0616 [0.0034; 0.3104] 0.0003	
ECOG						0.3520
0	5 / 251 (2.0)	NE [NE; NE]	17 / 246 (6.9)	NE [NE; NE]	0.2435 [0.0798; 0.6178] 0.0027	
>=1	3 / 178 (1.7)	NE [NE; NE]	19 / 163 (11.7)	NE [NE; NE]	0.1038 [0.0243; 0.3069] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Age at randomization						0.5106
<65 years of age	4 / 301 (1.3)	NE [NE; NE]	7 / 285 (2.5)	NE [NE; NE]	0.4121 [0.1066; 1.3821] 0.1493	
>=65 years of age	1 / 133 (0.8)	NE [NE; NE]	5 / 132 (3.8)	NE [NE; NE]	0.1754 [0.0092; 1.0886] 0.0723	
Race						0.0117
Asian	1 / 153 (0.7)	NE [NE; NE]	10 / 147 (6.8)	NE [NE; NE]	0.0801 [0.0044; 0.4199] 0.0020	
White	4 / 231 (1.7)	NE [NE; NE]	1 / 223 (0.4)	NE [NE; NE]	2.8351 [0.4144; 55.6973] 0.3323	
Other	0 / 50 (0.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0421
Asia	1 / 148 (0.7)	NE [NE; NE]	10 / 144 (6.9)	NE [NE; NE]	0.0811 [0.0044; 0.4249] 0.0022	
Europe	2 / 227 (0.9)	NE [NE; NE]	1 / 206 (0.5)	NE [NE; NE]	1.3847 [0.1311; 29.9922] 0.7906	
Rest of the World	2 / 59 (3.4)	NE [NE; NE]	1 / 67 (1.5)	NE [NE; NE]	1.5654 [0.1450; 34.2625] 0.7160	
HER2 IHC expression						0.6046
IHC 1+	2 / 239 (0.8)	NE [NE; NE]	8 / 226 (3.5)	NE [NE; NE]	0.1980 [0.0298; 0.7936] 0.0232	
IHC 2+/ISH-	2 / 116 (1.7)	NE [NE; NE]	3 / 115 (2.6)	NE [NE; NE]	0.4815 [0.0632; 2.9167] 0.4143	
IHC >0 <1+	1 / 76 (1.3)	NE [NE; NE]	1 / 74 (1.4)	NE [NE; NE]	0.7033 [0.0273; 18.1005] 0.8044	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2463
Yes	5 / 393 (1.3)	NE [NE; NE]	10 / 377 (2.7)	NE [NE; NE]	0.3550 [0.1099; 1.0070] 0.0502	
No	0 / 41 (0.0)	NE [NE; NE]	2 / 40 (5.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.1245
Yes	0 / 177 (0.0)	NE [NE; NE]	3 / 172 (1.7)	NE [NE; NE]	NE [NE; NE]	
No	5 / 257 (1.9)	NE [NE; NE]	9 / 245 (3.7)	NE [NE; NE]	0.4100 [0.1254; 1.1933] 0.1005	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1741
1	1 / 65 (1.5)	NE [NE; NE]	1 / 79 (1.3)	NE [NE; NE]	1.1843 [0.0468; 29.9483] 0.9047	
2	3 / 293 (1.0)	NE [NE; NE]	11 / 281 (3.9)	NE [NE; NE]	0.1983 [0.0447; 0.6392] 0.0061	
>=3	1 / 75 (1.3)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.3816
ER+, PR+	3 / 252 (1.2)	NE [NE; NE]	4 / 234 (1.7)	NE [NE; NE]	0.5065 [0.0983; 2.3339] 0.3701	
ER+, PR-	2 / 166 (1.2)	NE [NE; NE]	8 / 171 (4.7)	NE [NE; NE]	0.2197 [0.0331; 0.8799] 0.0358	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9328
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	4 / 362 (1.1)	NE [NE; NE]	10 / 343 (2.9)	NE [NE; NE]	0.2960 [0.0806; 0.8925] 0.0303	
Positive	1 / 51 (2.0)	NE [NE; NE]	2 / 60 (3.3)	NE [NE; NE]	0.4597 [0.0213; 4.8097] 0.5158	
Endocrine Resistance						0.4518
Primary	1 / 127 (0.8)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	0.1964 [0.0102; 1.2198] 0.0982	
Secondary	4 / 307 (1.3)	NE [NE; NE]	7 / 279 (2.5)	NE [NE; NE]	0.3833 [0.0998; 1.2786] 0.1146	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0215
Capecitabine	5 / 265 (1.9)	NE [NE; NE]	4 / 249 (1.6)	NE [NE; NE]	0.9050 [0.2385; 3.6693] 0.8821	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	8 / 101 (7.9)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.2497
Yes	1 / 197 (0.5)	NE [NE; NE]	6 / 198 (3.0)	NE [NE; NE]	0.1271 [0.0067; 0.7604] 0.0262	
No	4 / 237 (1.7)	NE [NE; NE]	6 / 219 (2.7)	NE [NE; NE]	0.4841 [0.1233; 1.7020] 0.2525	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0247
Yes	5 / 294 (1.7)	NE [NE; NE]	6 / 275 (2.2)	NE [NE; NE]	0.6095 [0.1744; 2.0366] 0.4117	
No	0 / 140 (0.0)	NE [NE; NE]	6 / 142 (4.2)	NE [NE; NE]	NE [NE; NE]	
ECOG						0.4539
0	4 / 251 (1.6)	NE [NE; NE]	7 / 246 (2.8)	NE [NE; NE]	0.4124 [0.1074; 1.3758] 0.1473	
>=1	1 / 178 (0.6)	NE [NE; NE]	4 / 163 (2.5)	NE [NE; NE]	0.2110 [0.0108; 1.4289] 0.1249	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Blood and lymphatic system disorders; PT: Anaemia						
Age at randomization						0.7746
<65 years of age	104 / 301 (34.6)	NE [21.5; NE]	64 / 285 (22.5)	NE [NE; NE]	1.3426 [0.9841; 1.8456] 0.0665	
>=65 years of age	55 / 133 (41.4)	NE [8.9; NE]	43 / 132 (32.6)	NE [14.3; NE]	1.2408 [0.8340; 1.8580] 0.2875	
Race						0.5801
Asian	68 / 153 (44.4)	16.1 [9.0; NE]	41 / 147 (27.9)	NE [NE; NE]	1.4201 [0.9673; 2.1106] 0.0763	
White	74 / 231 (32.0)	NE [21.5; NE]	57 / 223 (25.6)	NE [18.7; NE]	1.1418 [0.8087; 1.6203] 0.4576	
Other	17 / 50 (34.0)	NE [9.3; NE]	9 / 47 (19.1)	NE [NE; NE]	1.7013 [0.7673; 4.0243] 0.2004	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5267
Asia	67 / 148 (45.3)	16.1 [8.5; NE]	42 / 144 (29.2)	NE [NE; NE]	1.3676 [0.9327; 2.0281] 0.1122	
Europe	84 / 227 (37.0)	NE [21.5; NE]	55 / 206 (26.7)	NE [NE; NE]	1.2883 [0.9188; 1.8208] 0.1470	
Rest of the World	8 / 59 (13.6)	NE [NE; NE]	10 / 67 (14.9)	NE [18.7; NE]	0.7634 [0.2885; 1.9539] 0.5712	
HER2 IHC expression						0.4341
IHC 1+	90 / 239 (37.7)	25.9 [16.1; NE]	56 / 226 (24.8)	NE [NE; NE]	1.3781 [0.9890; 1.9368] 0.0597	
IHC 2+/ISH-	36 / 116 (31.0)	NE [21.5; NE]	30 / 115 (26.1)	NE [NE; NE]	1.0140 [0.6234; 1.6609] 0.9649	
IHC >0 <1+	32 / 76 (42.1)	NE [4.6; NE]	21 / 74 (28.4)	NE [18.7; NE]	1.4454 [0.8382; 2.5452] 0.1886	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.8734
Yes	141 / 393 (35.9)	NE [21.5; NE]	93 / 377 (24.7)	NE [NE; NE]	1.3026 [1.0032; 1.6990] 0.0486	
No	18 / 41 (43.9)	NE [2.9; NE]	14 / 40 (35.0)	18.7 [6.6; NE]	1.2057 [0.5989; 2.4762] 0.6066	
Prior Taxane Use In The Non-Metastatic Setting						0.3541
Yes	67 / 177 (37.9)	25.9 [16.1; NE]	40 / 172 (23.3)	NE [NE; NE]	1.4961 [1.0145; 2.2347] 0.0445	
No	92 / 257 (35.8)	NE [18.8; NE]	67 / 245 (27.3)	NE [18.7; NE]	1.1620 [0.8485; 1.5995] 0.3524	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.8659
1	26 / 65 (40.0)	NE [6.2; NE]	21 / 79 (26.6)	NE [NE; NE]	1.4650 [0.8223; 2.6398] 0.2003	
2	106 / 293 (36.2)	25.9 [21.5; NE]	72 / 281 (25.6)	NE [NE; NE]	1.2366 [0.9175; 1.6760] 0.1646	
>=3	26 / 75 (34.7)	NE [11.7; NE]	14 / 56 (25.0)	NE [NE; NE]	1.3039 [0.6909; 2.5679] 0.4256	
ER/PR status I						0.8247
ER+, PR+	92 / 252 (36.5)	NE [18.8; NE]	58 / 234 (24.8)	NE [NE; NE]	1.3372 [0.9645; 1.8688] 0.0842	
ER+, PR-	63 / 166 (38.0)	NE [16.1; NE]	46 / 171 (26.9)	NE [NE; NE]	1.2621 [0.8627; 1.8598] 0.2342	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9445
ER <=10%	7 / 21 (33.3)	NE [2.1; NE]	3 / 14 (21.4)	NE [1.9; NE]	1.3491 [0.3727; 6.2858] 0.6617	
ER >10%	137 / 362 (37.8)	25.9 [18.8; NE]	90 / 343 (26.2)	NE [NE; NE]	1.3015 [0.9983; 1.7051] 0.0533	
Positive	15 / 51 (29.4)	NE [11.7; NE]	14 / 60 (23.3)	NE [NE; NE]	1.1335 [0.5427; 2.3812] 0.7388	
Endocrine Resistance						0.1468
Primary	46 / 127 (36.2)	25.9 [16.1; NE]	43 / 137 (31.4)	NE [11.2; NE]	0.9624 [0.6306; 1.4704] 0.8544	
Secondary	113 / 307 (36.8)	NE [21.5; NE]	64 / 279 (22.9)	NE [NE; NE]	1.4826 [1.0941; 2.0265] 0.0116	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0654
Capecitabine	90 / 265 (34.0)	NE [NE; NE]	48 / 249 (19.3)	NE [NE; NE]	1.6350 [1.1570; 2.3394] 0.0056	
Nab-Paclitaxel	47 / 103 (45.6)	16.1 [6.3; NE]	37 / 101 (36.6)	NE [14.3; NE]	1.1127 [0.7209; 1.7297] 0.6332	
Paclitaxel	22 / 66 (33.3)	NE [21.5; NE]	22 / 67 (32.8)	NE [NE; NE]	0.8545 [0.4630; 1.5706] 0.6045	
Prior anthracycline use						0.2536
Yes	64 / 197 (32.5)	NE [25.9; NE]	51 / 198 (25.8)	NE [NE; NE]	1.1288 [0.7810; 1.6395] 0.5232	
No	95 / 237 (40.1)	21.5 [11.7; NE]	56 / 219 (25.6)	NE [18.7; NE]	1.4372 [1.0358; 2.0130] 0.0311	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.4392
Yes	106 / 294 (36.1)	25.9 [21.5; NE]	73 / 275 (26.5)	NE [NE; NE]	1.2181 [0.9047; 1.6490] 0.1995	
No	53 / 140 (37.9)	NE [16.1; NE]	34 / 142 (23.9)	NE [18.7; NE]	1.4371 [0.9370; 2.2338] 0.0985	
ECOG						0.8706
0	79 / 251 (31.5)	NE [25.9; NE]	54 / 246 (22.0)	NE [NE; NE]	1.2729 [0.9016; 1.8106] 0.1750	
>=1	77 / 178 (43.3)	21.5 [7.3; NE]	51 / 163 (31.3)	NE [NE; NE]	1.2642 [0.8890; 1.8129] 0.1950	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Age at randomization						0.8908
<65 years of age	18 / 301 (6.0)	NE [NE; NE]	4 / 285 (1.4)	NE [NE; NE]	2.8413 [1.0437; 9.9309] 0.0517	
>=65 years of age	9 / 133 (6.8)	NE [NE; NE]	3 / 132 (2.3)	NE [NE; NE]	2.6595 [0.7918; 12.0008] 0.1277	
Race						0.5143
Asian	2 / 153 (1.3)	NE [NE; NE]	0 / 147 (0.0)	NE [NE; NE]	NE [NE; NE]	
White	18 / 231 (7.8)	NE [NE; NE]	6 / 223 (2.7)	NE [NE; NE]	2.0844 [0.8669; 5.7825] 0.1144	
Other	7 / 50 (14.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	5.1648 [0.8921; 97.4541] 0.0916	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5748
Asia	2 / 148 (1.4)	NE [NE; NE]	0 / 144 (0.0)	NE [NE; NE]	NE [NE; NE]	
Europe	20 / 227 (8.8)	NE [NE; NE]	5 / 206 (2.4)	NE [NE; NE]	2.5866 [1.0371; 7.8255] 0.0510	
Rest of the World	5 / 59 (8.5)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	2.1566 [0.4550; 15.2450] 0.3529	
HER2 IHC expression						0.9003
IHC 1+	17 / 239 (7.1)	NE [NE; NE]	4 / 226 (1.8)	NE [NE; NE]	3.1919 [1.1742; 11.1342] 0.0283	
IHC 2+/ISH-	6 / 116 (5.2)	NE [NE; NE]	2 / 115 (1.7)	NE [NE; NE]	1.7772 [0.3971; 12.3576] 0.4841	
IHC >0 <1+	3 / 76 (3.9)	NE [NE; NE]	1 / 74 (1.4)	NE [NE; NE]	2.5949 [0.3316; 52.4952] 0.3917	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3043
Yes	25 / 393 (6.4)	NE [NE; NE]	7 / 377 (1.9)	NE [NE; NE]	2.5171 [1.1395; 6.3429] 0.0268	
No	2 / 41 (4.9)	NE [NE; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.5623
Yes	15 / 177 (8.5)	NE [NE; NE]	3 / 172 (1.7)	NE [NE; NE]	3.4091 [1.1076; 14.8462] 0.0420	
No	12 / 257 (4.7)	NE [NE; NE]	4 / 245 (1.6)	NE [NE; NE]	2.1693 [0.7483; 7.8085] 0.1727	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.6006
1	7 / 65 (10.8)	NE [NE; NE]	1 / 79 (1.3)	NE [NE; NE]	6.5053 [1.1422; 122.1694] 0.0456	
2	16 / 293 (5.5)	NE [NE; NE]	5 / 281 (1.8)	NE [NE; NE]	2.3119 [0.8981; 7.1088] 0.0950	
>=3	4 / 75 (5.3)	NE [NE; NE]	1 / 56 (1.8)	NE [NE; NE]	2.1956 [0.3171; 43.3382] 0.4747	
ER/PR status I						0.0110
ER+, PR+	19 / 252 (7.5)	NE [NE; NE]	1 / 234 (0.4)	NE [NE; NE]	13.4582 [2.7779; 242.1275] 0.0010	
ER+, PR-	7 / 166 (4.2)	NE [NE; NE]	5 / 171 (2.9)	NE [NE; NE]	1.0632 [0.3346; 3.6363] 0.9173	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2273
ER <=10%	3 / 21 (14.3)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	23 / 362 (6.4)	NE [NE; NE]	5 / 343 (1.5)	NE [NE; NE]	3.1244 [1.2771; 9.3548] 0.0159	
Positive	1 / 51 (2.0)	NE [NE; NE]	2 / 60 (3.3)	NE [NE; NE]	0.5809 [0.0270; 6.0636] 0.6534	
Endocrine Resistance						0.2589
Primary	12 / 127 (9.4)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	1.8566 [0.6789; 5.8984] 0.2440	
Secondary	15 / 307 (4.9)	NE [NE; NE]	2 / 279 (0.7)	NE [NE; NE]	5.2718 [1.4759; 33.5630] 0.0141	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.2627
Capecitabine	16 / 265 (6.0)	NE [NE; NE]	6 / 249 (2.4)	NE [NE; NE]	1.8634 [0.7624; 5.2175] 0.1887	
Nab-Paclitaxel	6 / 103 (5.8)	NE [NE; NE]	1 / 101 (1.0)	NE [NE; NE]	5.8295 [0.9960; 110.1441] 0.0640	
Paclitaxel	5 / 66 (7.6)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.5174
Yes	15 / 197 (7.6)	NE [NE; NE]	3 / 198 (1.5)	NE [NE; NE]	3.6151 [1.1802; 15.7016] 0.0314	
No	12 / 237 (5.1)	NE [NE; NE]	4 / 219 (1.8)	NE [NE; NE]	2.1747 [0.7512; 7.8220] 0.1708	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9990
Yes	20 / 294 (6.8)	NE [NE; NE]	5 / 275 (1.8)	NE [NE; NE]	2.6549 [1.0630; 8.0392] 0.0449	
No	7 / 140 (5.0)	NE [NE; NE]	2 / 142 (1.4)	NE [NE; NE]	2.9792 [0.7169; 20.0383] 0.1539	
ECOG						0.5217
0	14 / 251 (5.6)	NE [NE; NE]	3 / 246 (1.2)	NE [NE; NE]	3.4641 [1.1232; 15.0830] 0.0387	
>=1	12 / 178 (6.7)	NE [NE; NE]	4 / 163 (2.5)	NE [NE; NE]	2.0814 [0.7144; 7.5159] 0.1999	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Blood and lymphatic system disorders; PT: Lymphopenia						
Age at randomization						0.1084
<65 years of age	10 / 301 (3.3)	NE [NE; NE]	4 / 285 (1.4)	NE [NE; NE]	1.7489 [0.5766; 6.4397] 0.3438	
>=65 years of age	11 / 133 (8.3)	NE [NE; NE]	1 / 132 (0.8)	NE [NE; NE]	10.0029 [1.9428; 182.8517] 0.0065	
Race						0.5751
Asian	2 / 153 (1.3)	NE [NE; NE]	0 / 147 (0.0)	NE [NE; NE]	NE [NE; NE]	
White	13 / 231 (5.6)	NE [NE; NE]	4 / 223 (1.8)	NE [NE; NE]	2.3730 [0.8342; 8.4617] 0.1213	
Other	6 / 50 (12.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	4.3413 [0.7089; 83.1484] 0.1446	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5851
Asia	2 / 148 (1.4)	NE [NE; NE]	0 / 144 (0.0)	NE [NE; NE]	NE [NE; NE]	
Europe	14 / 227 (6.2)	NE [NE; NE]	3 / 206 (1.5)	NE [NE; NE]	3.0377 [0.9818; 13.2503] 0.0684	
Rest of the World	5 / 59 (8.5)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	2.5154 [0.5334; 17.6989] 0.2579	
HER2 IHC expression						0.4158
IHC 1+	12 / 239 (5.0)	NE [NE; NE]	3 / 226 (1.3)	NE [NE; NE]	2.9544 [0.9310; 13.0259] 0.0801	
IHC 2+/ISH-	5 / 116 (4.3)	NE [NE; NE]	2 / 115 (1.7)	NE [NE; NE]	1.8307 [0.3845; 12.9720] 0.4694	
IHC >0 <1+	3 / 76 (3.9)	NE [NE; NE]	0 / 74 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4147
Yes	17 / 393 (4.3)	NE [NE; NE]	3 / 377 (0.8)	NE [NE; NE]	4.3212 [1.4424; 18.5768] 0.0113	
No	4 / 41 (9.8)	NE [NE; NE]	2 / 40 (5.0)	NE [NE; NE]	1.7645 [0.3429; 12.7659] 0.5075	
Prior Taxane Use In The Non-Metastatic Setting						0.4830
Yes	9 / 177 (5.1)	NE [NE; NE]	3 / 172 (1.7)	NE [NE; NE]	2.5622 [0.7583; 11.5999] 0.1456	
No	12 / 257 (4.7)	NE [NE; NE]	2 / 245 (0.8)	NE [NE; NE]	4.3232 [1.1717; 27.8739] 0.0373	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5735
1	5 / 65 (7.7)	NE [NE; NE]	1 / 79 (1.3)	NE [NE; NE]	5.4033 [0.8617; 103.9056] 0.0859	
2	14 / 293 (4.8)	NE [NE; NE]	4 / 281 (1.4)	NE [NE; NE]	2.5011 [0.8881; 8.8808] 0.0972	
>=3	2 / 75 (2.7)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.3658
ER+, PR+	13 / 252 (5.2)	NE [NE; NE]	4 / 234 (1.7)	NE [NE; NE]	2.4769 [0.8718; 8.8245] 0.1024	
ER+, PR-	8 / 166 (4.8)	NE [NE; NE]	1 / 171 (0.6)	NE [NE; NE]	6.1477 [1.1094; 114.6620] 0.0528	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.8188
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	18 / 362 (5.0)	NE [NE; NE]	4 / 343 (1.2)	NE [NE; NE]	3.2767 [1.2142; 11.3907] 0.0239	
Positive	2 / 51 (3.9)	NE [NE; NE]	1 / 60 (1.7)	NE [NE; NE]	2.2945 [0.2198; 49.3517] 0.4843	
Endocrine Resistance						0.1726
Primary	5 / 127 (3.9)	NE [NE; NE]	3 / 137 (2.2)	NE [NE; NE]	1.3984 [0.3374; 6.9009] 0.6484	
Secondary	16 / 307 (5.2)	NE [NE; NE]	2 / 279 (0.7)	NE [NE; NE]	5.8525 [1.6564; 37.0985] 0.0078	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.6885
Capecitabine	15 / 265 (5.7)	NE [NE; NE]	4 / 249 (1.6)	NE [NE; NE]	2.9715 [1.0743; 10.4498] 0.0429	
Nab-Paclitaxel	4 / 103 (3.9)	NE [NE; NE]	1 / 101 (1.0)	NE [NE; NE]	3.6259 [0.5331; 71.0587] 0.2189	
Paclitaxel	2 / 66 (3.0)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.6617
Yes	10 / 197 (5.1)	NE [NE; NE]	3 / 198 (1.5)	NE [NE; NE]	2.6790 [0.8101; 12.0278] 0.1225	
No	11 / 237 (4.6)	NE [NE; NE]	2 / 219 (0.9)	NE [NE; NE]	4.0361 [1.0769; 26.1677] 0.0504	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.4433
Yes	13 / 294 (4.4)	NE [NE; NE]	2 / 275 (0.7)	NE [NE; NE]	4.7045 [1.2911; 30.1999] 0.0254	
No	8 / 140 (5.7)	NE [NE; NE]	3 / 142 (2.1)	NE [NE; NE]	2.2599 [0.6470; 10.3815] 0.2193	
ECOG						0.0109
0	9 / 251 (3.6)	NE [NE; NE]	5 / 246 (2.0)	NE [NE; NE]	1.4998 [0.5158; 4.8985] 0.4661	
>=1	11 / 178 (6.2)	NE [NE; NE]	0 / 163 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)						
Age at randomization						0.3832
<65 years of age	88 / 301 (29.2)	28.3 [19.3; NE]	89 / 285 (31.2)	26.5 [14.3; NE]	0.6598 [0.4884; 0.8910] 0.0063	
>=65 years of age	41 / 133 (30.8)	NE [16.6; NE]	44 / 132 (33.3)	14.3 [11.3; NE]	0.8040 [0.5224; 1.2348] 0.3148	
Race						0.7929
Asian	29 / 153 (19.0)	NE [28.3; NE]	28 / 147 (19.0)	27.9 [NE; NE]	0.7561 [0.4434; 1.2882] 0.3006	
White	80 / 231 (34.6)	19.3 [16.4; NE]	85 / 223 (38.1)	12.2 [9.5; NE]	0.6892 [0.5056; 0.9384] 0.0173	
Other	20 / 50 (40.0)	17.1 [9.5; NE]	20 / 47 (42.6)	10.3 [2.3; NE]	0.5541 [0.2873; 1.0644] 0.0716	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2986
Asia	28 / 148 (18.9)	NE [28.3; NE]	28 / 144 (19.4)	27.9 [26.5; NE]	0.7419 [0.4324; 1.2697] 0.2731	
Europe	73 / 227 (32.2)	NE [17.1; NE]	79 / 206 (38.3)	12.2 [9.1; 14.4]	0.5823 [0.4211; 0.8041] 0.0009	
Rest of the World	28 / 59 (47.5)	17.0 [5.5; 19.5]	26 / 67 (38.8)	11.3 [4.5; NE]	1.0376 [0.6029; 1.7900] 0.8970	
HER2 IHC expression						0.2665
IHC 1+	69 / 239 (28.9)	28.3 [19.1; NE]	68 / 226 (30.1)	NE [12.0; NE]	0.7531 [0.5355; 1.0587] 0.1009	
IHC 2+/ISH-	41 / 116 (35.3)	NE [14.6; NE]	38 / 115 (33.0)	14.4 [10.3; NE]	0.7333 [0.4673; 1.1527] 0.1753	
IHC >0 <1+	17 / 76 (22.4)	NE [19.5; NE]	27 / 74 (36.5)	26.5 [8.0; NE]	0.4514 [0.2404; 0.8242] 0.0089	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5768
Yes	121 / 393 (30.8)	NE [19.1; NE]	122 / 377 (32.4)	26.5 [12.5; NE]	0.7079 [0.5483; 0.9138] 0.0076	
No	8 / 41 (19.5)	NE [28.3; NE]	11 / 40 (27.5)	NE [9.6; NE]	0.5056 [0.1852; 1.2894] 0.1519	
Prior Taxane Use In The Non-Metastatic Setting						0.5273
Yes	45 / 177 (25.4)	NE [NE; NE]	53 / 172 (30.8)	NE [12.0; NE]	0.6687 [0.4456; 0.9989] 0.0486	
No	84 / 257 (32.7)	19.5 [17.1; NE]	80 / 245 (32.7)	26.5 [12.5; NE]	0.7136 [0.5229; 0.9744] 0.0325	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0810
1	16 / 65 (24.6)	NE [19.1; NE]	29 / 79 (36.7)	14.4 [7.3; NE]	0.5621 [0.2960; 1.0291] 0.0630	
2	90 / 293 (30.7)	28.3 [18.5; NE]	94 / 281 (33.5)	26.5 [11.9; NE]	0.6486 [0.4829; 0.8703] 0.0036	
>=3	23 / 75 (30.7)	NE [19.5; NE]	10 / 56 (17.9)	NE [14.3; NE]	1.4954 [0.7281; 3.3010] 0.2878	
ER/PR status I						0.1579
ER+, PR+	77 / 252 (30.6)	NE [17.1; NE]	69 / 234 (29.5)	26.5 [11.9; NE]	0.7763 [0.5591; 1.0800] 0.1296	
ER+, PR-	45 / 166 (27.1)	NE [19.5; NE]	60 / 171 (35.1)	27.9 [12.5; NE]	0.5755 [0.3854; 0.8522] 0.0056	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4863
ER <=10%	8 / 21 (38.1)	NE [4.8; NE]	3 / 14 (21.4)	NE [4.5; NE]	0.9477 [0.2475; 4.5242] 0.9416	
ER >10%	110 / 362 (30.4)	28.3 [19.3; NE]	109 / 343 (31.8)	26.5 [12.5; NE]	0.7102 [0.5422; 0.9300] 0.0123	
Positive	11 / 51 (21.6)	NE [NE; NE]	21 / 60 (35.0)	NE [6.5; NE]	0.4989 [0.2313; 1.0174] 0.0572	
Endocrine Resistance						0.9279
Primary	32 / 127 (25.2)	NE [19.1; NE]	37 / 137 (27.0)	NE [14.3; NE]	0.7296 [0.4496; 1.1772] 0.1951	
Secondary	97 / 307 (31.6)	28.3 [18.5; NE]	95 / 279 (34.1)	26.5 [11.9; NE]	0.6848 [0.5136; 0.9130] 0.0093	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0001
Capecitabine	100 / 265 (37.7)	19.3 [16.4; NE]	81 / 249 (32.5)	26.5 [11.9; NE]	0.9616 [0.7167; 1.2942] 0.7917	
Nab-Paclitaxel	13 / 103 (12.6)	NE [28.3; NE]	23 / 101 (22.8)	NE [14.4; NE]	0.4160 [0.1990; 0.8261] 0.0120	
Paclitaxel	16 / 66 (24.2)	NE [16.6; NE]	29 / 67 (43.3)	12.5 [2.1; NE]	0.1864 [0.0833; 0.3818] <.0001	
Prior anthracycline use						0.8017
Yes	57 / 197 (28.9)	NE [19.1; NE]	61 / 198 (30.8)	14.4 [12.0; NE]	0.7346 [0.5083; 1.0599] 0.0978	
No	72 / 237 (30.4)	28.3 [19.3; NE]	72 / 219 (32.9)	26.5 [12.2; NE]	0.6629 [0.4754; 0.9239] 0.0144	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.8985
Yes	86 / 294 (29.3)	28.3 [19.3; NE]	86 / 275 (31.3)	26.5 [12.2; NE]	0.6895 [0.5084; 0.9348] 0.0159	
No	43 / 140 (30.7)	NE [17.1; NE]	47 / 142 (33.1)	27.9 [9.6; NE]	0.7105 [0.4663; 1.0798] 0.1076	
ECOG						0.8974
0	72 / 251 (28.7)	28.3 [28.3; NE]	78 / 246 (31.7)	26.5 [14.3; NE]	0.6630 [0.4784; 0.9173] 0.0125	
>=1	55 / 178 (30.9)	NE [19.3; NE]	52 / 163 (31.9)	NE [10.3; NE]	0.7594 [0.5167; 1.1173] 0.1598	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia						
Age at randomization						0.6597
<65 years of age	21 / 301 (7.0)	NE [NE; NE]	29 / 285 (10.2)	NE [NE; NE]	0.4600 [0.2567; 0.8103] 0.0064	
>=65 years of age	11 / 133 (8.3)	NE [NE; NE]	16 / 132 (12.1)	NE [NE; NE]	0.5655 [0.2543; 1.2122] 0.1422	
Race						0.8604
Asian	4 / 153 (2.6)	NE [NE; NE]	6 / 147 (4.1)	NE [NE; NE]	0.4750 [0.1203; 1.6798] 0.2425	
White	23 / 231 (10.0)	NE [NE; NE]	35 / 223 (15.7)	NE [NE; NE]	0.4473 [0.2596; 0.7563] 0.0024	
Other	5 / 50 (10.0)	NE [NE; NE]	4 / 47 (8.5)	NE [NE; NE]	0.8566 [0.2181; 3.5500] 0.8219	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5742
Asia	4 / 148 (2.7)	NE [NE; NE]	6 / 144 (4.2)	NE [NE; NE]	0.4927 [0.1249; 1.7404] 0.2669	
Europe	17 / 227 (7.5)	NE [NE; NE]	26 / 206 (12.6)	NE [NE; NE]	0.3783 [0.1998; 0.6977] 0.0015	
Rest of the World	11 / 59 (18.6)	NE [19.1; NE]	13 / 67 (19.4)	NE [NE; NE]	0.8022 [0.3505; 1.8016] 0.5896	
HER2 IHC expression						0.6123
IHC 1+	14 / 239 (5.9)	NE [NE; NE]	25 / 226 (11.1)	NE [NE; NE]	0.3883 [0.1953; 0.7416] 0.0037	
IHC 2+/ISH-	10 / 116 (8.6)	NE [NE; NE]	13 / 115 (11.3)	NE [NE; NE]	0.5406 [0.2286; 1.2404] 0.1425	
IHC >0 <1+	7 / 76 (9.2)	NE [19.5; NE]	7 / 74 (9.5)	NE [NE; NE]	0.7496 [0.2545; 2.2069] 0.5916	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4794
Yes	28 / 393 (7.1)	NE [NE; NE]	41 / 377 (10.9)	NE [NE; NE]	0.4714 [0.2871; 0.7630] 0.0020	
No	4 / 41 (9.8)	NE [NE; NE]	4 / 40 (10.0)	NE [NE; NE]	0.7337 [0.1716; 3.1346] 0.6630	
Prior Taxane Use In The Non-Metastatic Setting						0.9480
Yes	9 / 177 (5.1)	NE [NE; NE]	13 / 172 (7.6)	NE [NE; NE]	0.5216 [0.2132; 1.2205] 0.1315	
No	23 / 257 (8.9)	NE [NE; NE]	32 / 245 (13.1)	NE [NE; NE]	0.4843 [0.2788; 0.8281] 0.0073	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.9133
1	3 / 65 (4.6)	NE [NE; NE]	7 / 79 (8.9)	NE [NE; NE]	0.3908 [0.0831; 1.4283] 0.1638	
2	25 / 293 (8.5)	NE [NE; NE]	34 / 281 (12.1)	NE [NE; NE]	0.4875 [0.2862; 0.8190] 0.0060	
>=3	4 / 75 (5.3)	NE [NE; NE]	4 / 56 (7.1)	NE [NE; NE]	0.6069 [0.1416; 2.5955] 0.4800	
ER/PR status I						0.3712
ER+, PR+	19 / 252 (7.5)	NE [NE; NE]	24 / 234 (10.3)	NE [NE; NE]	0.5262 [0.2830; 0.9646] 0.0356	
ER+, PR-	9 / 166 (5.4)	NE [NE; NE]	20 / 171 (11.7)	NE [NE; NE]	0.3399 [0.1454; 0.7344] 0.0057	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9134
ER <=10%	2 / 21 (9.5)	NE [9.5; NE]	1 / 14 (7.1)	NE [4.5; NE]	0.0000 [NE; 2.5488] 0.1306	
ER >10%	26 / 362 (7.2)	NE [NE; NE]	35 / 343 (10.2)	NE [NE; NE]	0.5050 [0.2992; 0.8414] 0.0080	
Positive	4 / 51 (7.8)	NE [NE; NE]	9 / 60 (15.0)	NE [NE; NE]	0.4236 [0.1143; 1.3064] 0.1421	
Endocrine Resistance						0.5309
Primary	8 / 127 (6.3)	NE [NE; NE]	10 / 137 (7.3)	NE [NE; NE]	0.6582 [0.2489; 1.6840] 0.3796	
Secondary	24 / 307 (7.8)	NE [NE; NE]	35 / 279 (12.5)	NE [NE; NE]	0.4439 [0.2596; 0.7463] 0.0019	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.5361
Capecitabine	25 / 265 (9.4)	NE [NE; NE]	32 / 249 (12.9)	NE [NE; NE]	0.5472 [0.3204; 0.9243] 0.0229	
Nab-Paclitaxel	2 / 103 (1.9)	NE [NE; NE]	4 / 101 (4.0)	NE [NE; NE]	0.4670 [0.0647; 2.3941] 0.3680	
Paclitaxel	5 / 66 (7.6)	NE [NE; NE]	9 / 67 (13.4)	NE [NE; NE]	0.2084 [0.0522; 0.6869] 0.0082	
Prior anthracycline use						0.2190
Yes	16 / 197 (8.1)	NE [NE; NE]	17 / 198 (8.6)	NE [NE; NE]	0.6390 [0.3158; 1.2860] 0.2037	
No	16 / 237 (6.8)	NE [NE; NE]	28 / 219 (12.8)	NE [NE; NE]	0.3940 [0.2075; 0.7227] 0.0023	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9857
Yes	23 / 294 (7.8)	NE [NE; NE]	31 / 275 (11.3)	NE [NE; NE]	0.4817 [0.2760; 0.8288] 0.0075	
No	9 / 140 (6.4)	NE [NE; NE]	14 / 142 (9.9)	NE [NE; NE]	0.4932 [0.2035; 1.1352] 0.0954	
ECOG						0.9426
0	18 / 251 (7.2)	NE [NE; NE]	28 / 246 (11.4)	NE [NE; NE]	0.4714 [0.2551; 0.8492] 0.0116	
>=1	12 / 178 (6.7)	NE [NE; NE]	17 / 163 (10.4)	NE [NE; NE]	0.4308 [0.1976; 0.9092] 0.0248	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Infections and infestations; PT: COVID-19						
Age at randomization						0.8150
<65 years of age	76 / 301 (25.2)	NE [18.6; NE]	33 / 285 (11.6)	NE [NE; NE]	1.4428 [0.9635; 2.2077] 0.0804	
>=65 years of age	30 / 133 (22.6)	NE [19.5; NE]	19 / 132 (14.4)	NE [NE; NE]	1.3241 [0.7500; 2.3959] 0.3385	
Race						0.7723
Asian	44 / 153 (28.8)	18.6 [16.1; NE]	26 / 147 (17.7)	NE [14.9; NE]	1.1857 [0.7331; 1.9561] 0.4944	
White	51 / 231 (22.1)	NE [NE; NE]	23 / 223 (10.3)	NE [NE; NE]	1.6451 [1.0157; 2.7473] 0.0465	
Other	11 / 50 (22.0)	NE [15.9; NE]	3 / 47 (6.4)	NE [NE; NE]	1.8160 [0.5377; 8.2773] 0.3696	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.5252
Asia	43 / 148 (29.1)	18.6 [16.1; NE]	24 / 144 (16.7)	NE [14.9; NE]	1.2745 [0.7777; 2.1379] 0.3439	
Europe	46 / 227 (20.3)	NE [NE; NE]	21 / 206 (10.2)	NE [NE; NE]	1.3665 [0.8225; 2.3456] 0.2384	
Rest of the World	17 / 59 (28.8)	NE [12.6; NE]	7 / 67 (10.4)	NE [13.7; NE]	2.2873 [0.9812; 5.9402] 0.0598	
HER2 IHC expression						0.6101
IHC 1+	67 / 239 (28.0)	20.0 [16.4; NE]	31 / 226 (13.7)	NE [19.3; NE]	1.5416 [1.0134; 2.3972] 0.0463	
IHC 2+/ISH-	22 / 116 (19.0)	NE [NE; NE]	13 / 115 (11.3)	NE [NE; NE]	1.1037 [0.5590; 2.2668] 0.7803	
IHC >0 <1+	17 / 76 (22.4)	NE [NE; NE]	8 / 74 (10.8)	NE [NE; NE]	1.5004 [0.6620; 3.7001] 0.3448	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.3545
Yes	96 / 393 (24.4)	NE [19.5; NE]	44 / 377 (11.7)	NE [NE; NE]	1.4859 [1.0439; 2.1484] 0.0300	
No	10 / 41 (24.4)	NE [20.0; NE]	8 / 40 (20.0)	19.3 [11.7; NE]	0.9092 [0.3550; 2.4022] 0.8425	
Prior Taxane Use In The Non-Metastatic Setting						0.4791
Yes	47 / 177 (26.6)	NE [16.1; NE]	20 / 172 (11.6)	NE [NE; NE]	1.5934 [0.9541; 2.7599] 0.0811	
No	59 / 257 (23.0)	NE [20.0; NE]	32 / 245 (13.1)	NE [NE; NE]	1.2878 [0.8405; 2.0087] 0.2527	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5289
1	17 / 65 (26.2)	19.5 [12.4; NE]	8 / 79 (10.1)	NE [19.3; NE]	2.0315 [0.8975; 5.0065] 0.0938	
2	73 / 293 (24.9)	NE [20.0; NE]	35 / 281 (12.5)	NE [NE; NE]	1.3864 [0.9308; 2.1043] 0.1137	
>=3	16 / 75 (21.3)	NE [15.6; NE]	9 / 56 (16.1)	NE [13.3; NE]	1.0790 [0.4833; 2.5631] 0.8588	
ER/PR status I						0.3526
ER+, PR+	56 / 252 (22.2)	NE [NE; NE]	31 / 234 (13.2)	NE [19.3; NE]	1.1729 [0.7589; 1.8459] 0.4793	
ER+, PR-	45 / 166 (27.1)	NE [18.6; NE]	21 / 171 (12.3)	NE [NE; NE]	1.6214 [0.9735; 2.7885] 0.0677	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.9846
ER <=10%	4 / 21 (19.0)	NE [12.4; NE]	1 / 14 (7.1)	NE [NE; NE]	1.3863 [0.1847; 28.1437] 0.7766	
ER >10%	93 / 362 (25.7)	NE [19.5; NE]	45 / 343 (13.1)	NE [NE; NE]	1.4032 [0.9857; 2.0265] 0.0636	
Positive	9 / 51 (17.6)	NE [12.8; NE]	6 / 60 (10.0)	NE [NE; NE]	1.5209 [0.5470; 4.5469] 0.4241	
Endocrine Resistance						0.3377
Primary	28 / 127 (22.0)	NE [16.4; NE]	12 / 137 (8.8)	NE [19.3; NE]	1.8445 [0.9554; 3.7855] 0.0737	
Secondary	78 / 307 (25.4)	NE [20.0; NE]	40 / 279 (14.3)	NE [NE; NE]	1.2740 [0.8731; 1.8876] 0.2159	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1015
Capecitabine	71 / 265 (26.8)	NE [16.4; NE]	29 / 249 (11.6)	NE [NE; NE]	1.7769 [1.1656; 2.7822] 0.0084	
Nab-Paclitaxel	24 / 103 (23.3)	20.0 [16.4; NE]	21 / 101 (20.8)	19.3 [19.3; NE]	0.8494 [0.4677; 1.5527] 0.5889	
Paclitaxel	11 / 66 (16.7)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	2.6570 [0.6565; 17.7835] 0.2047	
Prior anthracycline use						0.9072
Yes	49 / 197 (24.9)	NE [16.4; NE]	25 / 198 (12.6)	NE [NE; NE]	1.4052 [0.8726; 2.3193] 0.1687	
No	57 / 237 (24.1)	NE [20.0; NE]	27 / 219 (12.3)	NE [NE; NE]	1.4197 [0.9046; 2.2838] 0.1346	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.7197
Yes	69 / 294 (23.5)	NE [19.5; NE]	31 / 275 (11.3)	NE [NE; NE]	1.5097 [0.9947; 2.3435] 0.0568	
No	37 / 140 (26.4)	NE [20.0; NE]	21 / 142 (14.8)	NE [14.1; NE]	1.2687 [0.7458; 2.2145] 0.3874	
ECOG						0.8595
0	64 / 251 (25.5)	NE [19.5; NE]	33 / 246 (13.4)	NE [NE; NE]	1.3772 [0.9097; 2.1241] 0.1357	
>=1	39 / 178 (21.9)	NE [NE; NE]	17 / 163 (10.4)	NE [NE; NE]	1.5079 [0.8611; 2.7522] 0.1607	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Infections and infestations; PT: Cellulitis						
Age at randomization						0.4749
<65 years of age	1 / 301 (0.3)	NE [NE; NE]	7 / 285 (2.5)	NE [NE; NE]	0.0779 [0.0041; 0.4512] 0.0028	
>=65 years of age	1 / 133 (0.8)	NE [NE; NE]	3 / 132 (2.3)	NE [23.3; NE]	0.2107 [0.0100; 1.7487] 0.1541	
Race						0.1494
Asian	0 / 153 (0.0)	NE [NE; NE]	2 / 147 (1.4)	NE [NE; NE]	NE [NE; NE]	
White	1 / 231 (0.4)	NE [NE; NE]	8 / 223 (3.6)	NE [23.3; NE]	0.0888 [0.0048; 0.4914] 0.0046	
Other	1 / 50 (2.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1604
Asia	0 / 148 (0.0)	NE [NE; NE]	3 / 144 (2.1)	NE [NE; NE]	NE [NE; NE]	
Europe	0 / 227 (0.0)	NE [NE; NE]	3 / 206 (1.5)	NE [NE; NE]	NE [NE; NE]	
Rest of the World	2 / 59 (3.4)	NE [NE; NE]	4 / 67 (6.0)	NE [23.3; NE]	0.3964 [0.0541; 2.0719] 0.2754	
HER2 IHC expression						0.4983
IHC 1+	1 / 239 (0.4)	NE [NE; NE]	5 / 226 (2.2)	NE [NE; NE]	0.1339 [0.0069; 0.8440] 0.0331	
IHC 2+/ISH-	1 / 116 (0.9)	NE [NE; NE]	2 / 115 (1.7)	NE [NE; NE]	0.3886 [0.0180; 4.0767] 0.4245	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	3 / 74 (4.1)	NE [23.3; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1998
Yes	1 / 393 (0.3)	NE [NE; NE]	9 / 377 (2.4)	NE [NE; NE]	0.0741 [0.0040; 0.4005] 0.0015	
No	1 / 41 (2.4)	NE [NE; NE]	1 / 40 (2.5)	23.3 [NE; NE]	0.3030 [0.0106; 8.7041] 0.4120	
Prior Taxane Use In The Non-Metastatic Setting						0.8648
Yes	1 / 177 (0.6)	NE [NE; NE]	4 / 172 (2.3)	NE [NE; NE]	0.1872 [0.0094; 1.3017] 0.0999	
No	1 / 257 (0.4)	NE [NE; NE]	6 / 245 (2.4)	NE [23.3; NE]	0.0937 [0.0049; 0.5610] 0.0074	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5489
1	0 / 65 (0.0)	NE [NE; NE]	2 / 79 (2.5)	NE [NE; NE]	NE [NE; NE]	
2	2 / 293 (0.7)	NE [NE; NE]	7 / 281 (2.5)	NE [NE; NE]	0.1558 [0.0230; 0.6579] 0.0091	
>=3	0 / 75 (0.0)	NE [NE; NE]	1 / 56 (1.8)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.2635
ER+, PR+	2 / 252 (0.8)	NE [NE; NE]	7 / 234 (3.0)	NE [23.3; NE]	0.1548 [0.0227; 0.6551] 0.0089	
ER+, PR-	0 / 166 (0.0)	NE [NE; NE]	3 / 171 (1.8)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						1.0000
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	2 / 362 (0.6)	NE [NE; NE]	10 / 343 (2.9)	NE [NE; NE]	0.1170 [0.0177; 0.4556] 0.0013	
Positive	0 / 51 (0.0)	NE [NE; NE]	0 / 60 (0.0)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						0.5563
Primary	0 / 127 (0.0)	NE [NE; NE]	1 / 137 (0.7)	NE [NE; NE]	NE [NE; NE]	
Secondary	2 / 307 (0.7)	NE [NE; NE]	9 / 279 (3.2)	NE [NE; NE]	0.1281 [0.0193; 0.5059] 0.0023	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.3593
Capecitabine	2 / 265 (0.8)	NE [NE; NE]	6 / 249 (2.4)	NE [NE; NE]	0.2087 [0.0304; 0.9162] 0.0358	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	3 / 101 (3.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	1 / 67 (1.5)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.9522
Yes	1 / 197 (0.5)	NE [NE; NE]	5 / 198 (2.5)	NE [NE; NE]	0.1389 [0.0072; 0.8838] 0.0390	
No	1 / 237 (0.4)	NE [NE; NE]	5 / 219 (2.3)	NE [23.3; NE]	0.1136 [0.0059; 0.7196] 0.0186	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.2133
Yes	2 / 294 (0.7)	NE [NE; NE]	6 / 275 (2.2)	NE [NE; NE]	0.2025 [0.0293; 0.8956] 0.0330	
No	0 / 140 (0.0)	NE [NE; NE]	4 / 142 (2.8)	NE [23.3; NE]	NE [NE; NE]	
ECOG						0.1347
0	0 / 251 (0.0)	NE [NE; NE]	5 / 246 (2.0)	NE [23.3; NE]	NE [NE; NE]	
>=1	2 / 178 (1.1)	NE [NE; NE]	5 / 163 (3.1)	NE [NE; NE]	0.2614 [0.0371; 1.2320] 0.0885	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: General disorders and administration site conditions; PT: Oedema peripheral						
Age at randomization						0.3919
<65 years of age	23 / 301 (7.6)	NE [NE; NE]	30 / 285 (10.5)	NE [NE; NE]	0.5336 [0.3045; 0.9229] 0.0234	
>=65 years of age	13 / 133 (9.8)	NE [NE; NE]	29 / 132 (22.0)	NE [NE; NE]	0.3646 [0.1829; 0.6879] 0.0017	
Race						0.3720
Asian	11 / 153 (7.2)	NE [NE; NE]	18 / 147 (12.2)	NE [NE; NE]	0.4479 [0.2039; 0.9404] 0.0327	
White	23 / 231 (10.0)	NE [NE; NE]	34 / 223 (15.2)	NE [NE; NE]	0.5135 [0.2978; 0.8695] 0.0125	
Other	2 / 50 (4.0)	NE [NE; NE]	7 / 47 (14.9)	NE [NE; NE]	0.1624 [0.0228; 0.7186] 0.0156	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4043
Asia	10 / 148 (6.8)	NE [NE; NE]	16 / 144 (11.1)	NE [NE; NE]	0.4672 [0.2038; 1.0203] 0.0549	
Europe	18 / 227 (7.9)	NE [NE; NE]	33 / 206 (16.0)	NE [NE; NE]	0.3751 [0.2057; 0.6622] 0.0006	
Rest of the World	8 / 59 (13.6)	NE [NE; NE]	10 / 67 (14.9)	NE [12.4; NE]	0.7057 [0.2669; 1.8050] 0.4648	
HER2 IHC expression						0.7912
IHC 1+	19 / 239 (7.9)	NE [NE; NE]	28 / 226 (12.4)	NE [NE; NE]	0.5028 [0.2754; 0.8981] 0.0194	
IHC 2+/ISH-	12 / 116 (10.3)	NE [NE; NE]	20 / 115 (17.4)	NE [NE; NE]	0.4369 [0.2054; 0.8901] 0.0216	
IHC >0 <1+	5 / 76 (6.6)	NE [NE; NE]	11 / 74 (14.9)	NE [NE; NE]	0.3235 [0.1011; 0.8983] 0.0293	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.7165
Yes	34 / 393 (8.7)	NE [NE; NE]	54 / 377 (14.3)	NE [NE; NE]	0.4617 [0.2970; 0.7080] 0.0003	
No	2 / 41 (4.9)	NE [NE; NE]	5 / 40 (12.5)	NE [17.4; NE]	0.2680 [0.0378; 1.2723] 0.0975	
Prior Taxane Use In The Non-Metastatic Setting						0.9761
Yes	17 / 177 (9.6)	NE [NE; NE]	28 / 172 (16.3)	NE [NE; NE]	0.4483 [0.2385; 0.8180] 0.0084	
No	19 / 257 (7.4)	NE [NE; NE]	31 / 245 (12.7)	NE [NE; NE]	0.4430 [0.2451; 0.7800] 0.0044	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0206
1	10 / 65 (15.4)	NE [NE; NE]	7 / 79 (8.9)	NE [17.4; NE]	1.5934 [0.6045; 4.4246] 0.3455	
2	20 / 293 (6.8)	NE [NE; NE]	42 / 281 (14.9)	NE [NE; NE]	0.3209 [0.1836; 0.5420] <.0001	
>=3	6 / 75 (8.0)	NE [NE; NE]	10 / 56 (17.9)	NE [NE; NE]	0.3882 [0.1318; 1.0482] 0.0581	
ER/PR status I						0.0337
ER+, PR+	23 / 252 (9.1)	NE [NE; NE]	25 / 234 (10.7)	NE [NE; NE]	0.6631 [0.3723; 1.1755] 0.1560	
ER+, PR-	10 / 166 (6.0)	NE [NE; NE]	31 / 171 (18.1)	NE [17.4; NE]	0.2478 [0.1144; 0.4920] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.7501
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	2 / 14 (14.3)	NE [4.4; NE]	0.2336 [0.0108; 2.4756] 0.1999	
ER >10%	31 / 362 (8.6)	NE [NE; NE]	49 / 343 (14.3)	NE [NE; NE]	0.4524 [0.2845; 0.7087] 0.0005	
Positive	4 / 51 (7.8)	NE [NE; NE]	8 / 60 (13.3)	NE [NE; NE]	0.4851 [0.1288; 1.5497] 0.2296	
Endocrine Resistance						0.7004
Primary	11 / 127 (8.7)	NE [NE; NE]	18 / 137 (13.1)	NE [17.4; NE]	0.4578 [0.2064; 0.9697] 0.0406	
Secondary	25 / 307 (8.1)	NE [NE; NE]	41 / 279 (14.7)	NE [NE; NE]	0.4315 [0.2581; 0.7069] 0.0007	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.4795
Capecitabine	22 / 265 (8.3)	NE [NE; NE]	29 / 249 (11.6)	NE [NE; NE]	0.5712 [0.3236; 0.9940] 0.0462	
Nab-Paclitaxel	7 / 103 (6.8)	NE [NE; NE]	18 / 101 (17.8)	NE [17.4; NE]	0.3106 [0.1196; 0.7205] 0.0063	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	12 / 67 (17.9)	NE [NE; NE]	0.3018 [0.1059; 0.7867] 0.0125	
Prior anthracycline use						0.8092
Yes	19 / 197 (9.6)	NE [NE; NE]	33 / 198 (16.7)	NE [NE; NE]	0.4365 [0.2420; 0.7649] 0.0035	
No	17 / 237 (7.2)	NE [NE; NE]	26 / 219 (11.9)	NE [NE; NE]	0.4620 [0.2453; 0.8477] 0.0118	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.5134
Yes	26 / 294 (8.8)	NE [NE; NE]	37 / 275 (13.5)	NE [NE; NE]	0.4884 [0.2910; 0.8075] 0.0048	
No	10 / 140 (7.1)	NE [NE; NE]	22 / 142 (15.5)	NE [NE; NE]	0.3624 [0.1635; 0.7488] 0.0058	
ECOG						0.1898
0	17 / 251 (6.8)	NE [NE; NE]	36 / 246 (14.6)	NE [NE; NE]	0.3478 [0.1900; 0.6118] 0.0002	
>=1	19 / 178 (10.7)	NE [NE; NE]	21 / 163 (12.9)	NE [17.4; NE]	0.6601 [0.3496; 1.2378] 0.1913	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Psychiatric disorders; PT: Anxiety						
Age at randomization						0.0759
<65 years of age	8 / 301 (2.7)	NE [31.3; NE]	0 / 285 (0.0)	NE [NE; NE]	NE [NE; NE]	
>=65 years of age	4 / 133 (3.0)	NE [NE; NE]	2 / 132 (1.5)	NE [NE; NE]	1.7409 [0.3387; 12.5851] 0.5175	
Race						0.4393
Asian	2 / 153 (1.3)	NE [31.3; NE]	0 / 147 (0.0)	NE [NE; NE]	NE [NE; NE]	
White	8 / 231 (3.5)	NE [NE; NE]	1 / 223 (0.4)	NE [NE; NE]	6.5045 [1.1828; 120.9961] 0.0431	
Other	2 / 50 (4.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	0.8484 [0.0789; 18.5279] 0.8943	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.3082
Asia	2 / 148 (1.4)	NE [31.3; NE]	0 / 144 (0.0)	NE [NE; NE]	NE [NE; NE]	
Europe	7 / 227 (3.1)	NE [NE; NE]	2 / 206 (1.0)	NE [NE; NE]	2.4898 [0.5934; 16.8329] 0.2431	
Rest of the World	3 / 59 (5.1)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
HER2 IHC expression						0.3980
IHC 1+	6 / 239 (2.5)	NE [31.3; NE]	1 / 226 (0.4)	NE [NE; NE]	3.8239 [0.6393; 72.7485] 0.1853	
IHC 2+/ISH-	4 / 116 (3.4)	NE [NE; NE]	0 / 115 (0.0)	NE [NE; NE]	NE [NE; NE]	
IHC >0 <1+	2 / 76 (2.6)	NE [NE; NE]	1 / 74 (1.4)	NE [NE; NE]	1.5854 [0.1489; 34.4657] 0.7066	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.4292
Yes	10 / 393 (2.5)	NE [NE; NE]	2 / 377 (0.5)	NE [NE; NE]	3.7452 [0.9767; 24.4949] 0.0692	
No	2 / 41 (4.9)	31.3 [31.3; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.9765
Yes	6 / 177 (3.4)	NE [NE; NE]	1 / 172 (0.6)	NE [NE; NE]	4.3786 [0.7356; 83.2110] 0.1383	
No	6 / 257 (2.3)	NE [31.3; NE]	1 / 245 (0.4)	NE [NE; NE]	4.1921 [0.7020; 79.7461] 0.1529	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.5835
1	2 / 65 (3.1)	NE [NE; NE]	0 / 79 (0.0)	NE [NE; NE]	NE [NE; NE]	
2	9 / 293 (3.1)	31.3 [31.3; NE]	2 / 281 (0.7)	NE [NE; NE]	3.4143 [0.8686; 22.5380] 0.0976	
>=3	1 / 75 (1.3)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.4837
ER+, PR+	9 / 252 (3.6)	NE [NE; NE]	1 / 234 (0.4)	NE [NE; NE]	6.4625 [1.2044; 119.4620] 0.0426	
ER+, PR-	3 / 166 (1.8)	NE [31.3; NE]	1 / 171 (0.6)	NE [NE; NE]	1.9319 [0.2290; 40.3588] 0.5732	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.8079
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	11 / 362 (3.0)	NE [31.3; NE]	2 / 343 (0.6)	NE [NE; NE]	3.8792 [1.0244; 25.2626] 0.0601	
Positive	1 / 51 (2.0)	NE [NE; NE]	0 / 60 (0.0)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						0.2882
Primary	3 / 127 (2.4)	NE [NE; NE]	0 / 137 (0.0)	NE [NE; NE]	NE [NE; NE]	
Secondary	9 / 307 (2.9)	NE [31.3; NE]	2 / 279 (0.7)	NE [NE; NE]	3.1534 [0.8043; 20.7925] 0.1235	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.5832
Capecitabine	9 / 265 (3.4)	NE [NE; NE]	2 / 249 (0.8)	NE [NE; NE]	3.4159 [0.8750; 22.4763] 0.0960	
Nab-Paclitaxel	3 / 103 (2.9)	31.3 [31.3; NE]	0 / 101 (0.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.9754
Yes	6 / 197 (3.0)	NE [NE; NE]	1 / 198 (0.5)	NE [NE; NE]	4.5873 [0.7723; 87.1166] 0.1239	
No	6 / 237 (2.5)	NE [31.3; NE]	1 / 219 (0.5)	NE [NE; NE]	4.0314 [0.6747; 76.7079] 0.1664	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
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Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.1453
Yes	6 / 294 (2.0)	NE [31.3; NE]	0 / 275 (0.0)	NE [NE; NE]	NE [NE; NE]	
No	6 / 140 (4.3)	NE [NE; NE]	2 / 142 (1.4)	NE [NE; NE]	2.4918 [0.5689; 17.0889] 0.2499	
ECOG						0.0855
0	6 / 251 (2.4)	NE [31.3; NE]	0 / 246 (0.0)	NE [NE; NE]	NE [NE; NE]	
>=1	5 / 178 (2.8)	NE [NE; NE]	2 / 163 (1.2)	NE [NE; NE]	1.6396 [0.3460; 11.5975] 0.5553	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Vascular disorders; PT: Deep vein thrombosis						
Age at randomization						NE
<65 years of age	0 / 301 (0.0)	NE [NE; NE]	4 / 285 (1.4)	NE [NE; NE]	NE [NE; NE]	
>=65 years of age	0 / 133 (0.0)	NE [NE; NE]	6 / 132 (4.5)	NE [NE; NE]	NE [NE; NE]	
Race						NE
Asian	0 / 153 (0.0)	NE [NE; NE]	0 / 147 (0.0)	NE [NE; NE]	NE [NE; NE]	
White	0 / 231 (0.0)	NE [NE; NE]	10 / 223 (4.5)	NE [NE; NE]	NE [NE; NE]	
Other	0 / 50 (0.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						NE
Asia	0 / 148 (0.0)	NE [NE; NE]	0 / 144 (0.0)	NE [NE; NE]	NE [NE; NE]	
Europe	0 / 227 (0.0)	NE [NE; NE]	7 / 206 (3.4)	NE [NE; NE]	NE [NE; NE]	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	3 / 67 (4.5)	NE [NE; NE]	NE [NE; NE]	
HER2 IHC expression						1.0000
IHC 1+	0 / 239 (0.0)	NE [NE; NE]	3 / 226 (1.3)	NE [NE; NE]	NE [NE; NE]	
IHC 2+/ISH-	0 / 116 (0.0)	NE [NE; NE]	4 / 115 (3.5)	NE [NE; NE]	NE [NE; NE]	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	3 / 74 (4.1)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						1.0000
Yes	0 / 393 (0.0)	NE [NE; NE]	9 / 377 (2.4)	NE [NE; NE]	NE [NE; NE]	
No	0 / 41 (0.0)	NE [NE; NE]	1 / 40 (2.5)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.9998
Yes	0 / 177 (0.0)	NE [NE; NE]	5 / 172 (2.9)	NE [NE; NE]	NE [NE; NE]	
No	0 / 257 (0.0)	NE [NE; NE]	5 / 245 (2.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						NE
1	0 / 65 (0.0)	NE [NE; NE]	3 / 79 (3.8)	NE [NE; NE]	NE [NE; NE]	
2	0 / 293 (0.0)	NE [NE; NE]	5 / 281 (1.8)	NE [NE; NE]	NE [NE; NE]	
>=3	0 / 75 (0.0)	NE [NE; NE]	2 / 56 (3.6)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.9998
ER+, PR+	0 / 252 (0.0)	NE [NE; NE]	4 / 234 (1.7)	NE [NE; NE]	NE [NE; NE]	
ER+, PR-	0 / 166 (0.0)	NE [NE; NE]	5 / 171 (2.9)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						1.0000
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	1 / 14 (7.1)	NE [6.8; NE]	NE [NE; NE]	
ER >10%	0 / 362 (0.0)	NE [NE; NE]	6 / 343 (1.7)	NE [NE; NE]	NE [NE; NE]	
Positive	0 / 51 (0.0)	NE [NE; NE]	3 / 60 (5.0)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						0.9996
Primary	0 / 127 (0.0)	NE [NE; NE]	6 / 137 (4.4)	NE [NE; NE]	NE [NE; NE]	
Secondary	0 / 307 (0.0)	NE [NE; NE]	4 / 279 (1.4)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						1.0000
Capecitabine	0 / 265 (0.0)	NE [NE; NE]	7 / 249 (2.8)	NE [NE; NE]	NE [NE; NE]	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	2 / 101 (2.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	1 / 67 (1.5)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.9999
Yes	0 / 197 (0.0)	NE [NE; NE]	5 / 198 (2.5)	NE [NE; NE]	NE [NE; NE]	
No	0 / 237 (0.0)	NE [NE; NE]	5 / 219 (2.3)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.2 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9997
Yes	0 / 294 (0.0)	NE [NE; NE]	5 / 275 (1.8)	NE [NE; NE]	NE [NE; NE]	
No	0 / 140 (0.0)	NE [NE; NE]	5 / 142 (3.5)	NE [NE; NE]	NE [NE; NE]	
ECOG						0.9997
0	0 / 251 (0.0)	NE [NE; NE]	5 / 246 (2.0)	NE [NE; NE]	NE [NE; NE]	
>=1	0 / 178 (0.0)	NE [NE; NE]	5 / 163 (3.1)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 5:07; Program name: T.2.29.2_10TEAE_SAF_SUB.sas; Output name: T.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.29.3 Unerwünschte Ereignisse nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Subgruppenanalyse – Interaktions-p-Wert <0,05 – SAF

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: All (any PT)						
Age at randomization						0.0174
<65 years of age	269 / 301 (89.4)	0.1 [0.1; 0.1]	174 / 285 (61.1)	2.1 [1.2; 3.3]	2.5850 [2.1324; 3.1424] <.0001	
>=65 years of age	107 / 133 (80.5)	0.2 [0.1; 0.4]	82 / 132 (62.1)	1.2 [0.7; 4.3]	1.7520 [1.3144; 2.3438] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:00; Program name: T.2.29.3_10TEAE_SAF_SUB_SIG.sas; Output name: T.2.29.3_10TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Nausea						
Number of prior lines of endocrine therapy in the metastatic setting						0.0216
1	53 / 65 (81.5)	0.1 [0.1; 0.2]	22 / 79 (27.8)	NE [NE; NE]	5.6259 [3.4349; 9.5236] <.0001	
2	203 / 293 (69.3)	0.2 [0.1; 0.3]	82 / 281 (29.2)	NE [NE; NE]	3.4011 [2.6397; 4.4246] <.0001	
>=3	46 / 75 (61.3)	0.8 [0.2; 3.9]	22 / 56 (39.3)	14.0 [1.8; NE]	1.9980 [1.2160; 3.3853] 0.0067	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Constipation						
Prior Taxane Use In The Non-Metastatic Setting						0.0236
Yes	55 / 177 (31.1)	NE [NE; NE]	35 / 172 (20.3)	NE [NE; NE]	1.4729 [0.9662; 2.2746] 0.0741	
No	82 / 257 (31.9)	NE [23.5; NE]	27 / 245 (11.0)	NE [NE; NE]	2.8627 [1.8776; 4.5056] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior anthracycline use						0.0335
Yes	61 / 197 (31.0)	NE [NE; NE]	38 / 198 (19.2)	NE [NE; NE]	1.5628 [1.0452; 2.3661] 0.0306	
No	76 / 237 (32.1)	NE [23.5; NE]	24 / 219 (11.0)	NE [NE; NE]	2.9155 [1.8707; 4.7130] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:00; Program name: T.2.29.3_10TEAE_SAF_SUB_SIG.sas; Output name: T.2.29.3_10TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Vomiting						
Region						0.0439
Asia	48 / 148 (32.4)	NE [NE; NE]	8 / 144 (5.6)	NE [23.6; NE]	6.4820 [3.2460; 14.8275] <.0001	
Europe	73 / 227 (32.2)	NE [NE; NE]	29 / 206 (14.1)	NE [NE; NE]	2.3914 [1.5725; 3.7349] <.0001	
Rest of the World	25 / 59 (42.4)	18.6 [6.2; NE]	12 / 67 (17.9)	NE [NE; NE]	2.3710 [1.2113; 4.9047] 0.0119	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Gastrointestinal disorders; PT: Dyspepsia						
Race						0.0171
Asian	7 / 153 (4.6)	NE [NE; NE]	9 / 147 (6.1)	NE [NE; NE]	0.6639 [0.2366; 1.7865] 0.4144	
White	41 / 231 (17.7)	NE [NE; NE]	10 / 223 (4.5)	NE [NE; NE]	3.5711 [1.8604; 7.5562] 0.0001	
Other	2 / 50 (4.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	1.2054 [0.1036; 27.2290] 0.8832	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.0240
Yes	50 / 393 (12.7)	NE [NE; NE]	18 / 377 (4.8)	NE [NE; NE]	2.3021 [1.3656; 4.0608] 0.0019	
No	0 / 41 (0.0)	NE [NE; NE]	2 / 40 (5.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: All (any PT)						
Region						0.0161
Asia	84 / 148 (56.8)	5.6 [4.0; 14.6]	37 / 144 (25.7)	NE [NE; NE]	2.3775 [1.6277; 3.5428] <.0001	
Europe	80 / 227 (35.2)	NE [20.3; NE]	53 / 206 (25.7)	NE [NE; NE]	1.2126 [0.8573; 1.7288] 0.2786	
Rest of the World	33 / 59 (55.9)	5.7 [1.4; NE]	17 / 67 (25.4)	20.8 [20.8; NE]	2.4511 [1.3810; 4.5116] 0.0020	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
HER2 IHC expression						0.0331
IHC 1+	103 / 239 (43.1)	19.1 [12.1; NE]	54 / 226 (23.9)	NE [NE; NE]	1.7690 [1.2766; 2.4789] 0.0006	
IHC 2+/ISH-	61 / 116 (52.6)	9.0 [4.4; NE]	25 / 115 (21.7)	NE [NE; NE]	2.4474 [1.5532; 3.9739] 0.0001	
IHC >0 <1+	32 / 76 (42.1)	18.9 [6.2; NE]	28 / 74 (37.8)	20.8 [4.1; NE]	1.0169 [0.6115; 1.7009] 0.9451	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Endocrine Resistance						0.0174
Primary	51 / 127 (40.2)	14.6 [11.1; NE]	44 / 137 (32.1)	NE [9.8; NE]	1.1070 [0.7375; 1.6684] 0.6221	
Secondary	146 / 307 (47.6)	14.0 [7.9; NE]	63 / 279 (22.6)	NE [NE; NE]	2.1385 [1.5989; 2.8955] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0498
Yes	127 / 294 (43.2)	18.9 [13.1; NE]	76 / 275 (27.6)	NE [NE; NE]	1.4631 [1.1021; 1.9553] 0.0088	
No	70 / 140 (50.0)	10.0 [5.6; NE]	31 / 142 (21.8)	NE [20.8; NE]	2.3942 [1.5833; 3.7070] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Race						0.0239
Asian	50 / 153 (32.7)	NE [NE; NE]	12 / 147 (8.2)	NE [NE; NE]	4.3076 [2.3742; 8.4810] <.0001	
White	54 / 231 (23.4)	NE [NE; NE]	29 / 223 (13.0)	NE [NE; NE]	1.7301 [1.1098; 2.7530] 0.0161	
Other	10 / 50 (20.0)	NE [NE; NE]	7 / 47 (14.9)	NE [NE; NE]	1.2134 [0.4566; 3.3873] 0.7017	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0009
Asia	46 / 148 (31.1)	NE [NE; NE]	11 / 144 (7.6)	NE [NE; NE]	4.3148 [2.3198; 8.7752] <.0001	
Europe	47 / 227 (20.7)	NE [NE; NE]	32 / 206 (15.5)	NE [NE; NE]	1.2558 [0.8033; 1.9879] 0.3212	
Rest of the World	21 / 59 (35.6)	NE [10.3; NE]	5 / 67 (7.5)	NE [NE; NE]	5.0305 [2.0464; 15.0863] 0.0003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0006
Yes	64 / 294 (21.8)	NE [NE; NE]	38 / 275 (13.8)	NE [NE; NE]	1.5024 [1.0096; 2.2663] 0.0465	
No	50 / 140 (35.7)	NE [NE; NE]	10 / 142 (7.0)	NE [NE; NE]	5.5005 [2.9143; 11.5160] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: All (any PT)						
T-DXd vs. each Investigator's choice chemotherapy						0.0109
Capecitabine	174 / 265 (65.7)	4.2 [2.7; 5.5]	77 / 249 (30.9)	23.3 [14.0; 26.2]	2.4287 [1.8647; 3.1944] <.0001	
Nab-Paclitaxel	72 / 103 (69.9)	2.6 [0.6; 4.9]	50 / 101 (49.5)	7.7 [0.9; NE]	1.4526 [1.0144; 2.0962] 0.0412	
Paclitaxel	35 / 66 (53.0)	7.6 [5.1; NE]	24 / 67 (35.8)	NE [3.6; NE]	1.0801 [0.6347; 1.8639] 0.7751	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 11:00; Program name: T.2.29.3_10TEAE_SAF_SUB_SIG.sas; Output name: T.2.29.3_10TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Race						0.0065
Asian	54 / 153 (35.3)	NE [NE; NE]	28 / 147 (19.0)	NE [NE; NE]	1.8618 [1.1897; 2.9791] 0.0068	
White	49 / 231 (21.2)	NE [22.6; NE]	16 / 223 (7.2)	NE [NE; NE]	2.5781 [1.4948; 4.6900] 0.0007	
Other	14 / 50 (28.0)	NE [19.8; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0108
Asia	52 / 148 (35.1)	NE [NE; NE]	27 / 144 (18.8)	NE [NE; NE]	1.8799 [1.1915; 3.0352] 0.0069	
Europe	60 / 227 (26.4)	27.7 [22.6; NE]	11 / 206 (5.3)	NE [NE; NE]	4.3955 [2.4010; 8.8517] <.0001	
Rest of the World	5 / 59 (8.5)	NE [20.5; NE]	6 / 67 (9.0)	NE [NE; NE]	0.8187 [0.2348; 2.7310] 0.7419	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Alanine aminotransferase increased						
Race						0.0077
Asian	50 / 153 (32.7)	NE [NE; NE]	34 / 147 (23.1)	NE [NE; NE]	1.3981 [0.9077; 2.1793] 0.1307	
White	33 / 231 (14.3)	NE [NE; NE]	14 / 223 (6.3)	NE [NE; NE]	2.0648 [1.1268; 3.9916] 0.0206	
Other	10 / 50 (20.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Endocrine Resistance						0.0236
Primary	26 / 127 (20.5)	NE [NE; NE]	24 / 137 (17.5)	NE [NE; NE]	1.0620 [0.6069; 1.8658] 0.8310	
Secondary	67 / 307 (21.8)	NE [NE; NE]	24 / 279 (8.6)	NE [NE; NE]	2.4660 [1.5692; 4.0106] 0.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Gamma-glutamyltransferase increased						
Prior Taxane Use In The Non-Metastatic Setting						0.0420
Yes	17 / 177 (9.6)	NE [NE; NE]	7 / 172 (4.1)	NE [NE; NE]	1.7047 [0.7245; 4.4581] 0.2369	
No	23 / 257 (8.9)	NE [NE; NE]	2 / 245 (0.8)	NE [NE; NE]	8.8506 [2.6081; 55.2448] 0.0004	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0394
Capecitabine	19 / 265 (7.2)	NE [NE; NE]	1 / 249 (0.4)	NE [NE; NE]	14.7995 [3.0642; 266.0065] 0.0005	
Nab-Paclitaxel	17 / 103 (16.5)	NE [25.2; NE]	8 / 101 (7.9)	NE [NE; NE]	1.6133 [0.7035; 4.0063] 0.2697	
Paclitaxel	4 / 66 (6.1)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.0127
Yes	18 / 197 (9.1)	NE [NE; NE]	8 / 198 (4.0)	NE [NE; NE]	1.7691 [0.7853; 4.3496] 0.1797	
No	22 / 237 (9.3)	NE [NE; NE]	1 / 219 (0.5)	NE [NE; NE]	15.6066 [3.2679; 279.6789] 0.0003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Blood alkaline phosphatase increased						
Endocrine Resistance						0.0156
Primary	14 / 127 (11.0)	NE [25.2; NE]	11 / 137 (8.0)	NE [NE; NE]	0.9850 [0.4363; 2.2627] 0.9700	
Secondary	34 / 307 (11.1)	NE [NE; NE]	6 / 279 (2.2)	NE [NE; NE]	4.0164 [1.8088; 10.6566] 0.0007	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior anthracycline use						0.0120
Yes	20 / 197 (10.2)	NE [NE; NE]	13 / 198 (6.6)	NE [NE; NE]	1.1883 [0.5917; 2.4668] 0.6326	
No	28 / 237 (11.8)	NE [NE; NE]	4 / 219 (1.8)	NE [NE; NE]	4.9691 [1.9413; 16.8222] 0.0009	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Weight decreased						
Prior CDK4/6 inhibitor use						0.0446
Yes	25 / 393 (6.4)	NE [NE; NE]	8 / 377 (2.1)	NE [23.7; NE]	2.3042 [1.0805; 5.4802] 0.0356	
No	7 / 41 (17.1)	NE [24.4; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Endocrine Resistance						0.0061
Primary	12 / 127 (9.4)	NE [NE; NE]	0 / 137 (0.0)	NE [NE; NE]	NE [NE; NE]	
Secondary	20 / 307 (6.5)	NE [NE; NE]	8 / 279 (2.9)	NE [23.7; NE]	1.7131 [0.7767; 4.1586] 0.1965	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: All (any PT)						
Region						0.0379
Asia	45 / 148 (30.4)	NE [NE; NE]	57 / 144 (39.6)	11.8 [7.7; NE]	0.6684 [0.4489; 0.9893] 0.0433	
Europe	88 / 227 (38.8)	22.0 [13.9; NE]	100 / 206 (48.5)	7.4 [3.4; 12.5]	0.6108 [0.4559; 0.8168] 0.0008	
Rest of the World	36 / 59 (61.0)	5.3 [2.0; 9.3]	31 / 67 (46.3)	7.2 [2.3; NE]	1.2617 [0.7776; 2.0573] 0.3506	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:00; Program name: T.2.29.3_10TEAE_SAF_SUB_SIG.sas; Output name: T.2.29.3_10TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.0125
1	30 / 65 (46.2)	11.3 [3.7; NE]	33 / 79 (41.8)	8.0 [4.9; NE]	0.9975 [0.6008; 1.6481] 0.9848	
2	118 / 293 (40.3)	NE [14.5; NE]	122 / 281 (43.4)	9.5 [5.8; 20.9]	0.7932 [0.6142; 1.0240] 0.0726	
>=3	21 / 75 (28.0)	NE [14.9; NE]	32 / 56 (57.1)	4.1 [2.2; 10.9]	0.3009 [0.1680; 0.5268] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						<.0001
Capecitabine	125 / 265 (47.2)	13.4 [6.5; NE]	87 / 249 (34.9)	18.1 [10.9; NE]	1.2718 [0.9678; 1.6788] 0.0886	
Nab-Paclitaxel	22 / 103 (21.4)	NE [NE; NE]	51 / 101 (50.5)	6.6 [4.6; 11.9]	0.2997 [0.1763; 0.4926] <.0001	
Paclitaxel	22 / 66 (33.3)	NE [13.1; NE]	50 / 67 (74.6)	1.4 [1.0; 2.1]	0.2045 [0.1148; 0.3499] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0020
0	107 / 251 (42.6)	22.0 [11.3; NE]	100 / 246 (40.7)	14.3 [7.7; NE]	0.9529 [0.7242; 1.2550] 0.7179	
>=1	61 / 178 (34.3)	NE [14.2; NE]	85 / 163 (52.1)	4.0 [2.8; 9.1]	0.4664 [0.3319; 0.6512] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 11:00; Program name: T.2.29.3_10TEAE_SAF_SUB_SIG.sas; Output name: T.2.29.3_10TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Dysgeusia						
Region						0.0172
Asia	15 / 148 (10.1)	NE [NE; NE]	4 / 144 (2.8)	NE [NE; NE]	3.4084 [1.2350; 11.9687] 0.0207	
Europe	27 / 227 (11.9)	NE [NE; NE]	19 / 206 (9.2)	NE [NE; NE]	1.0595 [0.5898; 1.9418] 0.8473	
Rest of the World	9 / 59 (15.3)	NE [NE; NE]	1 / 67 (1.5)	NE [NE; NE]	9.5313 [1.7840; 175.9174] 0.0090	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:00; Program name: T.2.29.3_10TEAE_SAF_SUB_SIG.sas; Output name: T.2.29.3_10TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0067
Capecitabine	40 / 265 (15.1)	NE [NE; NE]	11 / 249 (4.4)	NE [NE; NE]	3.0479 [1.6183; 6.2490] 0.0006	
Nab-Paclitaxel	4 / 103 (3.9)	NE [NE; NE]	3 / 101 (3.0)	NE [NE; NE]	1.1650 [0.2544; 5.9541] 0.8423	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	10 / 67 (14.9)	NE [NE; NE]	0.5482 [0.1958; 1.4471] 0.2240	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Headache						
T-DXd vs. each Investigator's choice chemotherapy						0.0168
Capecitabine	56 / 265 (21.1)	NE [28.1; NE]	23 / 249 (9.2)	NE [NE; NE]	2.1809 [1.3596; 3.6186] 0.0013	
Nab-Paclitaxel	11 / 103 (10.7)	NE [25.9; NE]	8 / 101 (7.9)	NE [NE; NE]	1.1382 [0.4461; 2.9966] 0.7871	
Paclitaxel	7 / 66 (10.6)	NE [NE; NE]	11 / 67 (16.4)	NE [NE; NE]	0.5067 [0.1855; 1.2940] 0.1546	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:00; Program name: T.2.29.3_10TEAE_SAF_SUB_SIG.sas; Output name: T.2.29.3_10TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Race						0.0117
Asian	1 / 153 (0.7)	NE [NE; NE]	10 / 147 (6.8)	NE [NE; NE]	0.0801 [0.0044; 0.4199] 0.0020	
White	4 / 231 (1.7)	NE [NE; NE]	1 / 223 (0.4)	NE [NE; NE]	2.8351 [0.4144; 55.6973] 0.3323	
Other	0 / 50 (0.0)	NE [NE; NE]	1 / 47 (2.1)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.0421
Asia	1 / 148 (0.7)	NE [NE; NE]	10 / 144 (6.9)	NE [NE; NE]	0.0811 [0.0044; 0.4249] 0.0022	
Europe	2 / 227 (0.9)	NE [NE; NE]	1 / 206 (0.5)	NE [NE; NE]	1.3847 [0.1311; 29.9922] 0.7906	
Rest of the World	2 / 59 (3.4)	NE [NE; NE]	1 / 67 (1.5)	NE [NE; NE]	1.5654 [0.1450; 34.2625] 0.7160	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0215
Capecitabine	5 / 265 (1.9)	NE [NE; NE]	4 / 249 (1.6)	NE [NE; NE]	0.9050 [0.2385; 3.6693] 0.8821	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	8 / 101 (7.9)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.0247
Yes	5 / 294 (1.7)	NE [NE; NE]	6 / 275 (2.2)	NE [NE; NE]	0.6095 [0.1744; 2.0366] 0.4117	
No	0 / 140 (0.0)	NE [NE; NE]	6 / 142 (4.2)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Number of prior lines of endocrine therapy in the metastatic setting						0.0153
1	4 / 65 (6.2)	NE [NE; NE]	6 / 79 (7.6)	NE [NE; NE]	0.6843 [0.1733; 2.4184] 0.5577	
2	4 / 293 (1.4)	NE [NE; NE]	22 / 281 (7.8)	NE [NE; NE]	0.1346 [0.0393; 0.3532] <.0001	
>=3	0 / 75 (0.0)	NE [NE; NE]	8 / 56 (14.3)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0043
Capecitabine	7 / 265 (2.6)	NE [NE; NE]	11 / 249 (4.4)	NE [NE; NE]	0.4542 [0.1663; 1.1601] 0.0964	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	13 / 101 (12.9)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	1 / 66 (1.5)	NE [NE; NE]	12 / 67 (17.9)	NE [NE; NE]	0.0666 [0.0036; 0.3394] 0.0006	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Paraesthesia						
Age at randomization						0.0182
<65 years of age	8 / 301 (2.7)	NE [NE; NE]	18 / 285 (6.3)	NE [NE; NE]	0.2981 [0.1207; 0.6738] 0.0031	
>=65 years of age	4 / 133 (3.0)	NE [29.7; NE]	1 / 132 (0.8)	NE [NE; NE]	3.0804 [0.4503; 60.5138] 0.2918	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:00; Program name: T.2.29.3_10TEAE_SAF_SUB_SIG.sas; Output name: T.2.29.3_10TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
T-DXd vs. each Investigator's choice chemotherapy						0.0057
Capecitabine	8 / 265 (3.0)	NE [NE; NE]	13 / 249 (5.2)	NE [NE; NE]	0.5122 [0.2023; 1.2181] 0.1305	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	11 / 101 (10.9)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	4 / 66 (6.1)	NE [NE; NE]	25 / 67 (37.3)	NE [2.7; NE]	0.0831 [0.0238; 0.2222] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:00; Program name: T.2.29.3_10TEAE_SAF_SUB_SIG.sas; Output name: T.2.29.3_10TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia						
Region						0.0423
Asia	70 / 148 (47.3)	NE [2.3; NE]	33 / 144 (22.9)	NE [NE; NE]	2.1777 [1.4521; 3.3350] 0.0002	
Europe	109 / 227 (48.0)	9.7 [3.5; NE]	47 / 206 (22.8)	NE [NE; NE]	2.2457 [1.6065; 3.1908] <.0001	
Rest of the World	31 / 59 (52.5)	4.4 [1.0; NE]	7 / 67 (10.4)	NE [NE; NE]	6.1432 [2.8631; 15.2121] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						<.0001
Capecitabine	135 / 265 (50.9)	5.5 [2.2; NE]	7 / 249 (2.8)	NE [NE; NE]	23.1606 [11.6856; 54.7105] <.0001	
Nab-Paclitaxel	41 / 103 (39.8)	NE [5.4; NE]	46 / 101 (45.5)	NE [1.1; NE]	0.7691 [0.5031; 1.1717] 0.2220	
Paclitaxel	34 / 66 (51.5)	7.4 [1.4; NE]	34 / 67 (50.7)	2.3 [1.0; NE]	0.7746 [0.4780; 1.2544] 0.2986	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ECOG						0.0019
0	122 / 251 (48.6)	11.7 [2.8; NE]	38 / 246 (15.4)	NE [NE; NE]	3.5678 [2.5042; 5.2026] <.0001	
>=1	85 / 178 (47.8)	9.7 [2.6; NE]	49 / 163 (30.1)	NE [NE; NE]	1.6018 [1.1321; 2.2916] 0.0081	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)						
Age at randomization						0.0156
<65 years of age	182 / 301 (60.5)	2.2 [1.4; 3.8]	183 / 285 (64.2)	2.1 [1.4; 2.8]	0.8241 [0.6701; 1.0133] 0.0625	
>=65 years of age	68 / 133 (51.1)	6.3 [3.3; NE]	95 / 132 (72.0)	1.4 [1.2; 2.1]	0.4920 [0.3573; 0.6737] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Rash						
T-DXd vs. each Investigator's choice chemotherapy						0.0064
Capecitabine	18 / 265 (6.8)	NE [NE; NE]	10 / 249 (4.0)	NE [NE; NE]	1.2475 [0.5842; 2.8207] 0.5765	
Nab-Paclitaxel	3 / 103 (2.9)	NE [NE; NE]	11 / 101 (10.9)	NE [NE; NE]	0.2212 [0.0496; 0.7161] 0.0121	
Paclitaxel	5 / 66 (7.6)	NE [NE; NE]	10 / 67 (14.9)	NE [7.9; NE]	0.1693 [0.0403; 0.5765] 0.0038	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome						
Region						0.0404
Asia	0 / 148 (0.0)	NE [NE; NE]	52 / 144 (36.1)	NE [9.5; NE]	NE [NE; NE]	
Europe	4 / 227 (1.8)	NE [NE; NE]	62 / 206 (30.1)	NE [12.5; NE]	0.0369 [0.0111; 0.0902] <.0001	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	32 / 67 (47.8)	5.2 [2.1; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)						
T-DXd vs. each Investigator's choice chemotherapy						0.0013
Capecitabine	138 / 265 (52.1)	11.8 [8.2; 14.9]	65 / 249 (26.1)	NE [20.4; NE]	1.7127 [1.2805; 2.3152] 0.0003	
Nab-Paclitaxel	46 / 103 (44.7)	15.4 [8.1; 23.5]	17 / 101 (16.8)	NE [NE; NE]	2.3245 [1.3537; 4.1824] 0.0024	
Paclitaxel	25 / 66 (37.9)	NE [10.5; NE]	24 / 67 (35.8)	NE [3.9; NE]	0.6564 [0.3670; 1.1730] 0.1511	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Number of prior lines of endocrine therapy in the metastatic setting						0.0371
1	4 / 65 (6.2)	NE [NE; NE]	4 / 79 (5.1)	NE [NE; NE]	1.1023 [0.2602; 4.6687] 0.8907	
2	36 / 293 (12.3)	NE [NE; NE]	7 / 281 (2.5)	NE [NE; NE]	3.5439 [1.6697; 8.7240] 0.0012	
>=3	4 / 75 (5.3)	NE [26.8; NE]	4 / 56 (7.1)	NE [NE; NE]	0.5605 [0.1281; 2.4263] 0.4173	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea						
ER/PR status I						0.0221
ER+, PR+	18 / 252 (7.1)	NE [NE; NE]	20 / 234 (8.5)	NE [NE; NE]	0.6935 [0.3622; 1.3183] 0.2599	
ER+, PR-	4 / 166 (2.4)	NE [NE; NE]	19 / 171 (11.1)	NE [20.4; NE]	0.1642 [0.0470; 0.4438] 0.0003	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 11:00; Program name: T.2.29.3_10TEAE_SAF_SUB_SIG.sas; Output name: T.2.29.3_10TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)						
T-DXd vs. each Investigator's choice chemotherapy						0.0001
Capecitabine	100 / 265 (37.7)	19.3 [16.4; NE]	81 / 249 (32.5)	26.5 [11.9; NE]	0.9616 [0.7167; 1.2942] 0.7917	
Nab-Paclitaxel	13 / 103 (12.6)	NE [28.3; NE]	23 / 101 (22.8)	NE [14.4; NE]	0.4160 [0.1990; 0.8261] 0.0120	
Paclitaxel	16 / 66 (24.2)	NE [16.6; NE]	29 / 67 (43.3)	12.5 [2.1; NE]	0.1864 [0.0833; 0.3818] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: General disorders and administration site conditions; PT: Oedema peripheral						
Number of prior lines of endocrine therapy in the metastatic setting						0.0206
1	10 / 65 (15.4)	NE [NE; NE]	7 / 79 (8.9)	NE [17.4; NE]	1.5934 [0.6045; 4.4246] 0.3455	
2	20 / 293 (6.8)	NE [NE; NE]	42 / 281 (14.9)	NE [NE; NE]	0.3209 [0.1836; 0.5420] <.0001	
>=3	6 / 75 (8.0)	NE [NE; NE]	10 / 56 (17.9)	NE [NE; NE]	0.3882 [0.1318; 1.0482] 0.0581	
ER/PR status I						0.0337
ER+, PR+	23 / 252 (9.1)	NE [NE; NE]	25 / 234 (10.7)	NE [NE; NE]	0.6631 [0.3723; 1.1755] 0.1560	
ER+, PR-	10 / 166 (6.0)	NE [NE; NE]	31 / 171 (18.1)	NE [17.4; NE]	0.2478 [0.1144; 0.4920] <.0001	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 11:00; Program name: T.2.29.3_10TEAE_SAF_SUB_SIG.sas; Output name: T.2.29.3_10TEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
ER/PR status I						0.0110
ER+, PR+	19 / 252 (7.5)	NE [NE; NE]	1 / 234 (0.4)	NE [NE; NE]	13.4582 [2.7779; 242.1275] 0.0010	
ER+, PR-	7 / 166 (4.2)	NE [NE; NE]	5 / 171 (2.9)	NE [NE; NE]	1.0632 [0.3346; 3.6363] 0.9173	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

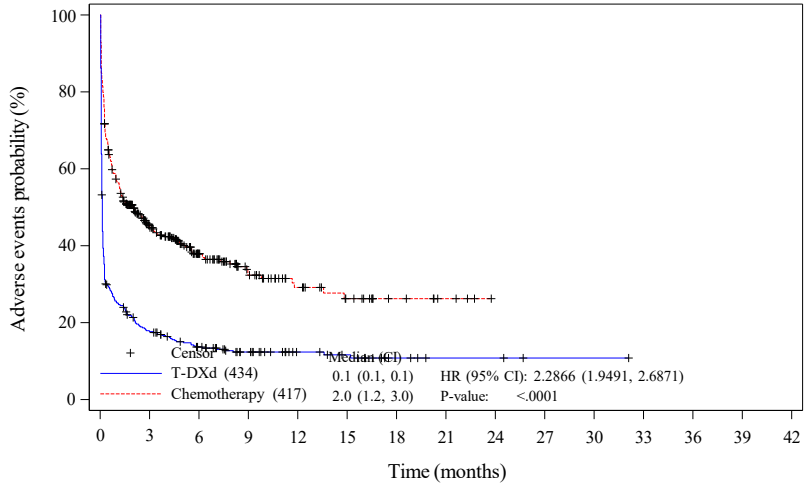
Table 2.29.3 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Blood and lymphatic system disorders; PT: Lymphopenia						
ECOG						0.0109
0	9 / 251 (3.6)	NE [NE; NE]	5 / 246 (2.0)	NE [NE; NE]	1.4998 [0.5158; 4.8985] 0.4661	
>=1	11 / 178 (6.2)	NE [NE; NE]	0 / 163 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Abbildung 2.29.1 Unerwünschte Ereignisse nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Kaplan-Meier-Plot – SAF

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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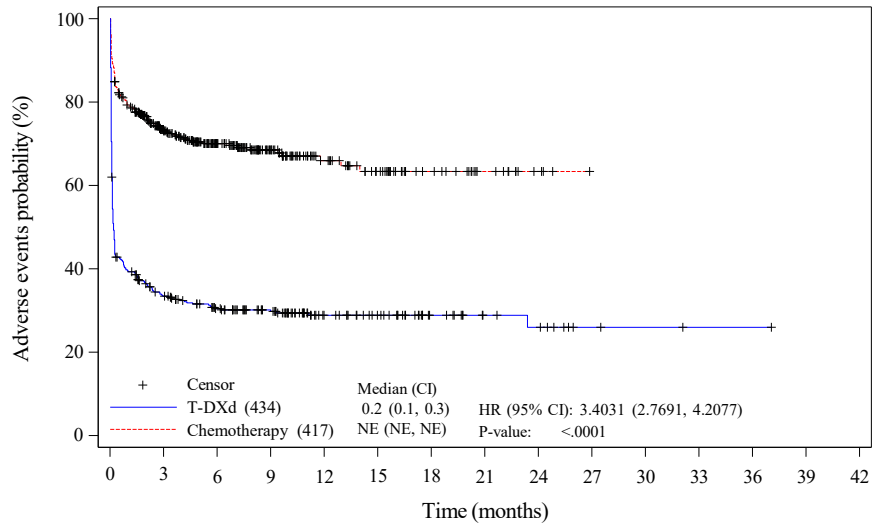
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Nausea



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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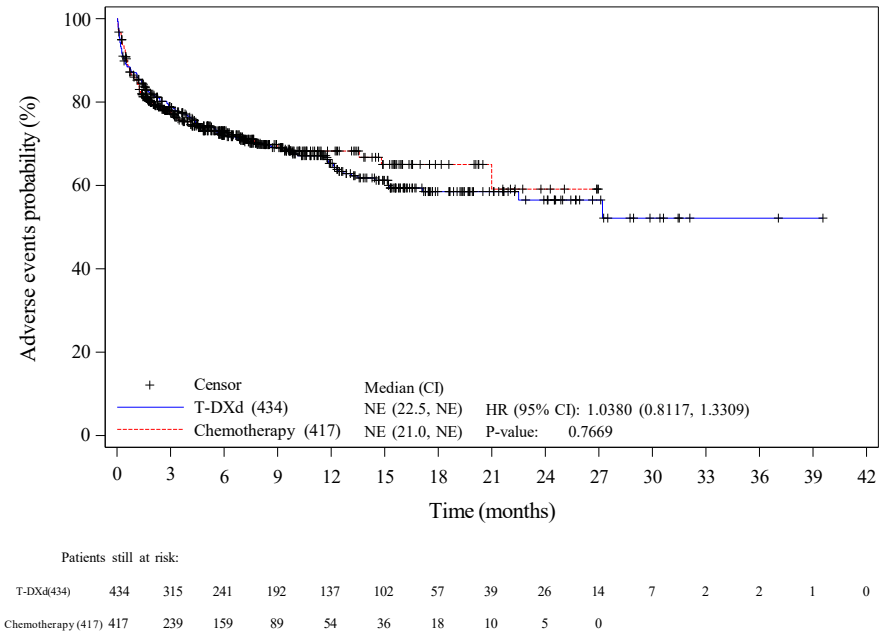
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Diarrhoea



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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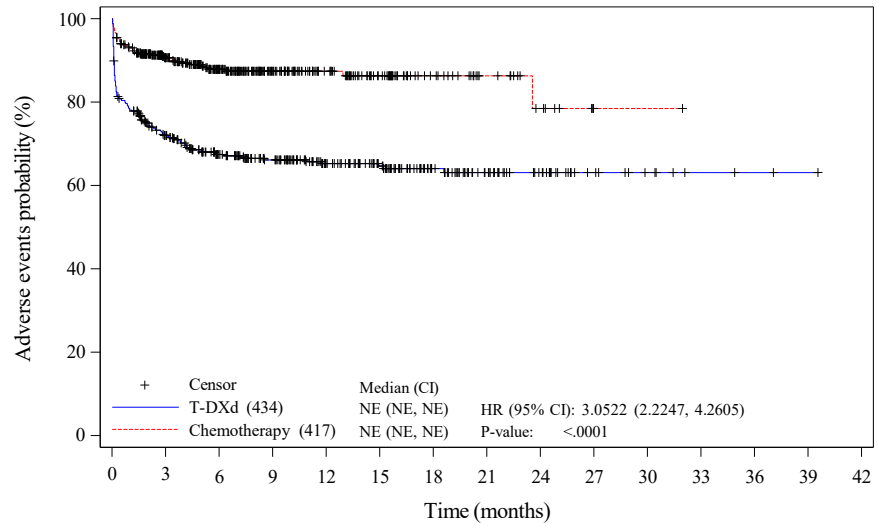
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Vomiting



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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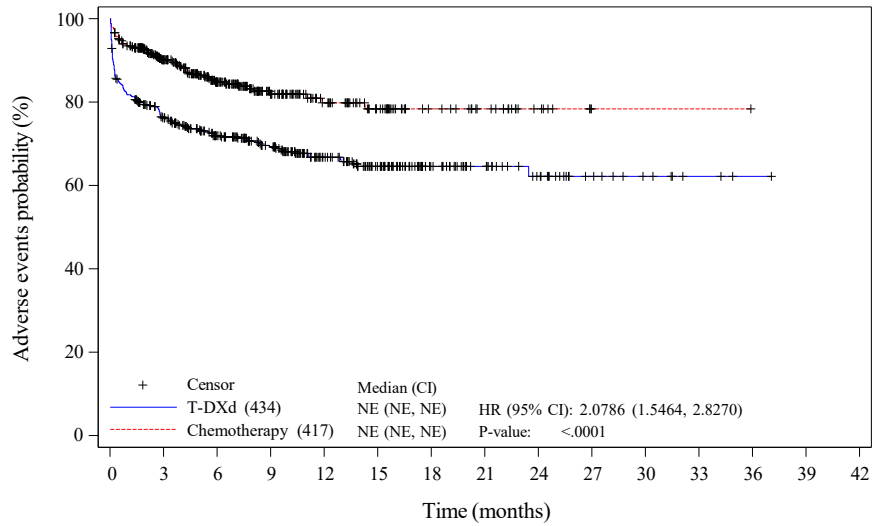
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Constipation



Patients still at risk:

T-DXd(434)	434	306	244	193	134	96	53	37	24	12	7	3	1	0
Chemotherapy (417)	417	290	192	116	72	48	27	19	8	1	1	1	0	

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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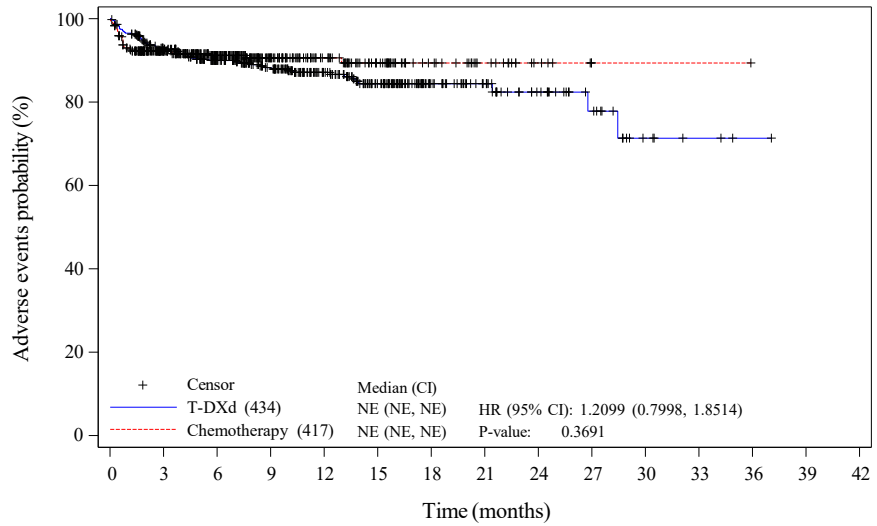
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Stomatitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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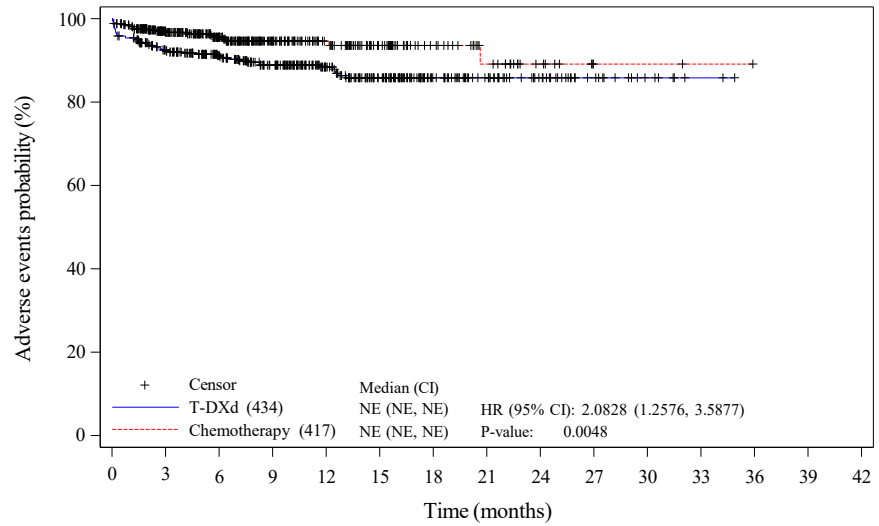
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia



Patients still at risk:

T-DXd(434)	434	365	301	241	179	131	74	52	31	16	7	2	0
Chemotherapy (417)	417	309	217	135	90	58	33	20	9	2	2	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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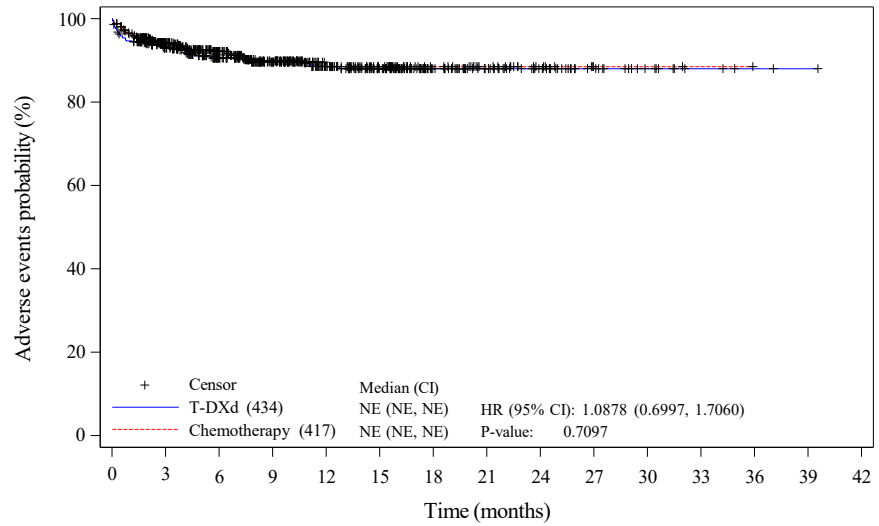
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Abdominal pain



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
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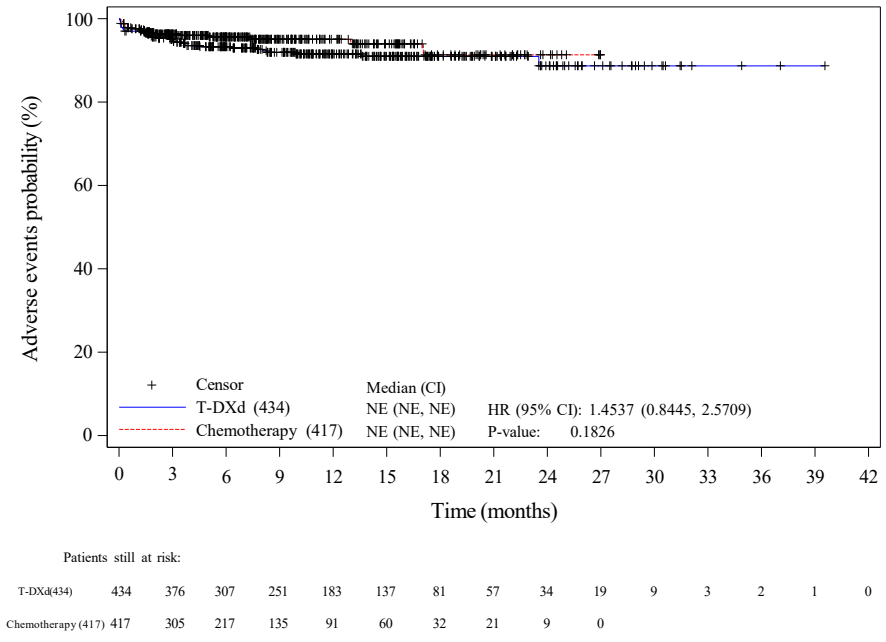
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Abdominal pain upper



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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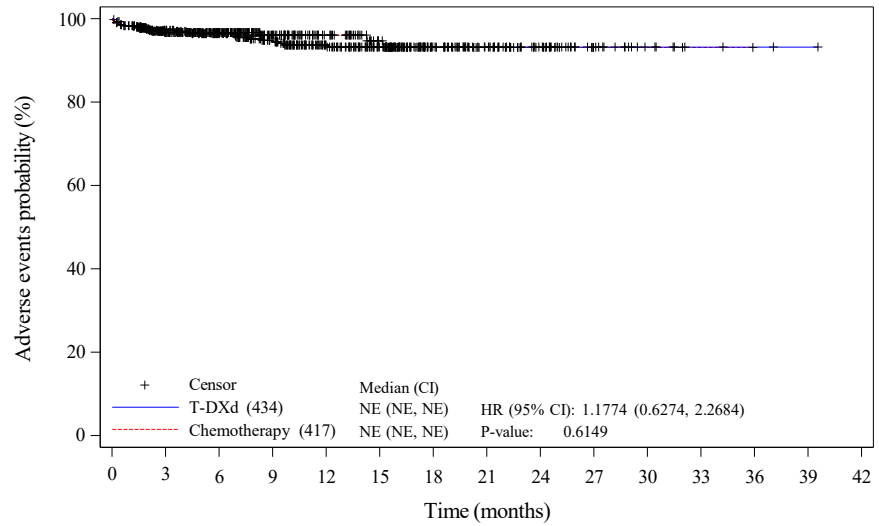
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dry mouth



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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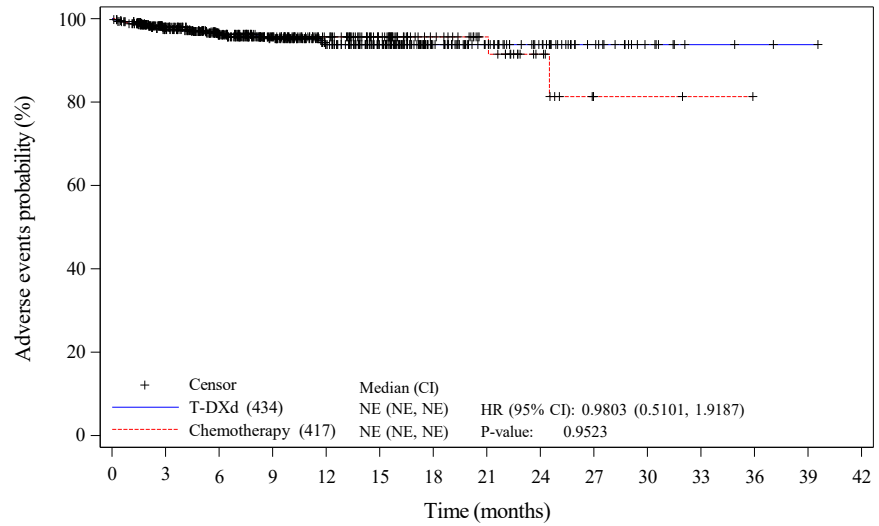
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Abdominal distension



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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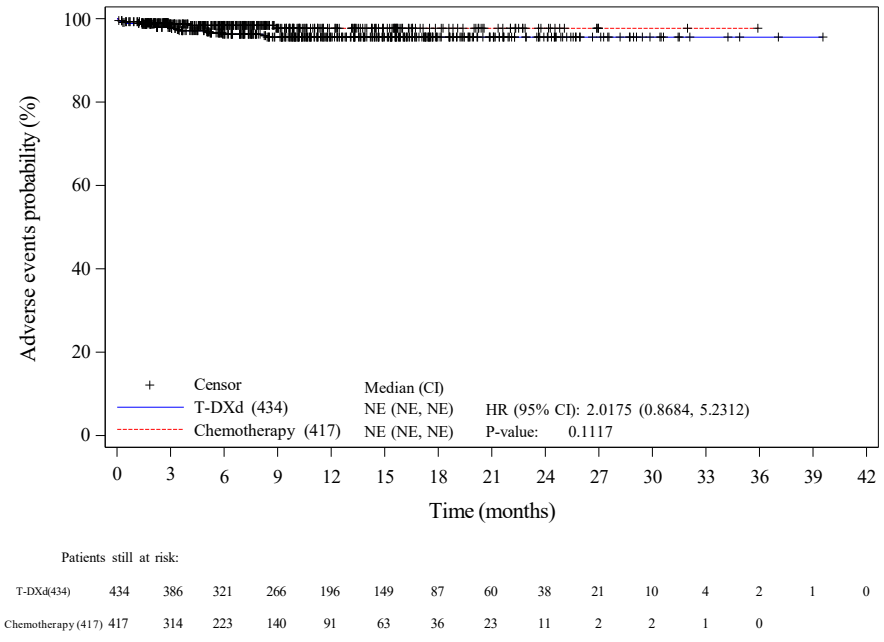
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Gastrooesophageal reflux disease



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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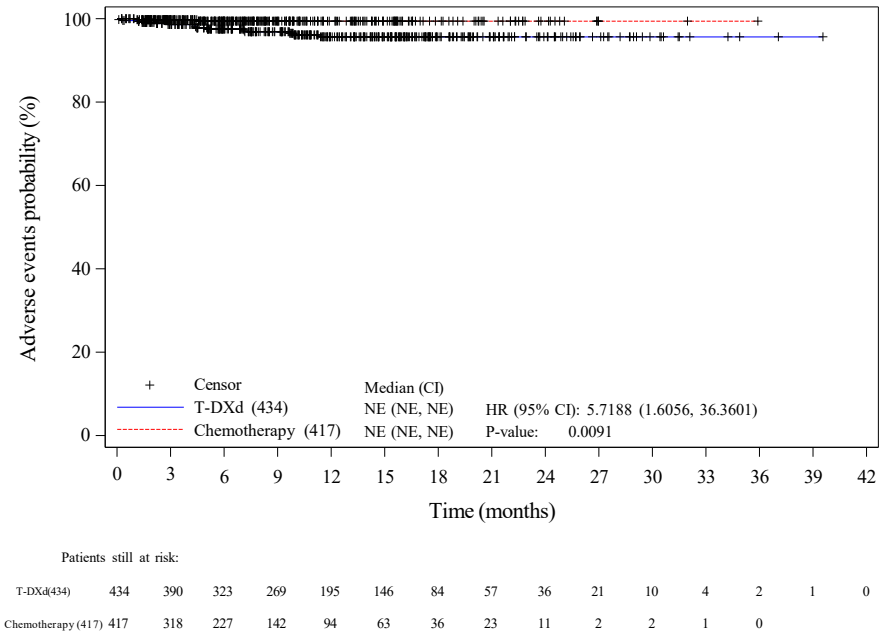
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Haemorrhoids



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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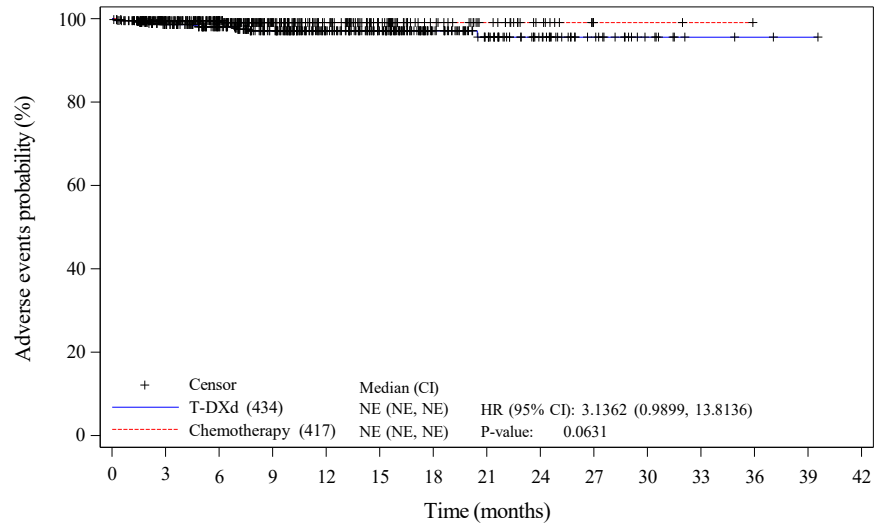
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Abdominal discomfort



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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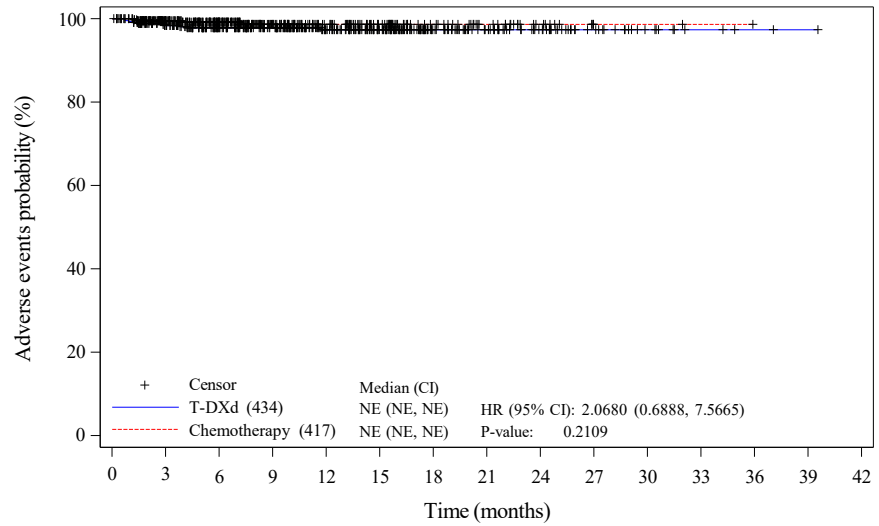
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Flatulence



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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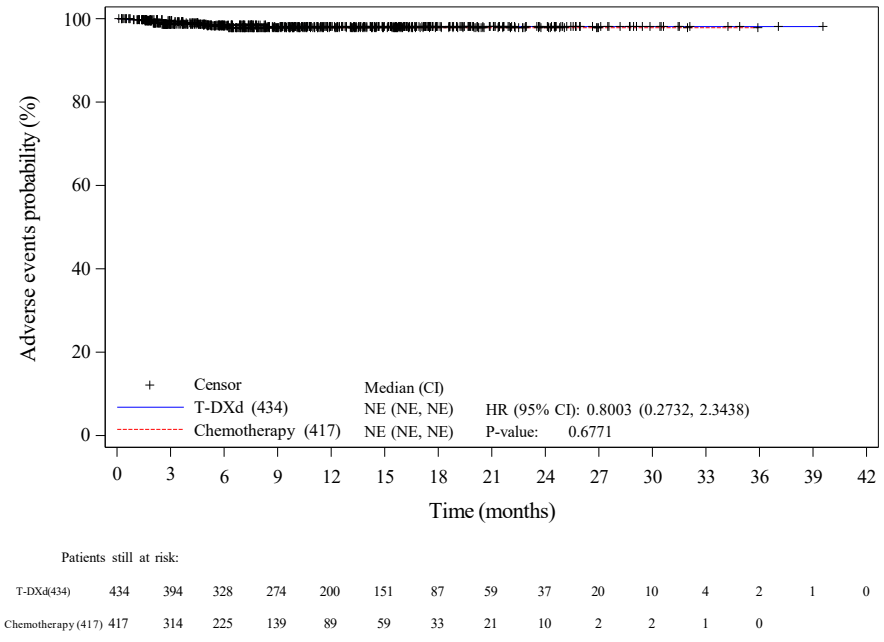
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Mouth ulceration



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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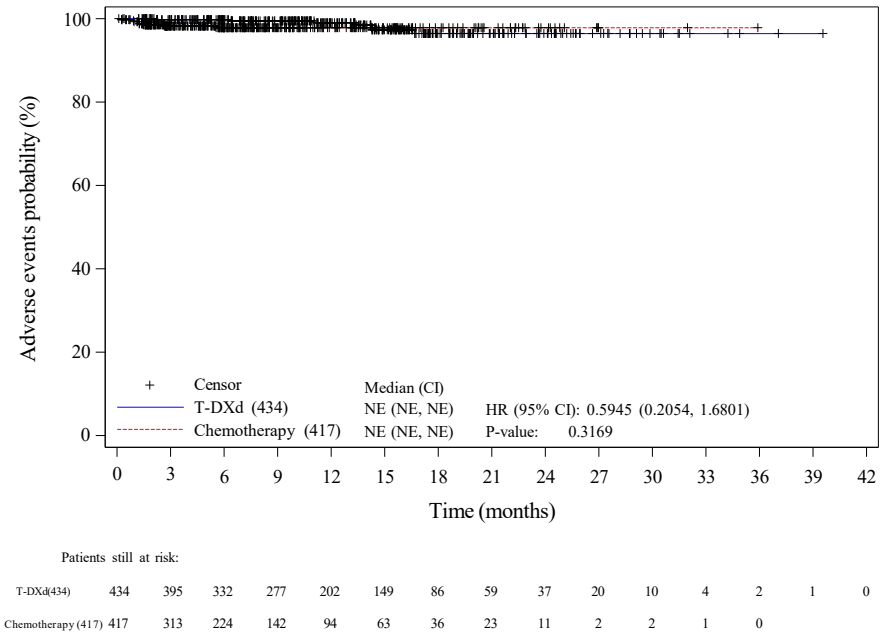
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Toothache



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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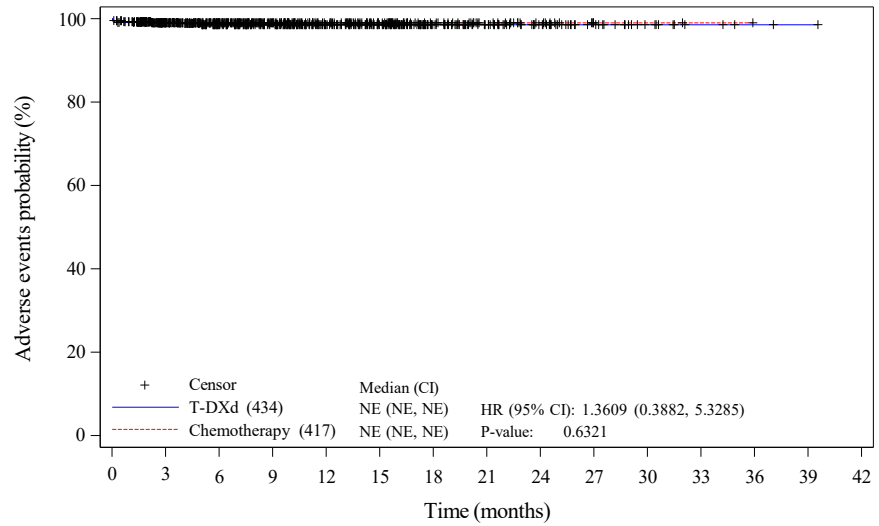
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Gastrointestinal pain



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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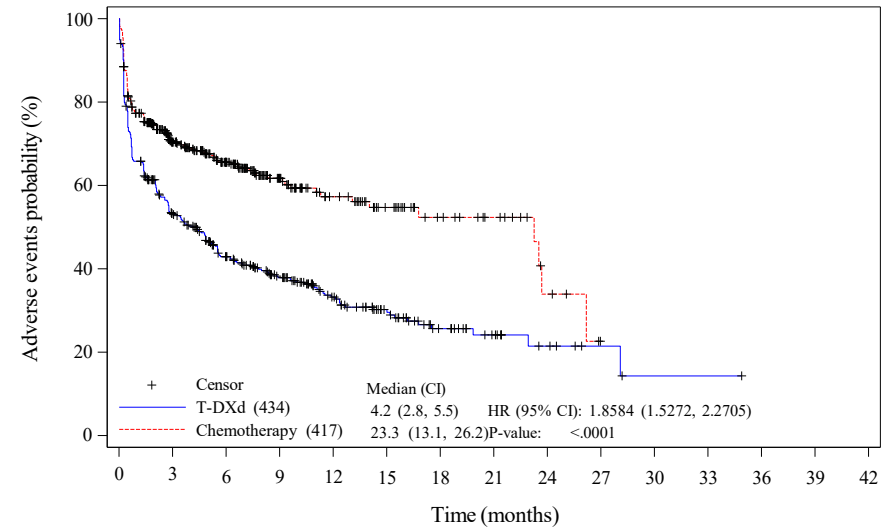
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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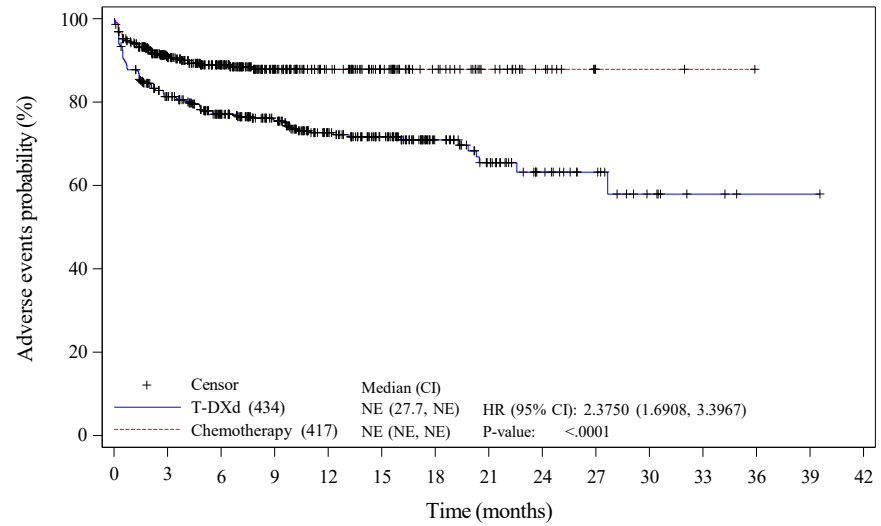
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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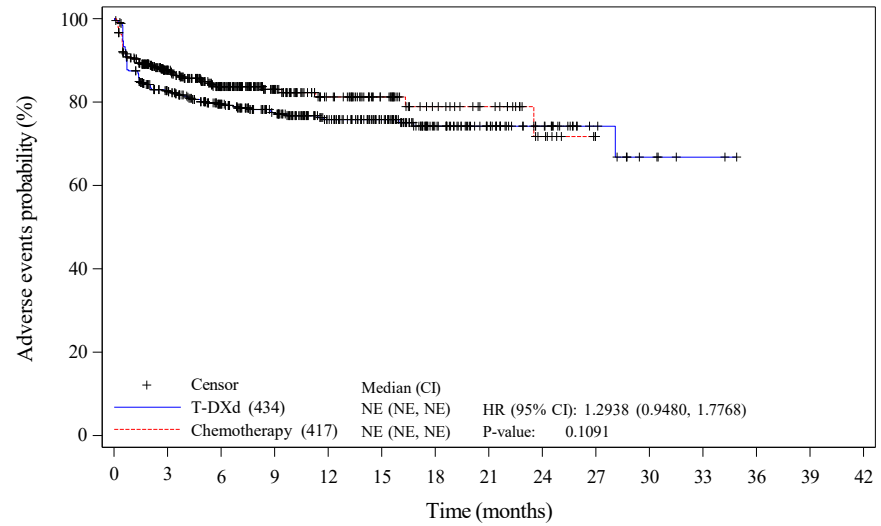
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Neutrophil count decreased



Patients still at risk:

T-DXd(434)	434	325	262	213	156	119	68	44	26	11	5	2	0
Chemotherapy (417)	417	276	187	114	72	47	28	20	8	0			

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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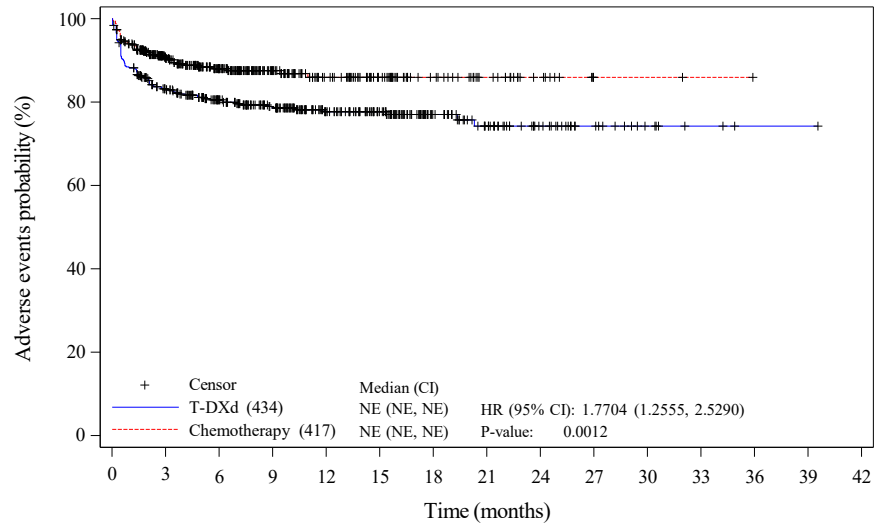
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Alanine aminotransferase increased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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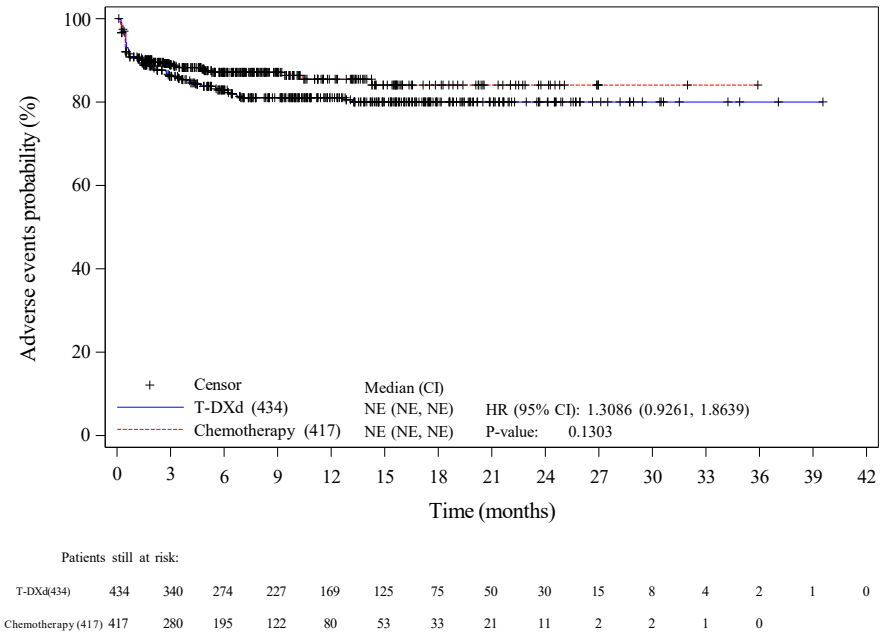
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: White blood cell count decreased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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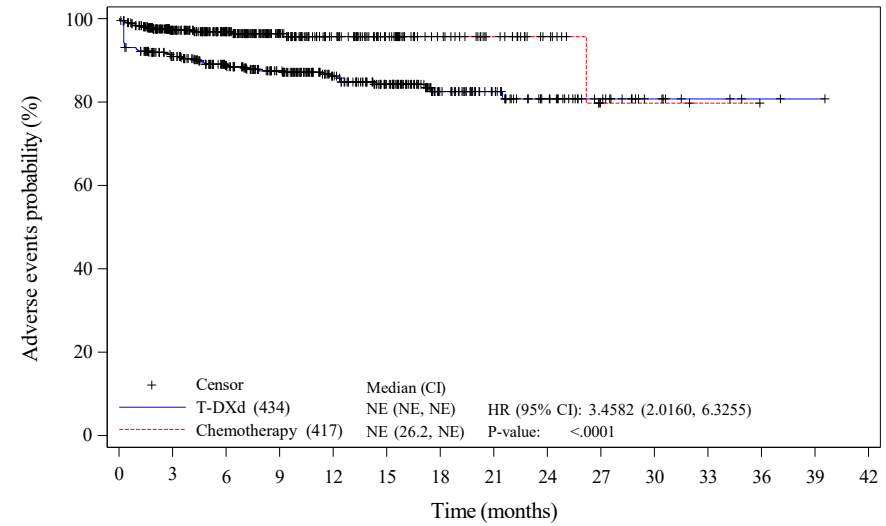
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Platelet count decreased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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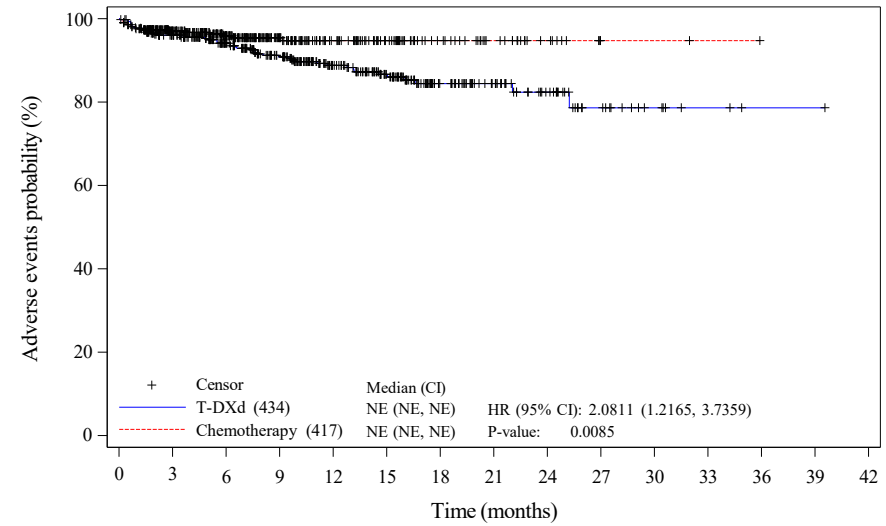
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Blood alkaline phosphatase increased



Patients still at risk:

T-DXd(434)	434	382	313	252	182	136	76	52	31	15	7	3	1	1	0
Chemotherapy (417)	417	309	220	140	90	61	35	22	11	2	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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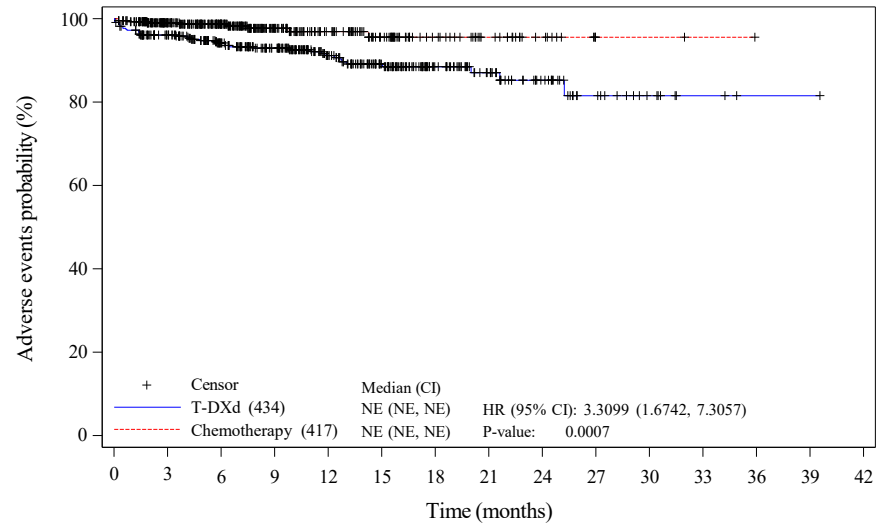
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Gamma-glutamyltransferase increased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
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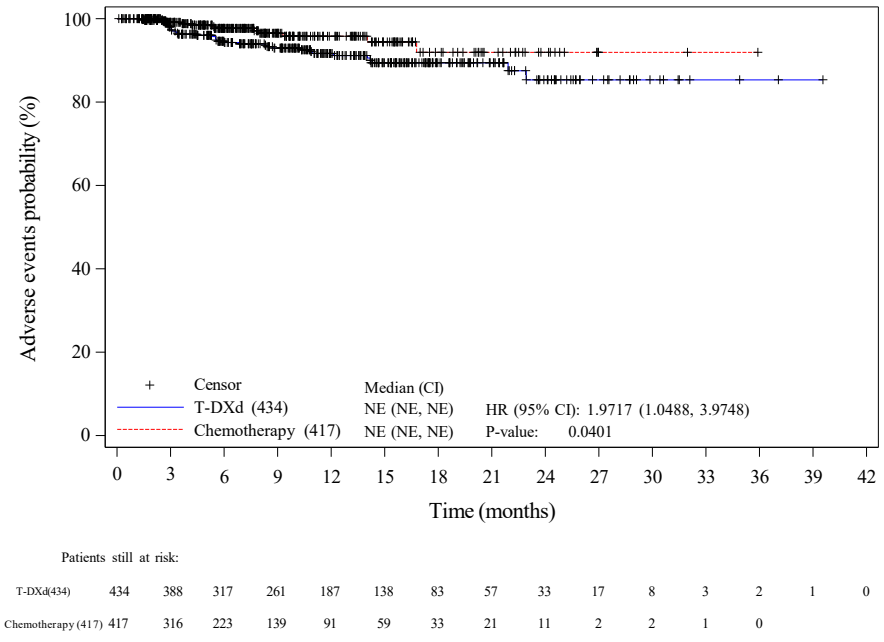
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Ejection fraction decreased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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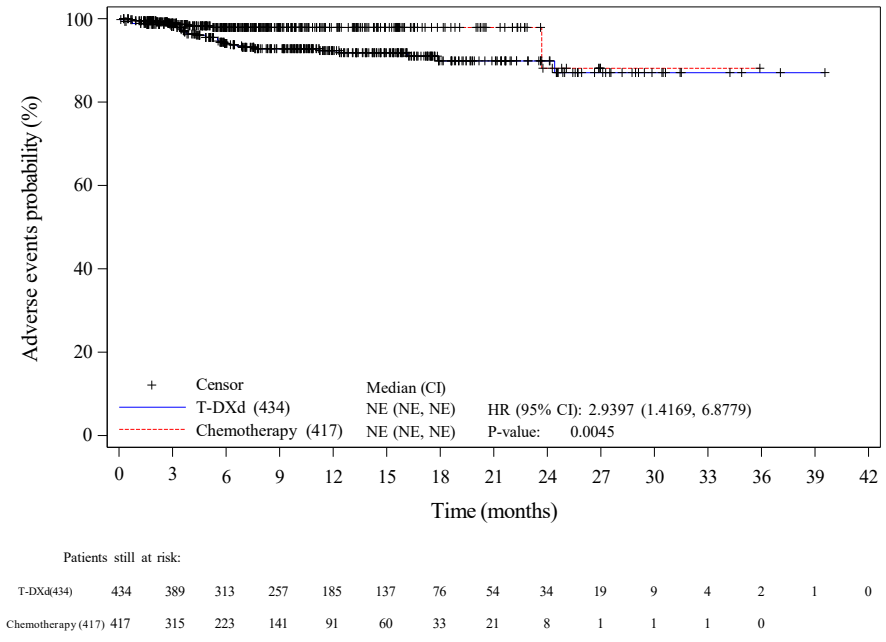
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Weight decreased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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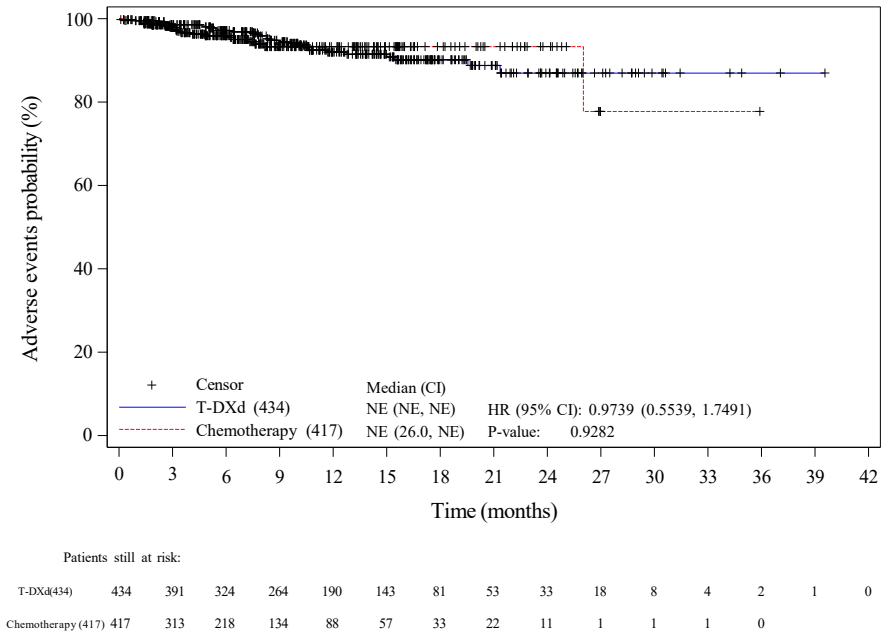
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Blood bilirubin increased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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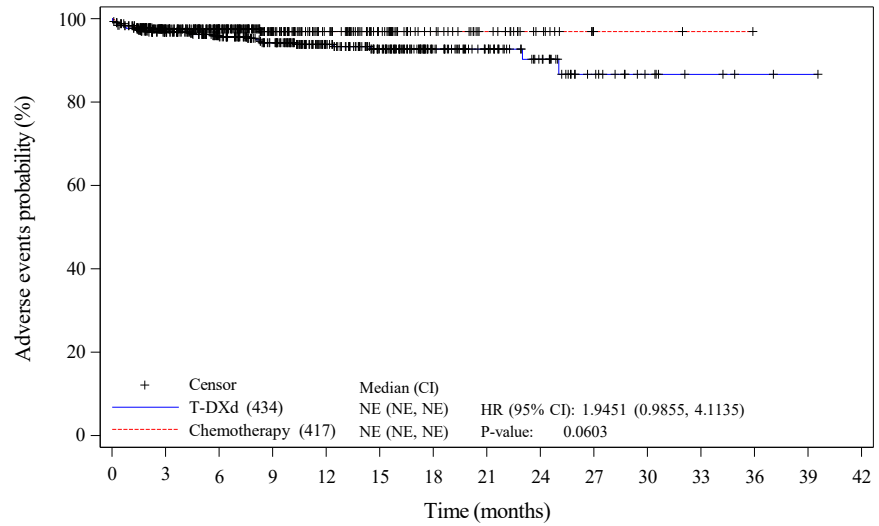
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Lymphocyte count decreased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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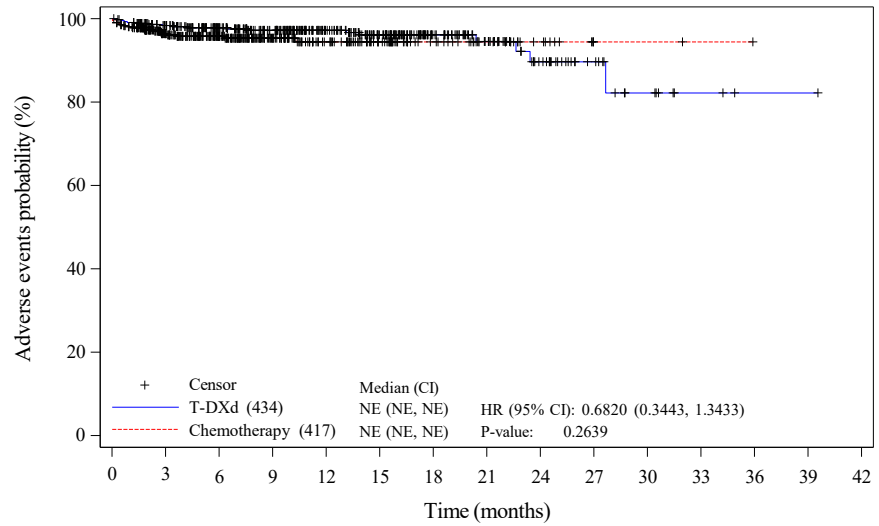
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Blood lactate dehydrogenase increased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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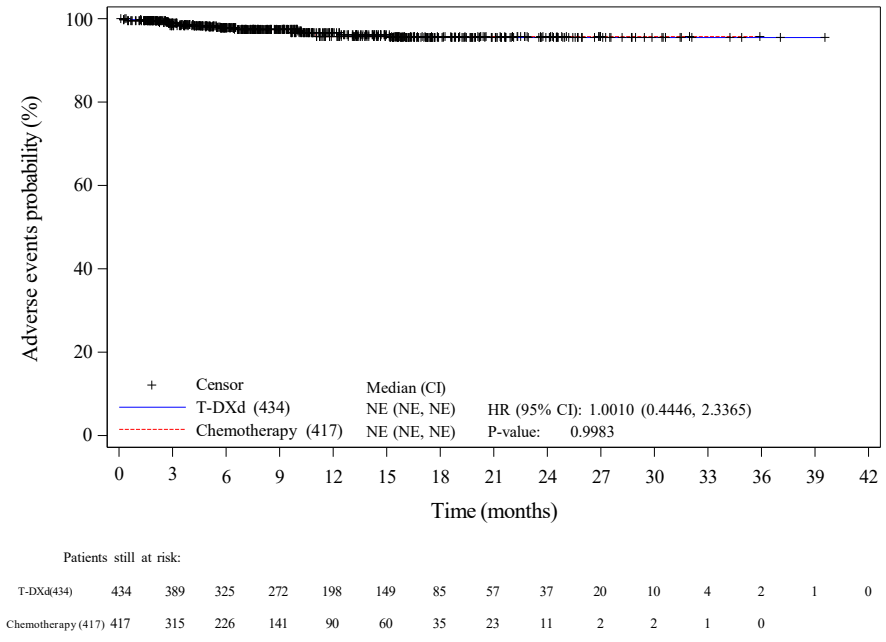
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Weight increased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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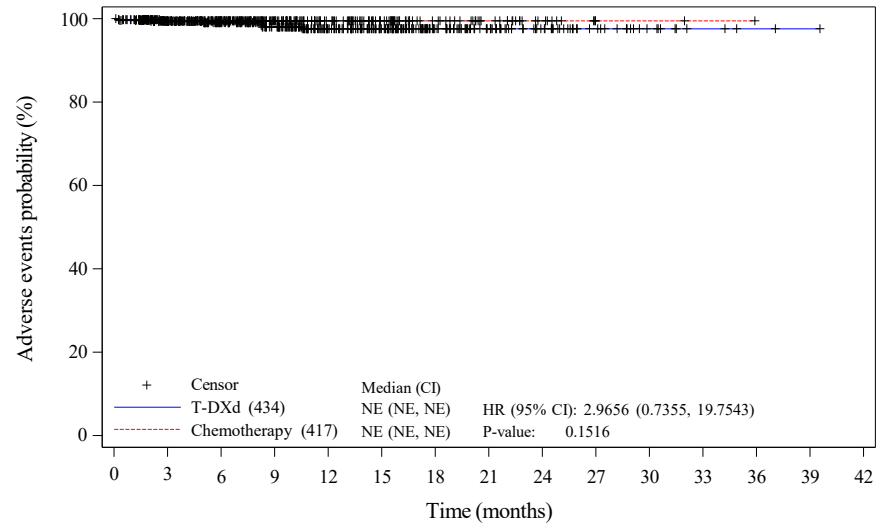
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Bilirubin conjugated increased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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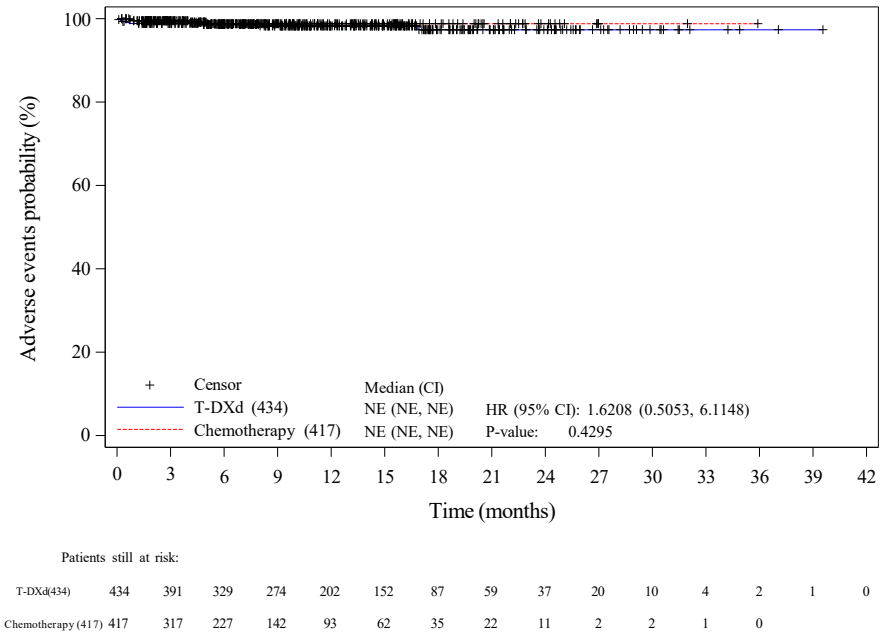
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Transaminases increased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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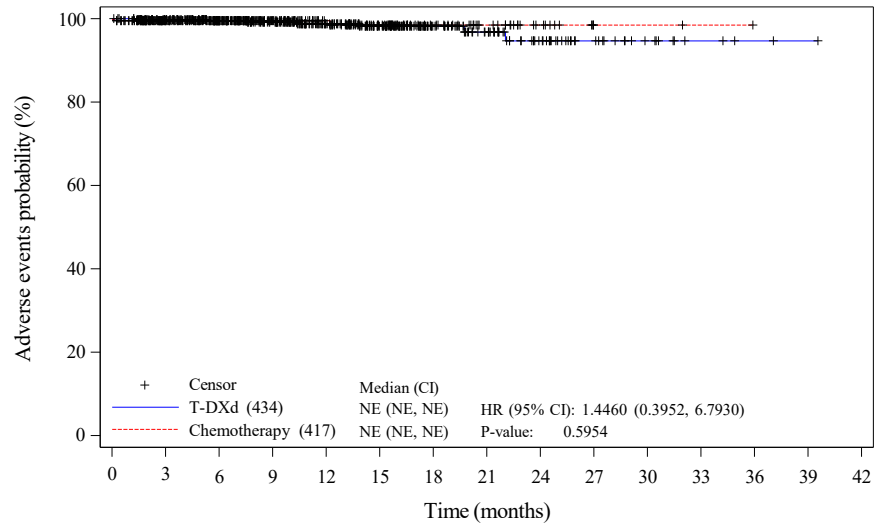
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Blood cholesterol increased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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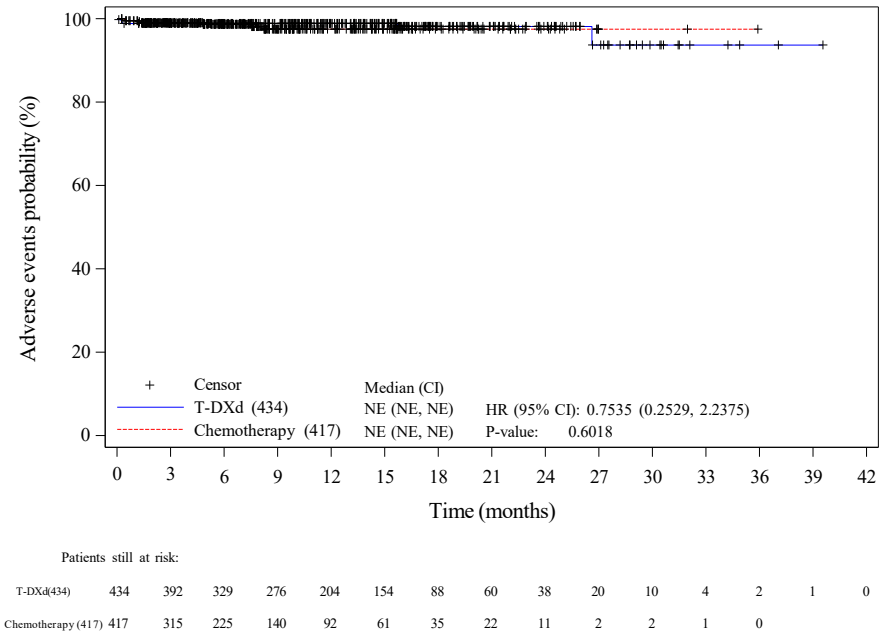
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Blood creatinine increased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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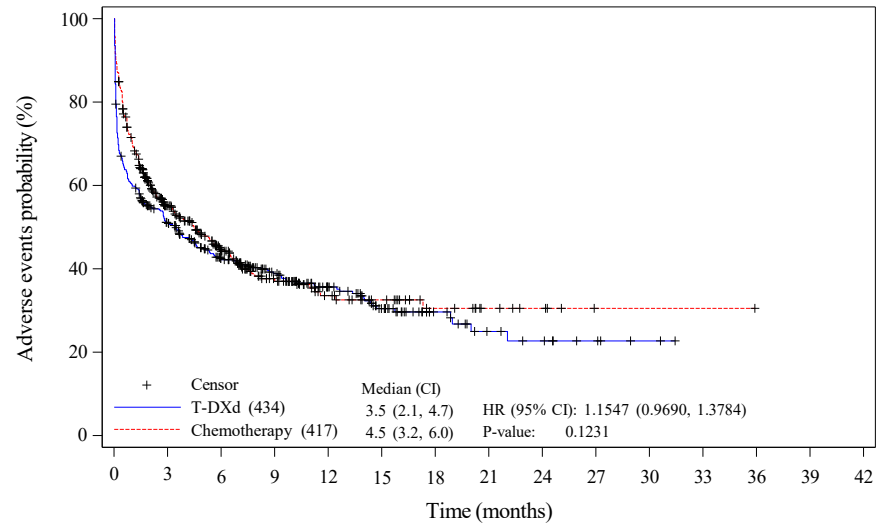
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: All (any PT)



Patients still at risk:

T-DXd(434)	434	203	142	105	71	44	22	12	9	5	2	0
Chemotherapy (417)	417	173	103	58	35	25	14	8	5	1	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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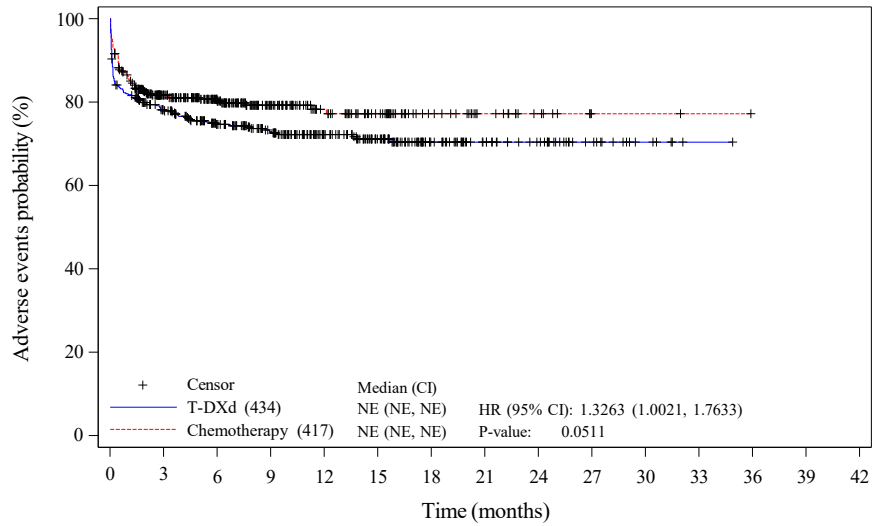
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Fatigue



Patients still at risk:

T-DXd(434)	434	308	248	203	150	110	62	41	30	15	6	1	0
Chemotherapy (417)	417	262	186	117	74	52	28	17	9	2	2	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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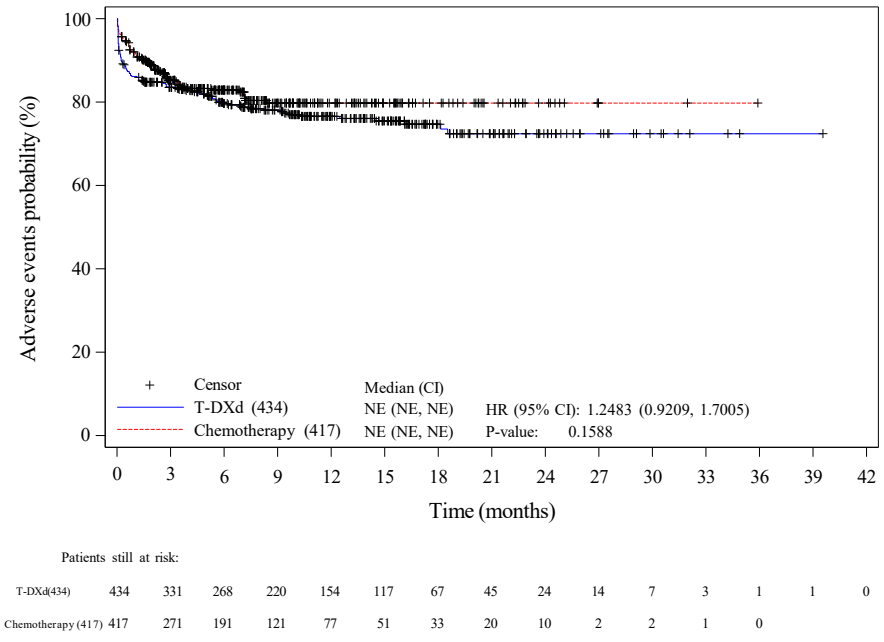
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Asthenia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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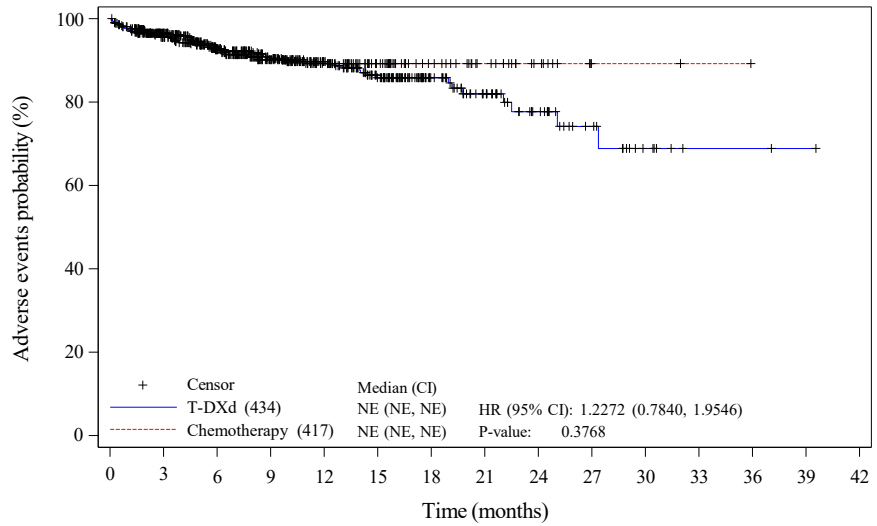
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Pyrexia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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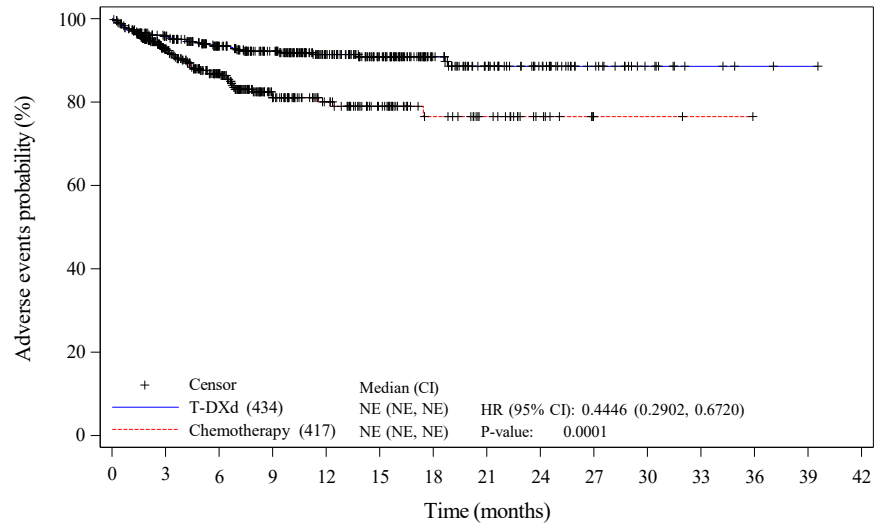
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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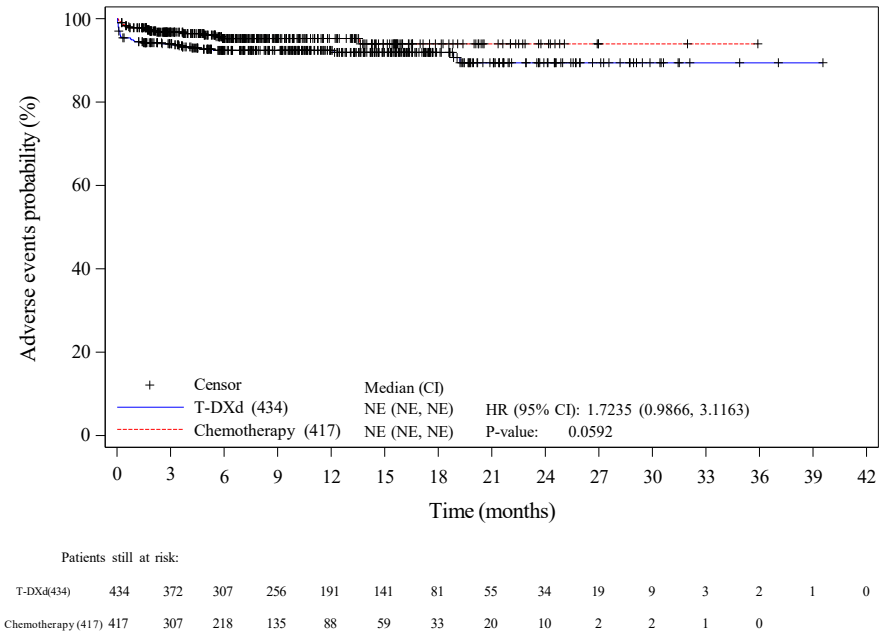
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Malaise



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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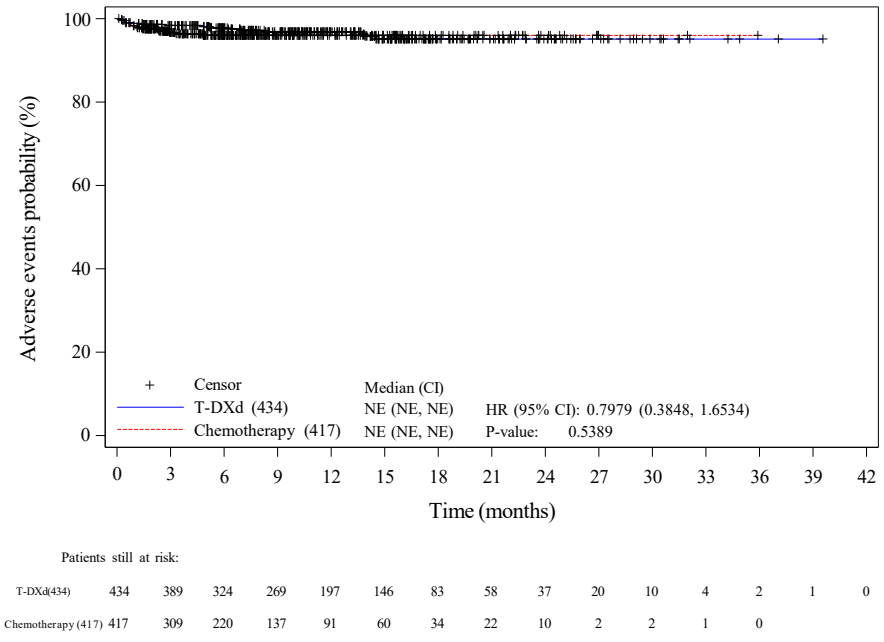
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Mucosal inflammation



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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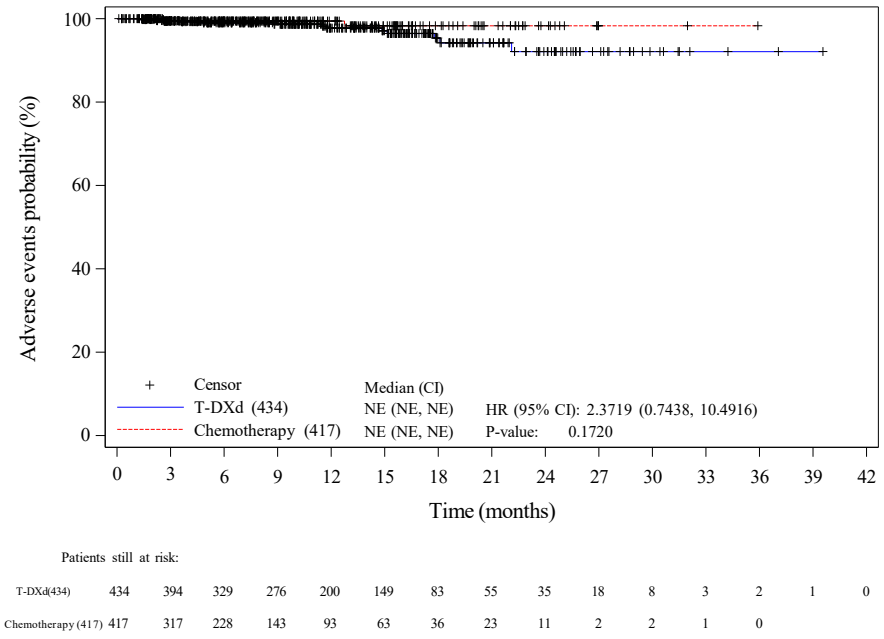
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Influenza like illness



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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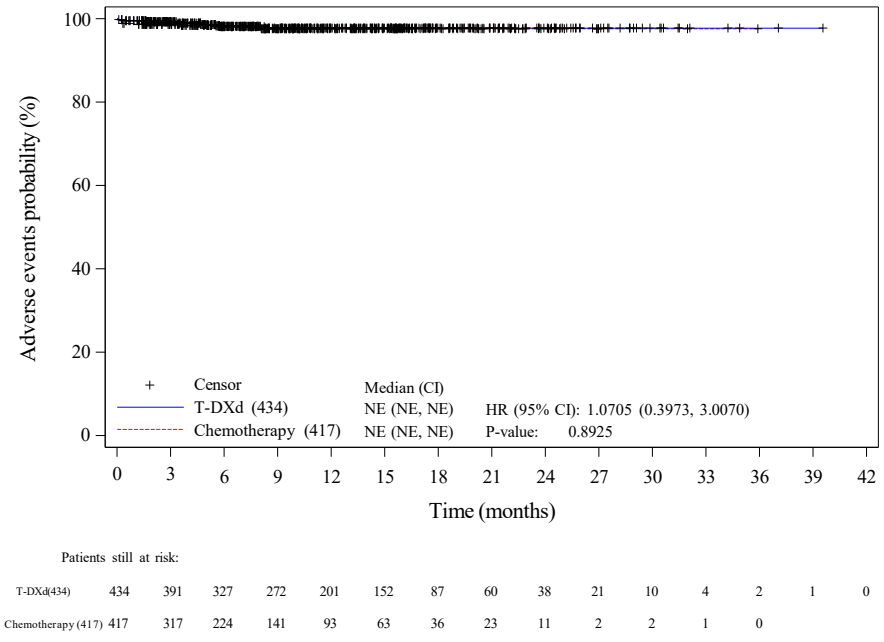
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Chest discomfort



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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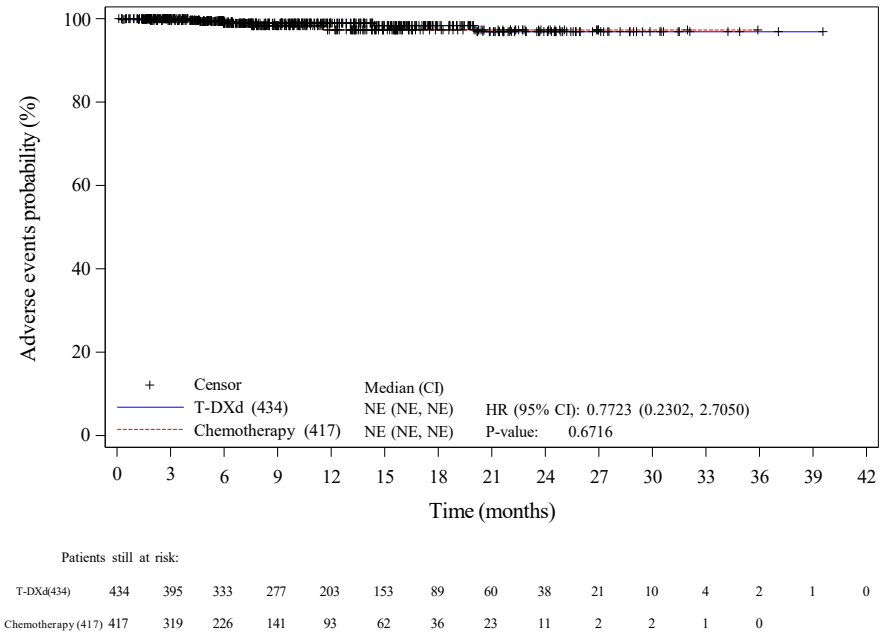
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Peripheral swelling



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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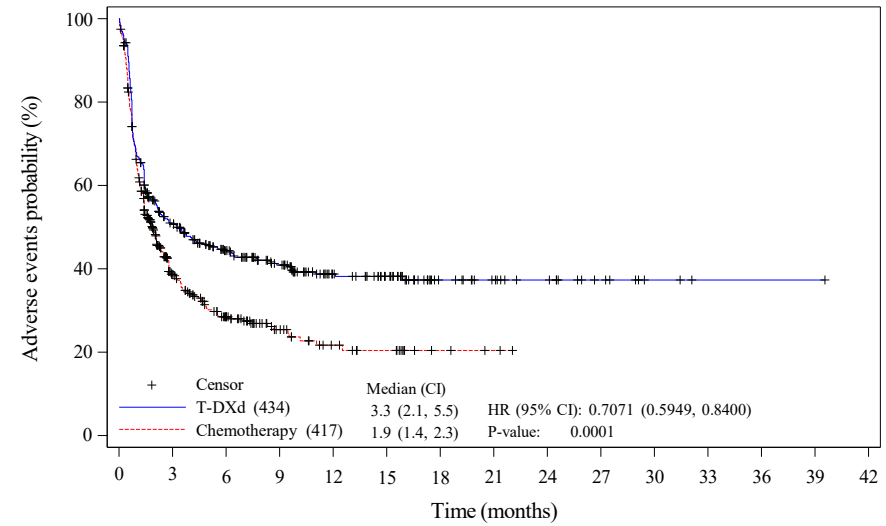
Run date: 16DEC2024 7:29; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)



Patients still at risk:

T-DXd(434)	434	198	141	106	70	55	27	20	15	8	3	1	1	1	0
Chemotherapy (417)	417	113	62	32	18	13	4	2	0						

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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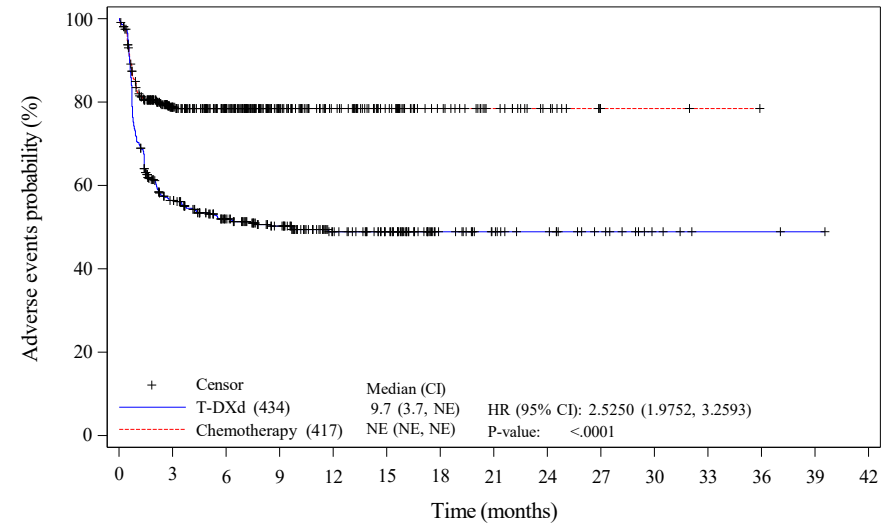
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Patients still at risk:

T-DXd(434)	434	220	167	132	89	70	34	24	19	12	5	2	2	1	0
Chemotherapy (417)	417	249	185	118	82	57	34	21	11	2	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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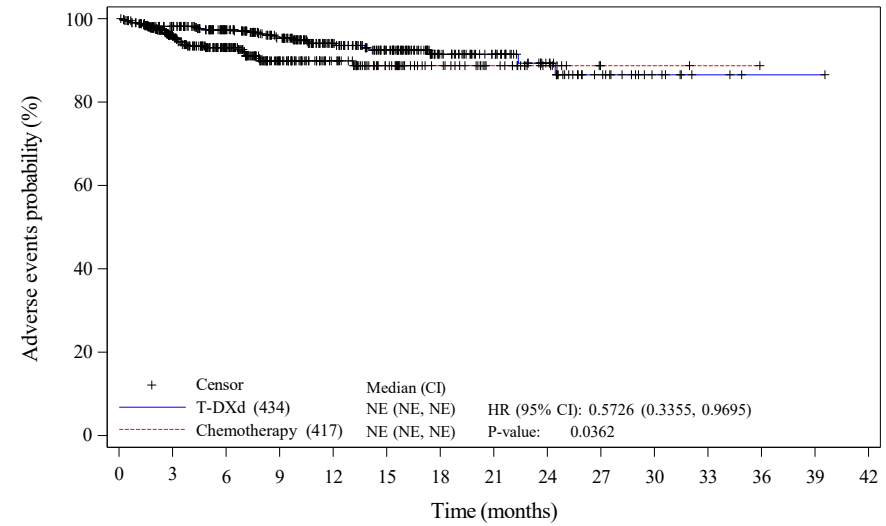
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Rash



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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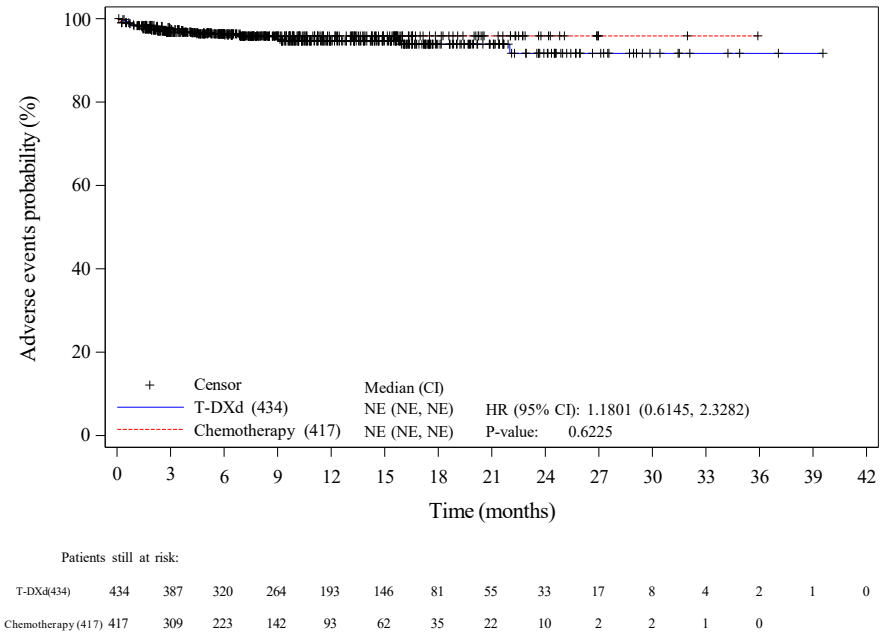
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Dry skin



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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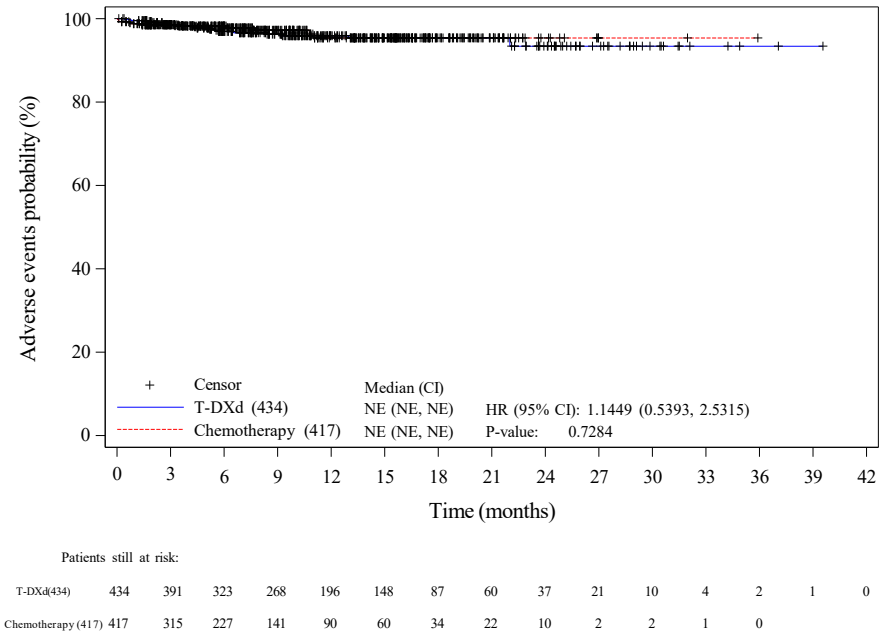
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Pruritus



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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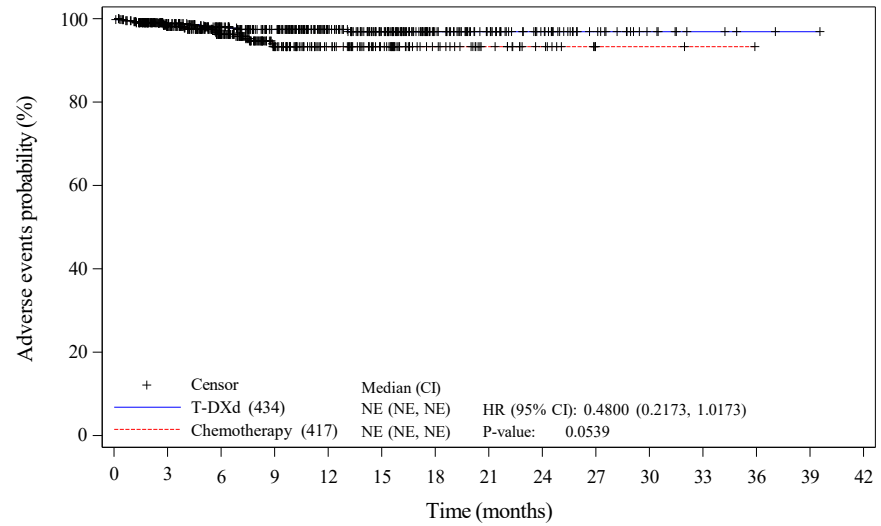
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Nail disorder



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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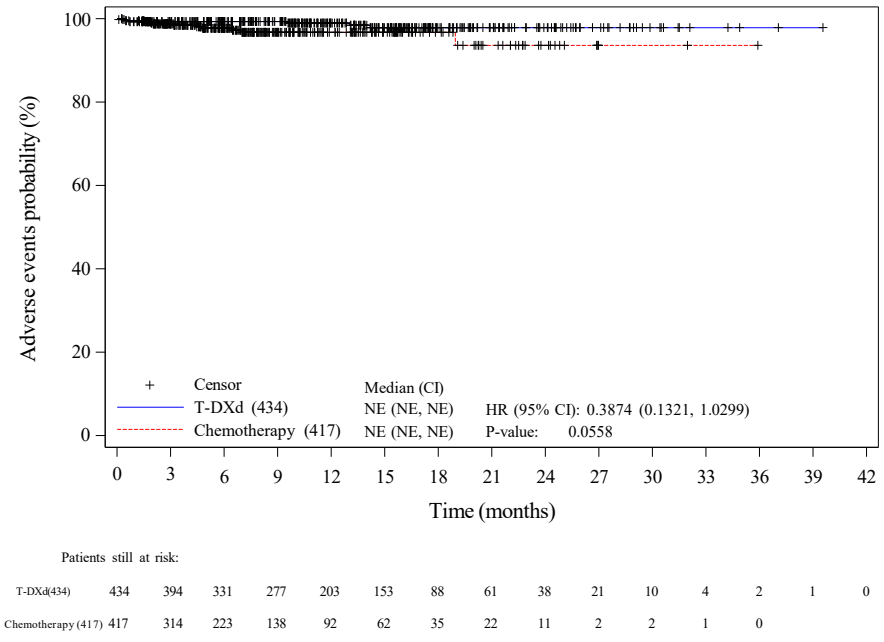
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Erythema



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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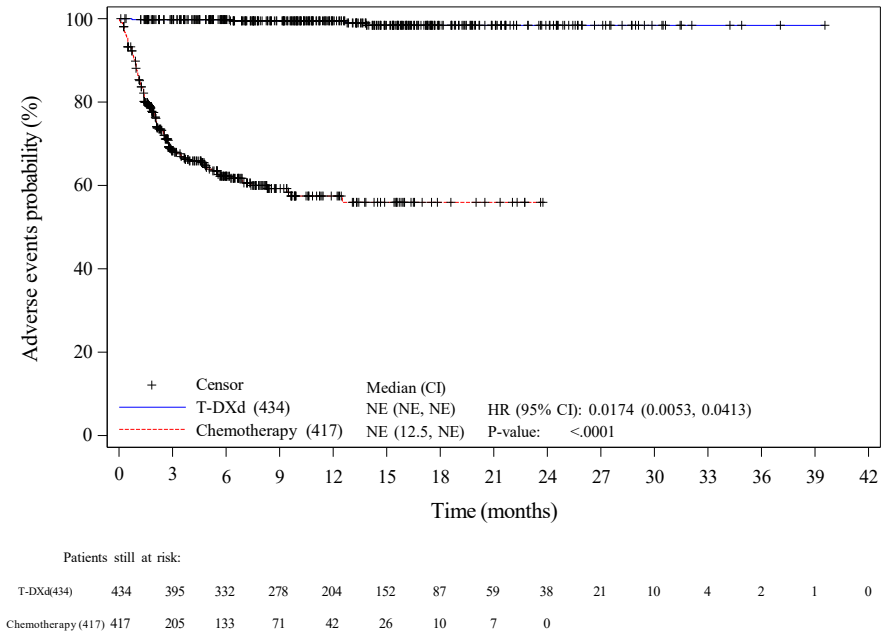
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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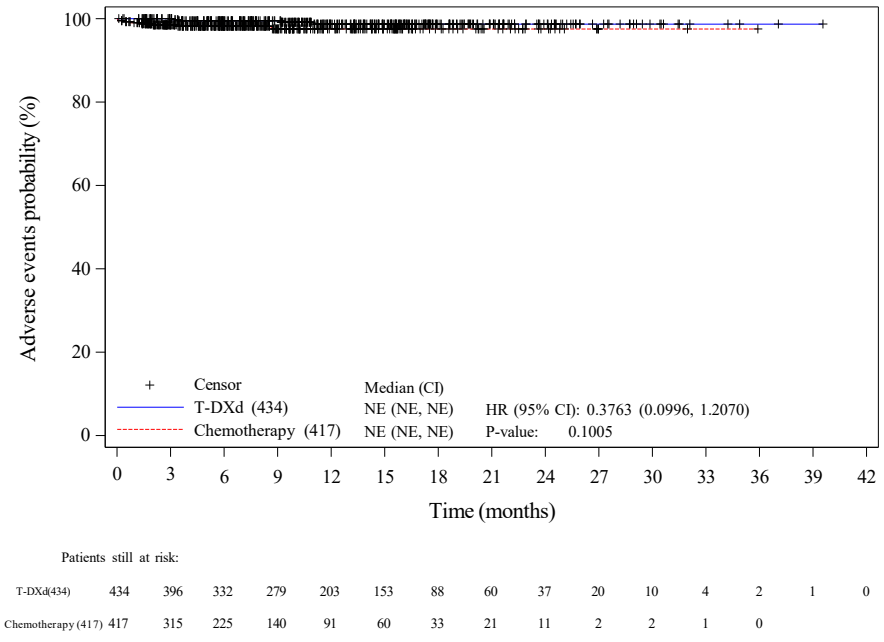
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Skin hyperpigmentation



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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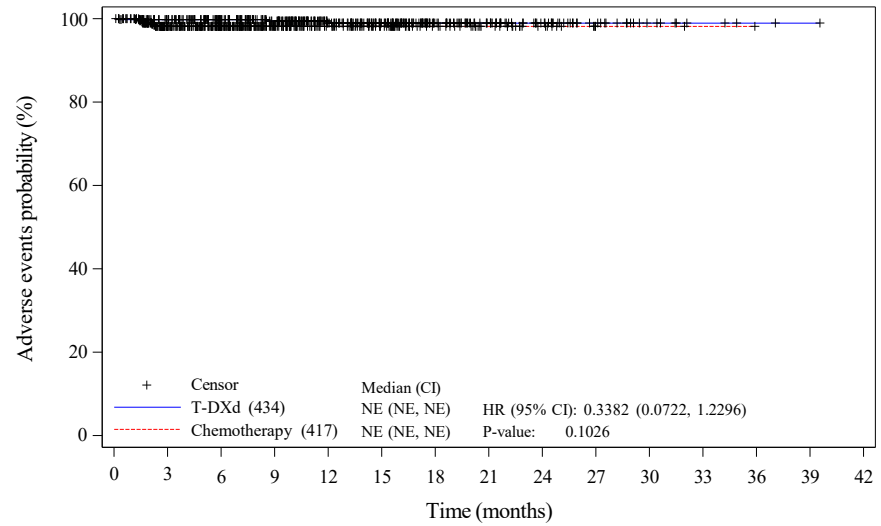
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Skin fissures



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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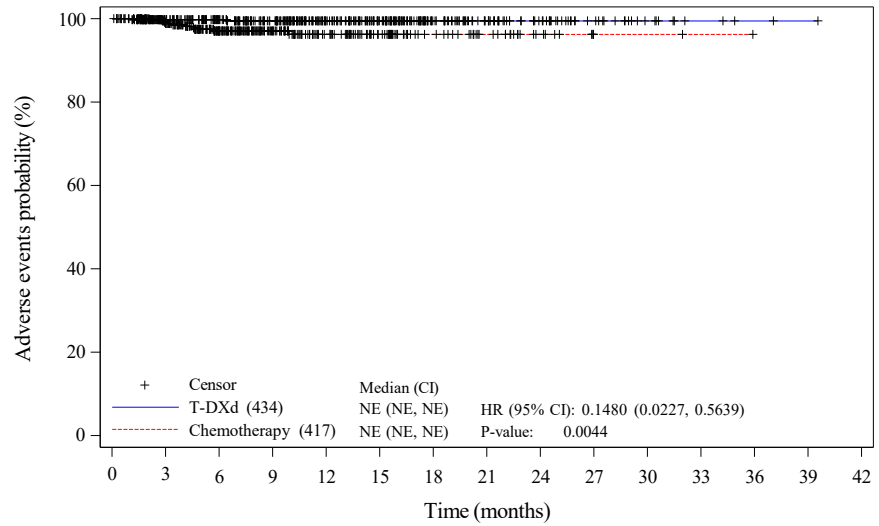
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Nail discolouration



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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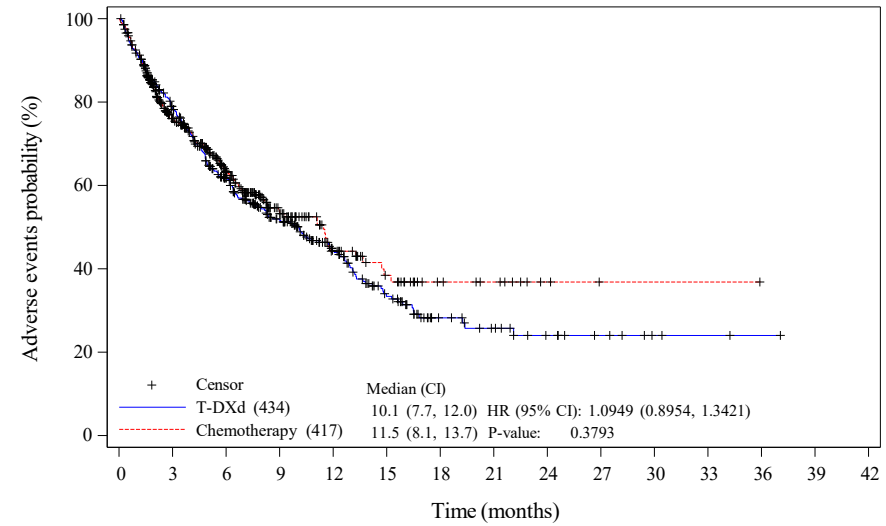
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: All (any PT)



Patients still at risk:

T-DXd(434)	434	311	210	144	89	53	25	18	11	7	3	2	1	0
Chemotherapy (417)	417	241	149	76	41	24	12	9	3	1	1	1	0	

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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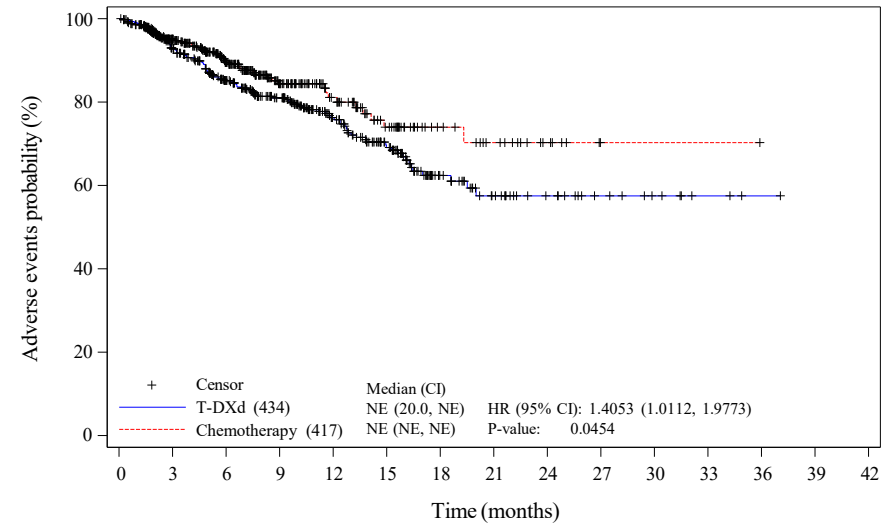
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: COVID-19



Patients still at risk:

T-DXd(434)	434	367	286	222	151	106	46	28	18	11	7	3	1	0
Chemotherapy (417)	417	302	204	117	71	43	22	15	7	1	1	1	0	

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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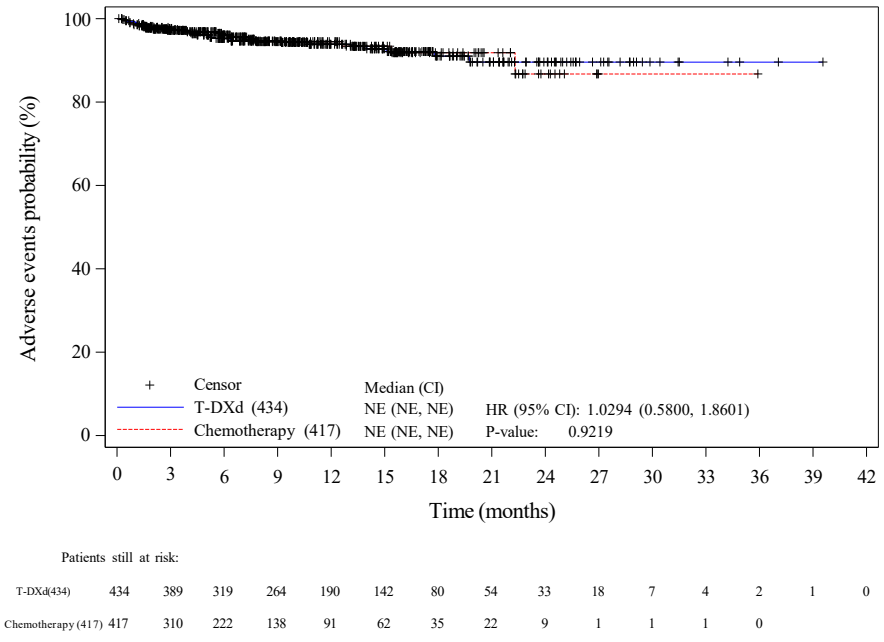
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Urinary tract infection



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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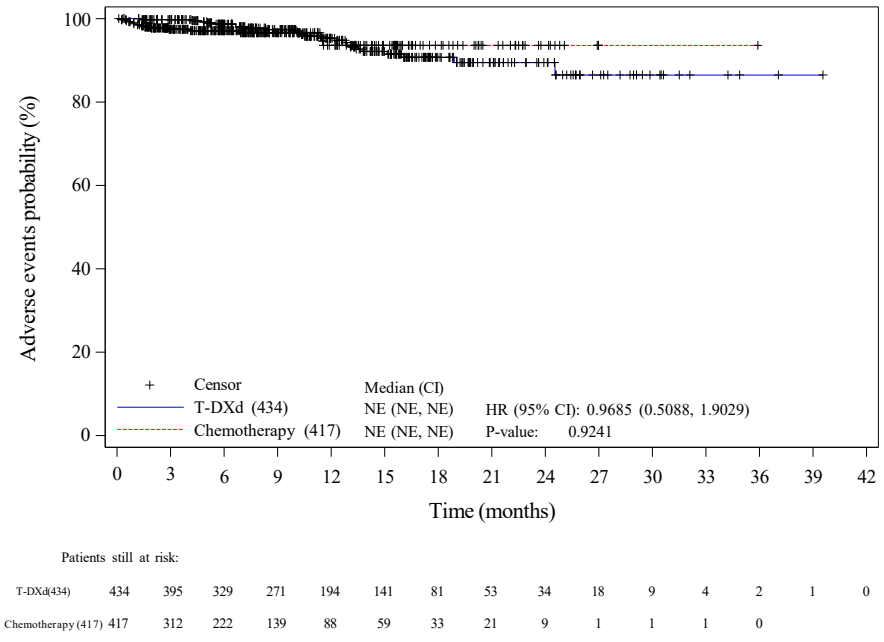
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Nasopharyngitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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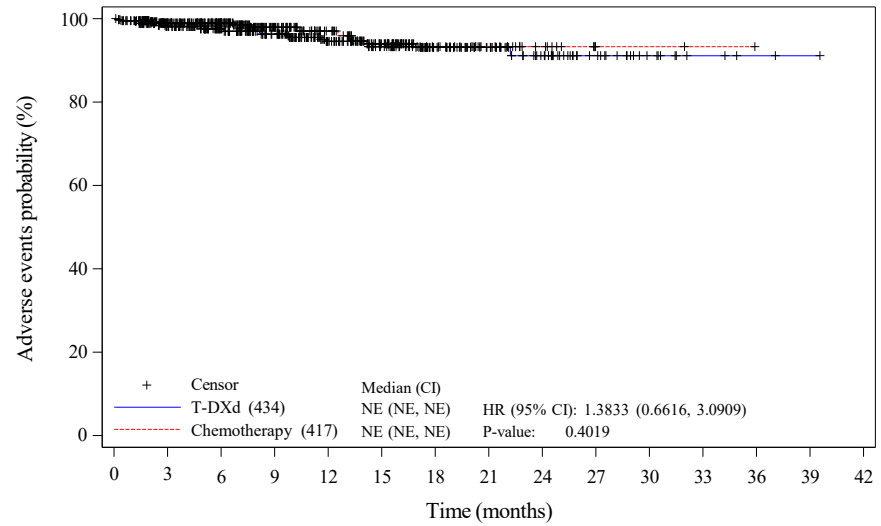
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Upper respiratory tract infection



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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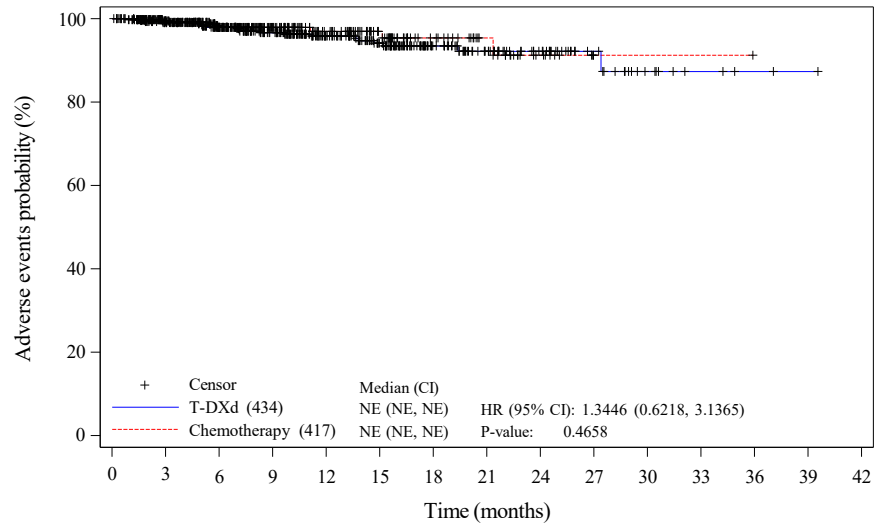
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Pneumonia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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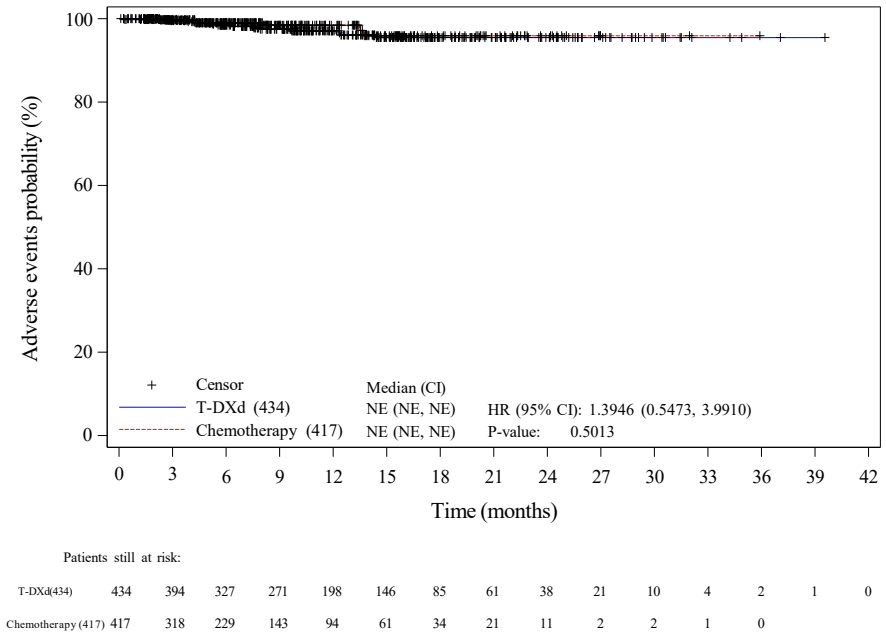
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Influenza



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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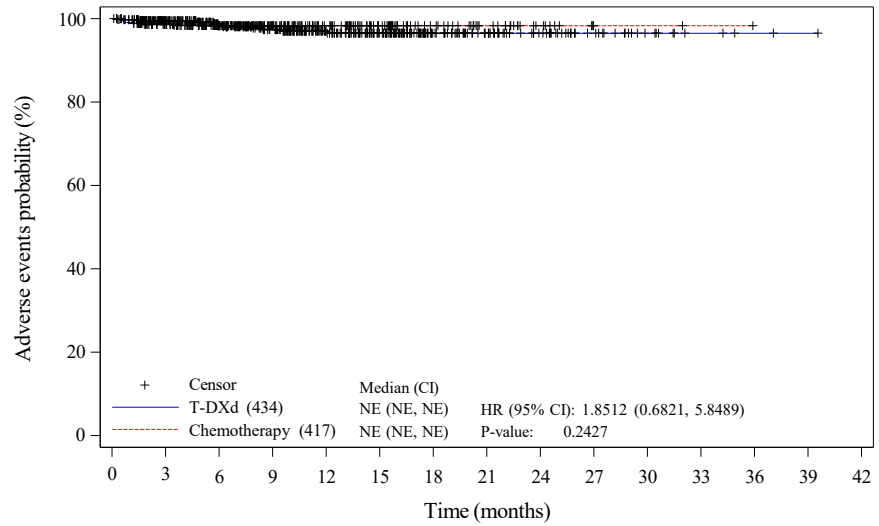
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Cystitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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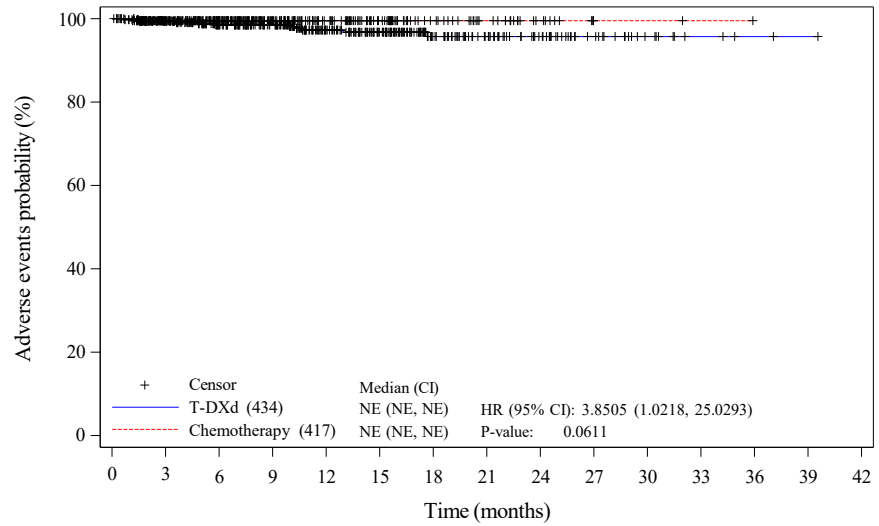
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: COVID-19 pneumonia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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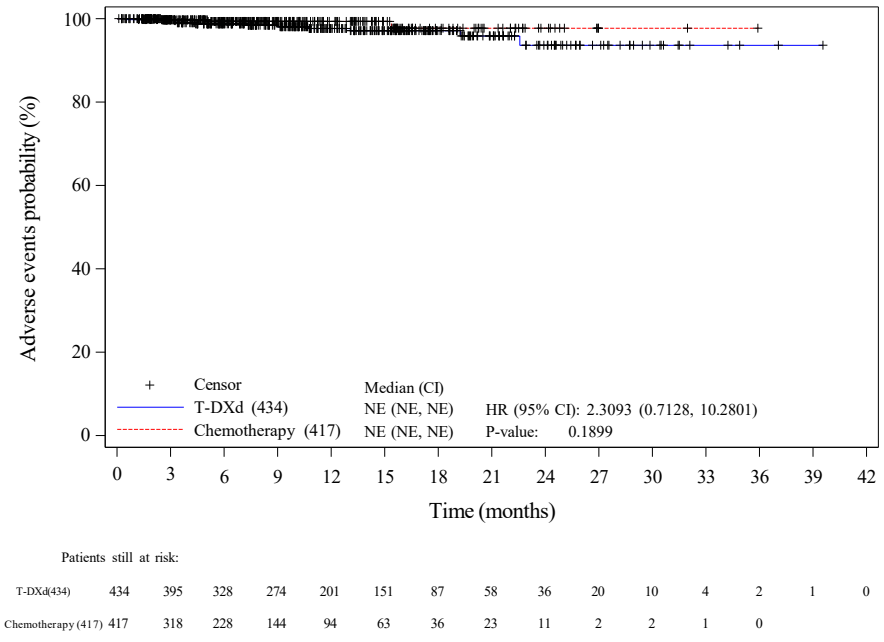
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Sinusitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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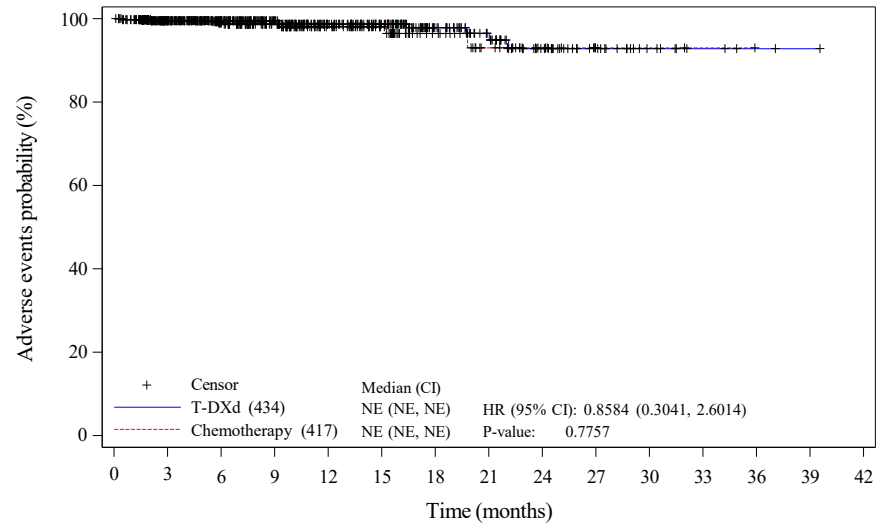
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Bronchitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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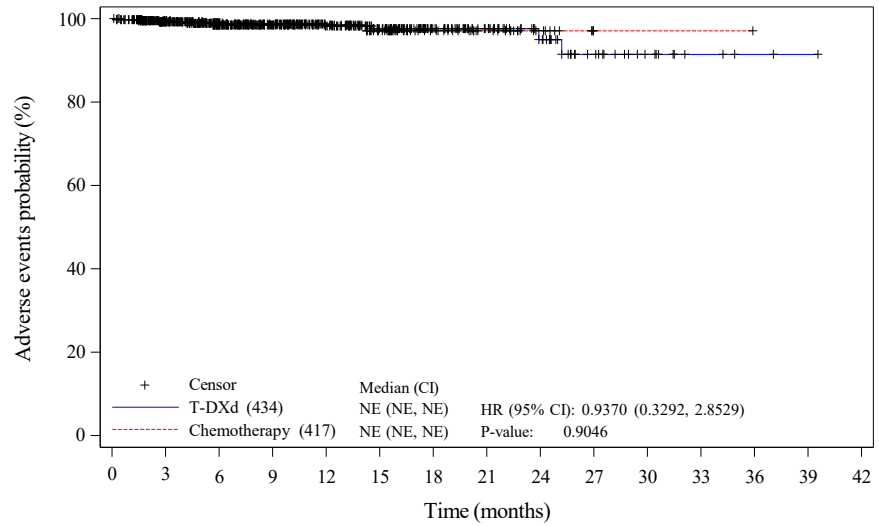
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Herpes zoster



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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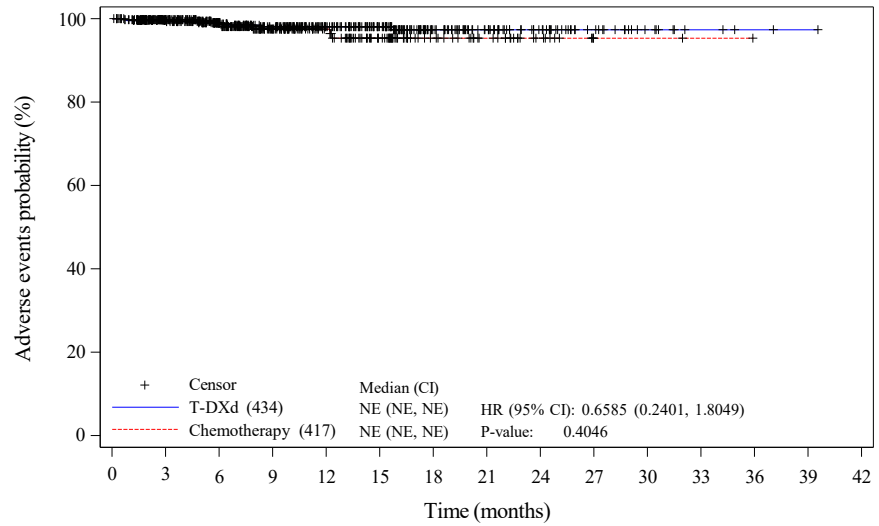
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Conjunctivitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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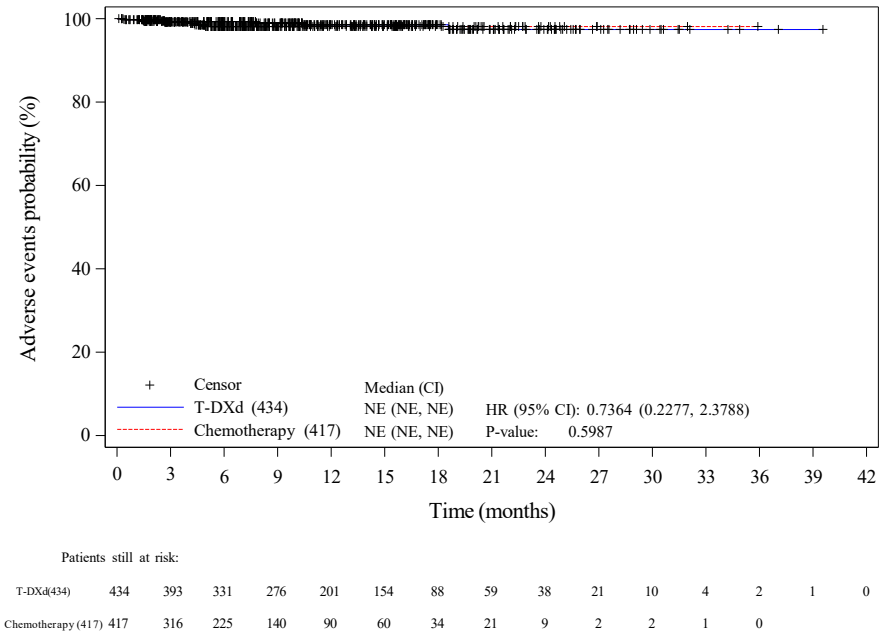
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Gastroenteritis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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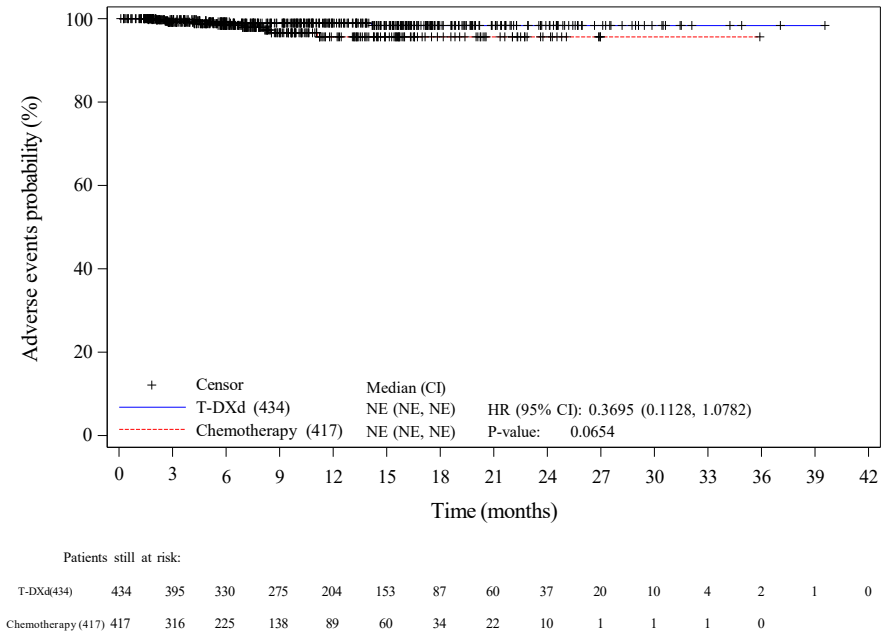
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Paronychia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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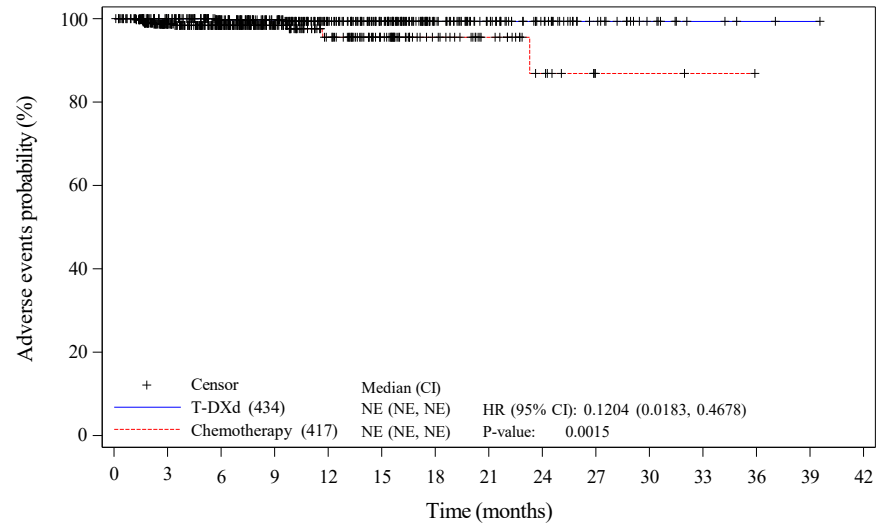
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: Cellulitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
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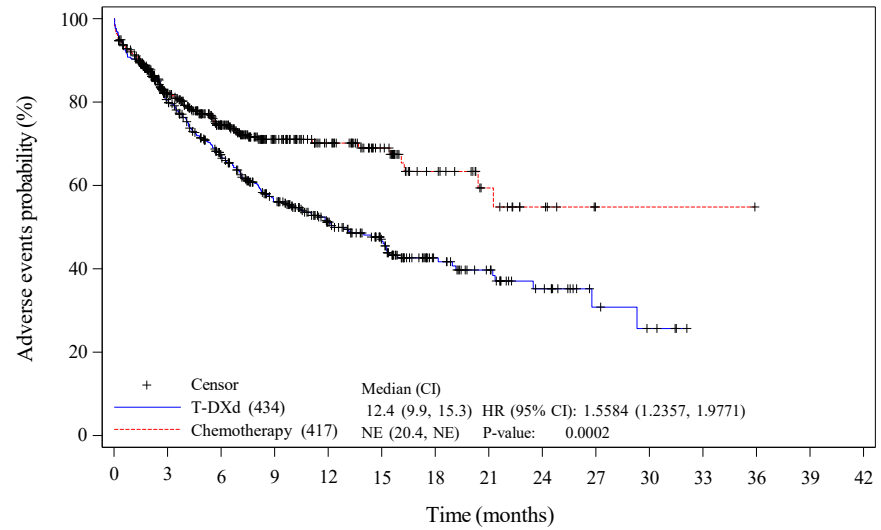
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
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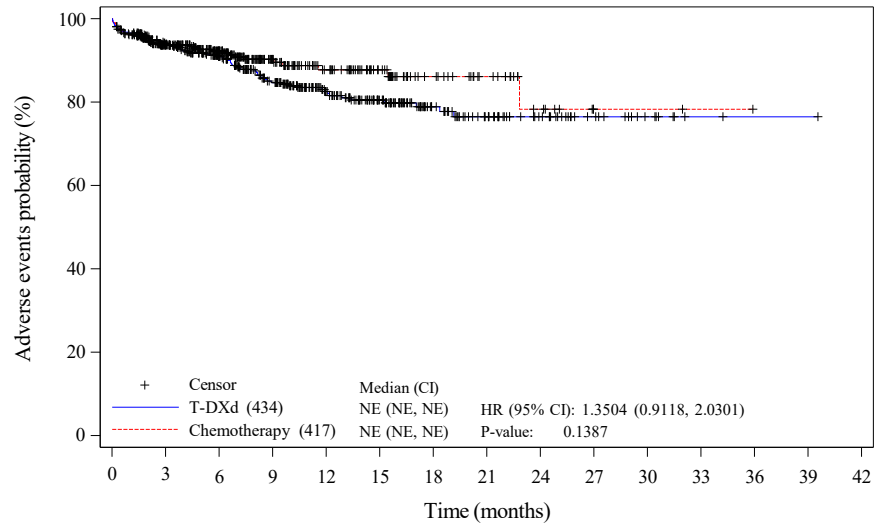
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Cough



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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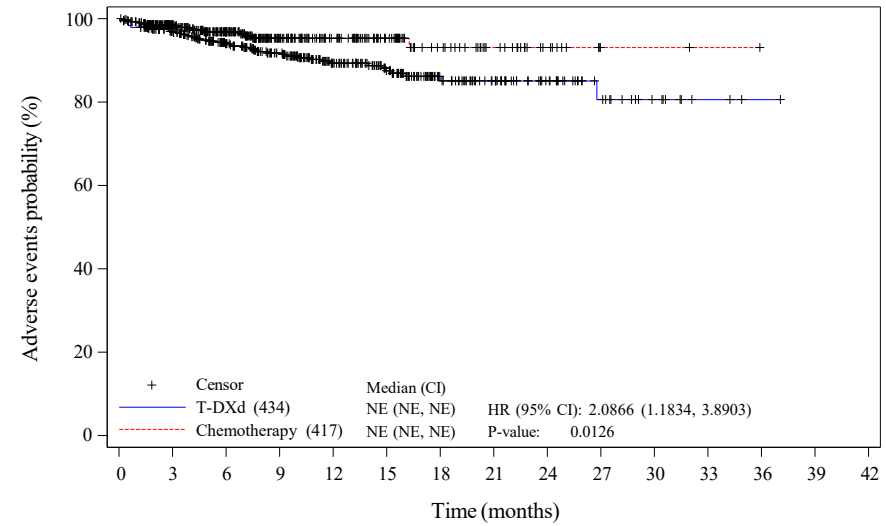
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis



Patients still at risk:

T-DXd(434)	434	385	315	257	186	140	80	56	34	18	9	3	1	0
Chemotherapy (417)	417	313	222	136	91	60	34	21	10	2	2	1	0	

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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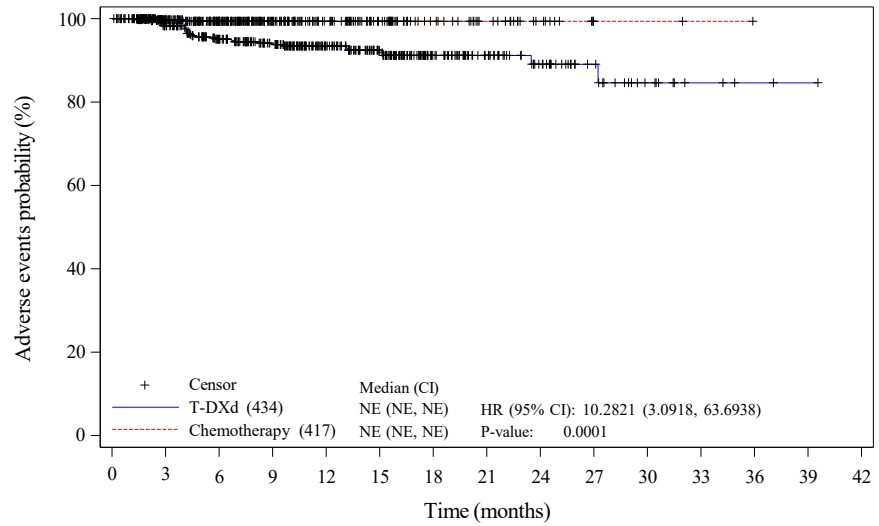
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease



Patients still at risk:

T-DXd(434)	434	391	325	272	200	150	87	59	37	21	10	4	2	1	0
Chemotherapy (417)	417	318	228	143	93	62	35	23	11	2	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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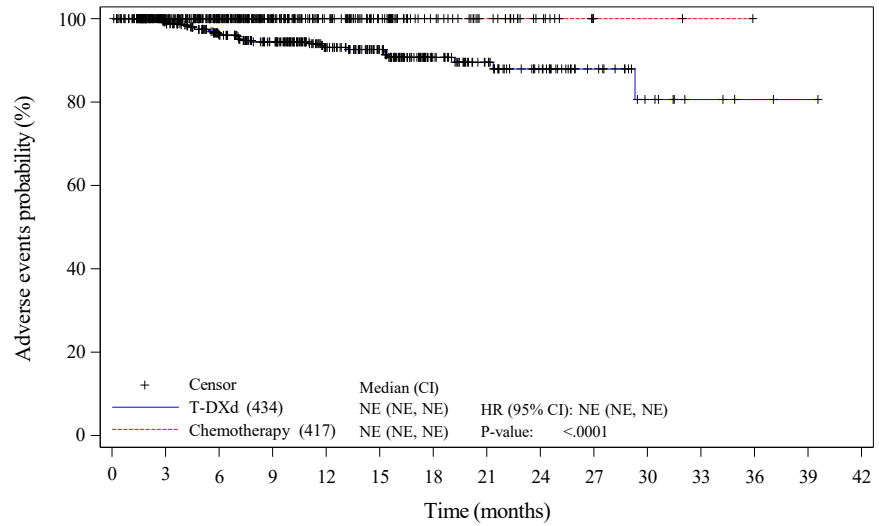
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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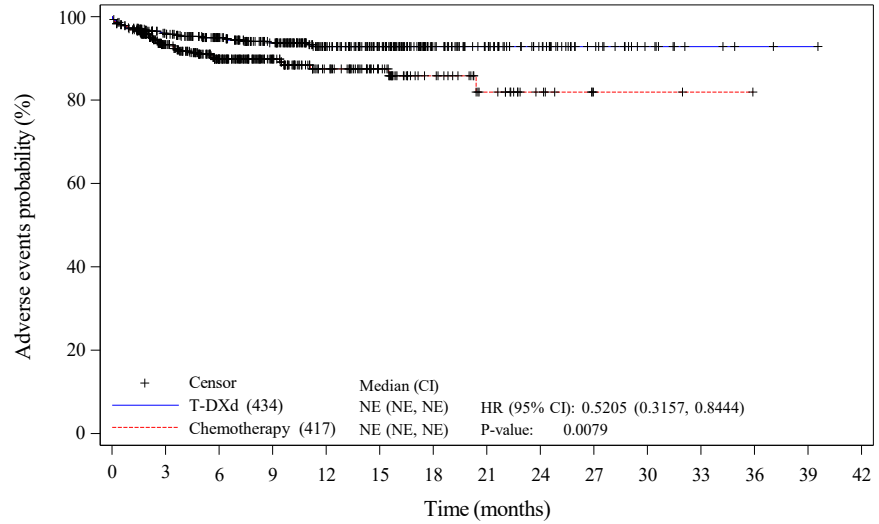
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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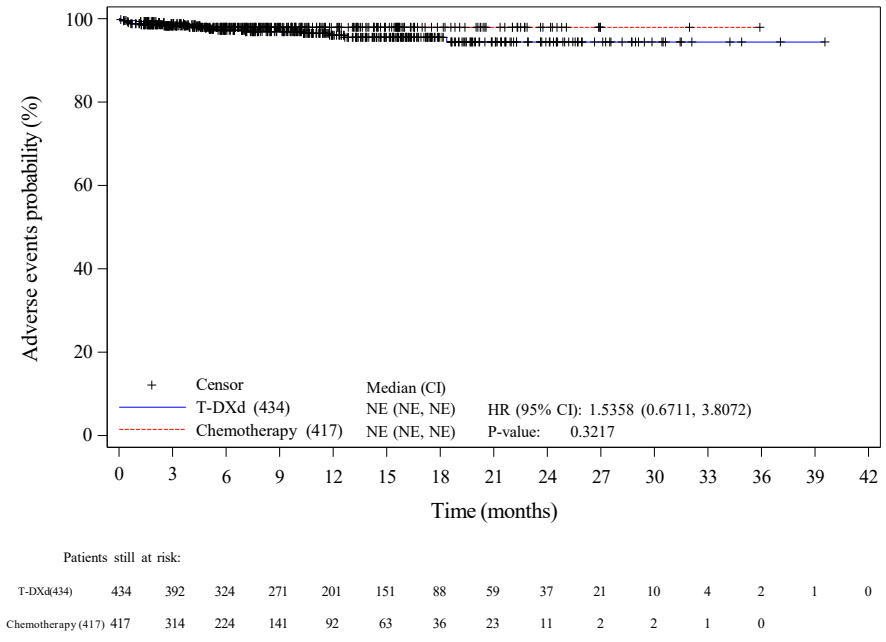
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Oropharyngeal pain



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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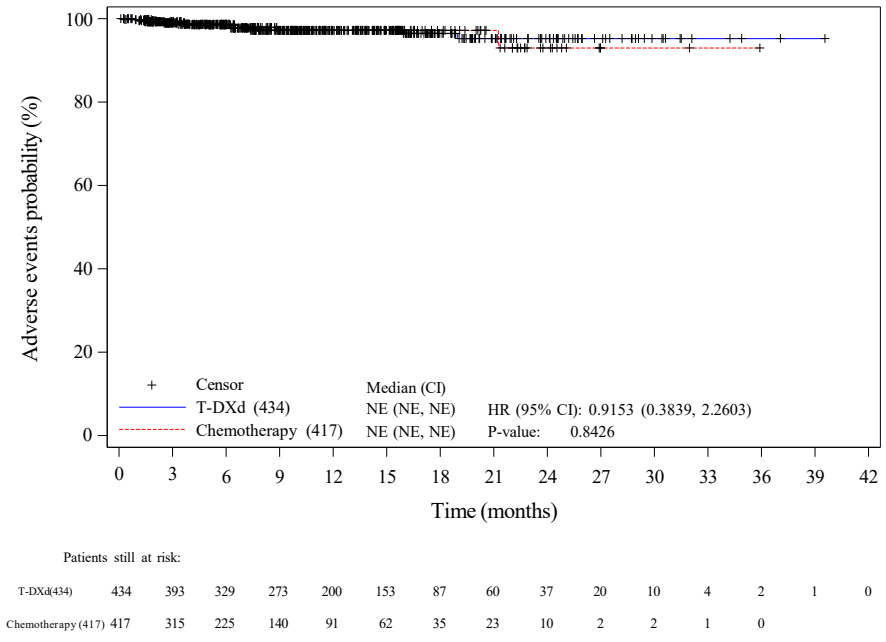
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Rhinorrhoea



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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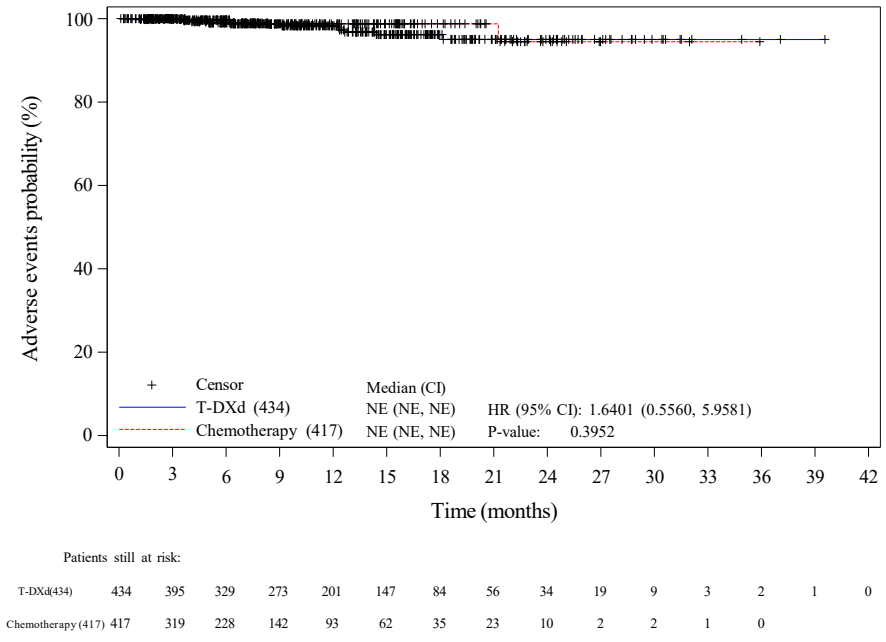
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Nasal congestion



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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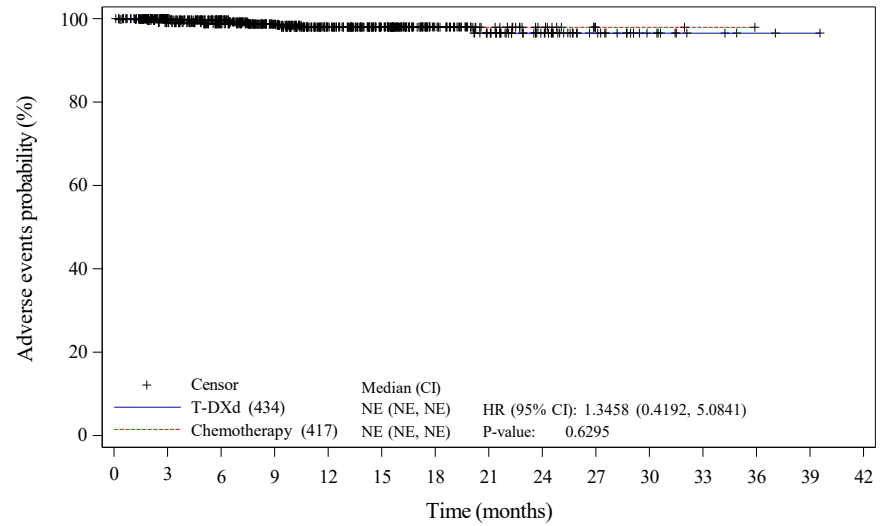
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Productive cough



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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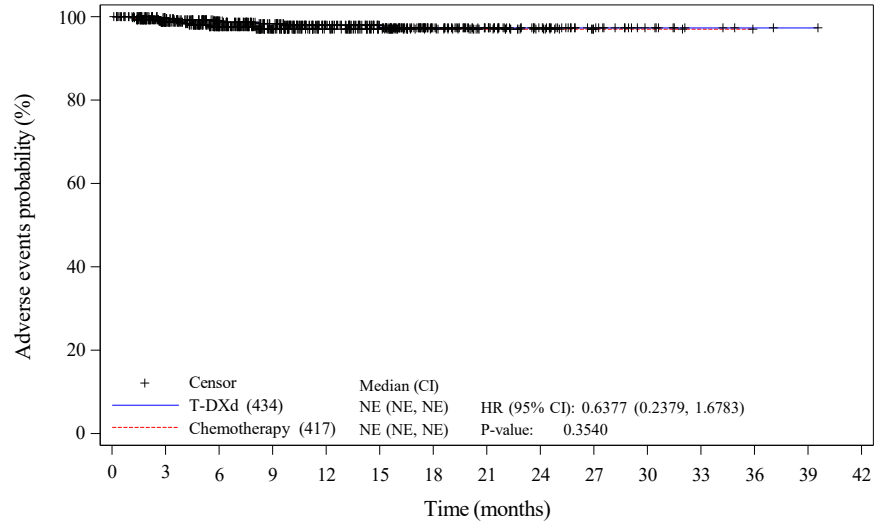
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pulmonary embolism



Patients still at risk:

T-DXd(434)	434	395	330	276	203	154	88	60	38	21	10	4	2	1	0
Chemotherapy (417)	417	315	226	141	91	60	35	22	11	2	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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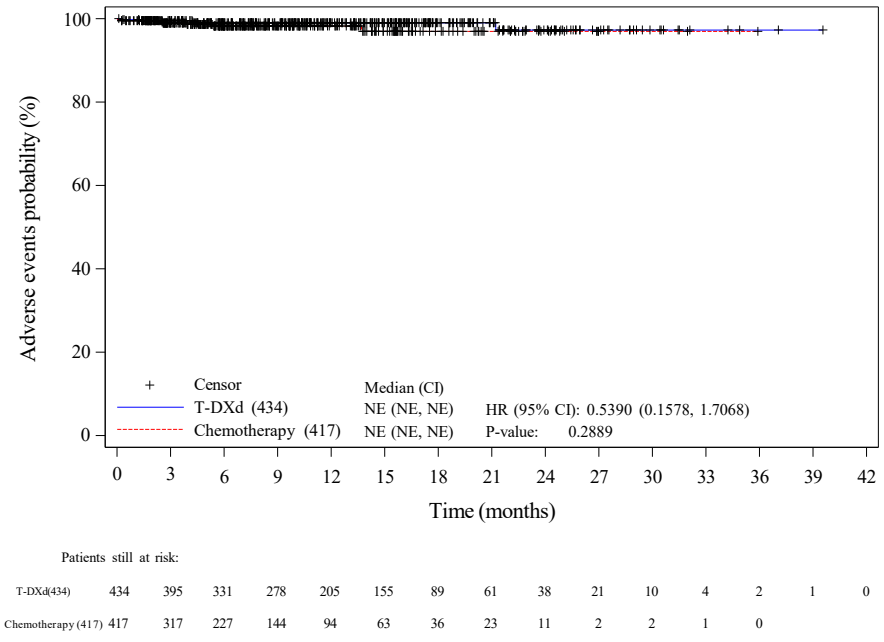
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pleural effusion



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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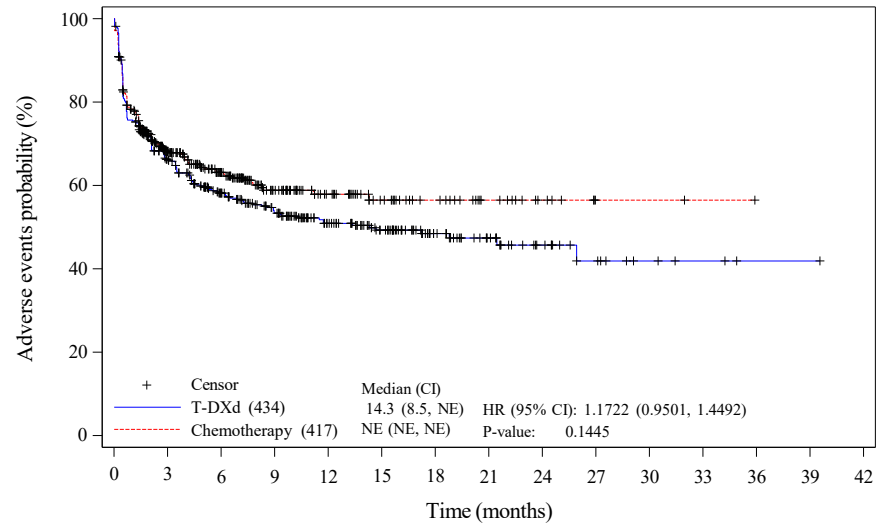
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: All (any PT)



Patients still at risk:

T-DXd(434)	434	263	197	155	112	83	48	32	18	10	5	3	1	1	0
Chemotherapy (417)	417	215	147	87	55	36	25	15	8	2	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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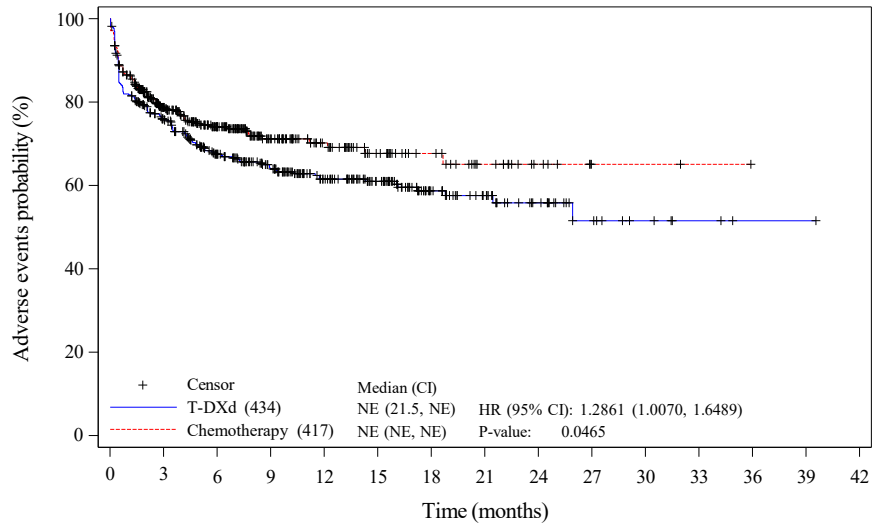
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Anaemia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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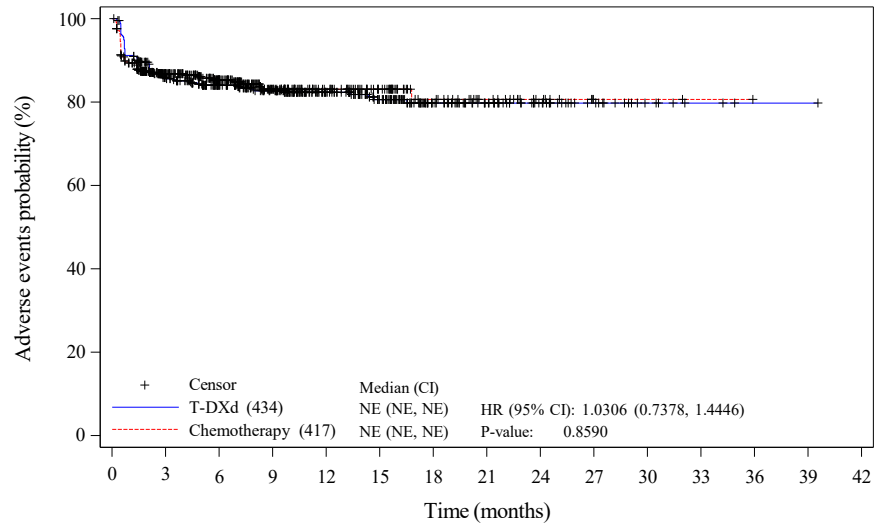
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Neutropenia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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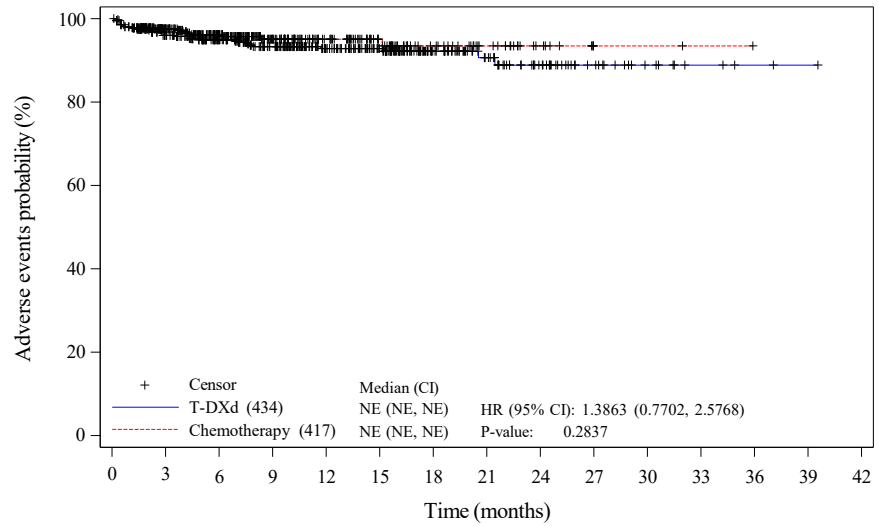
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Leukopenia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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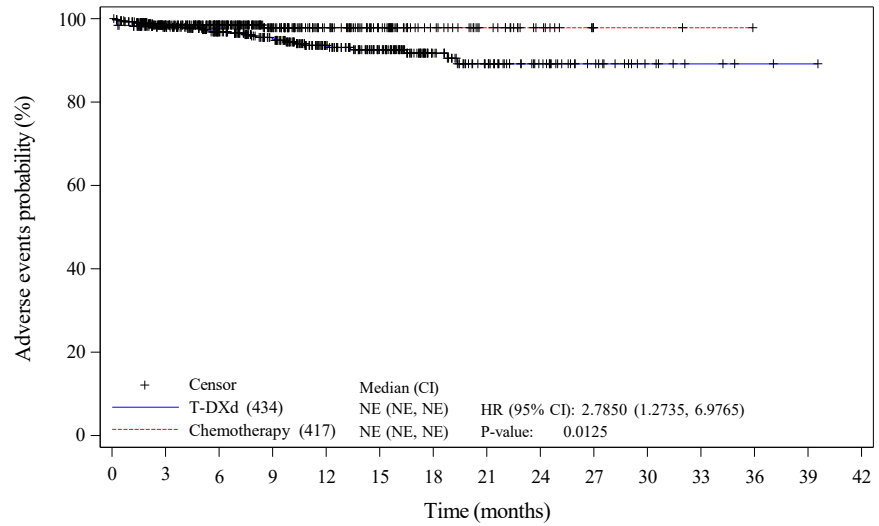
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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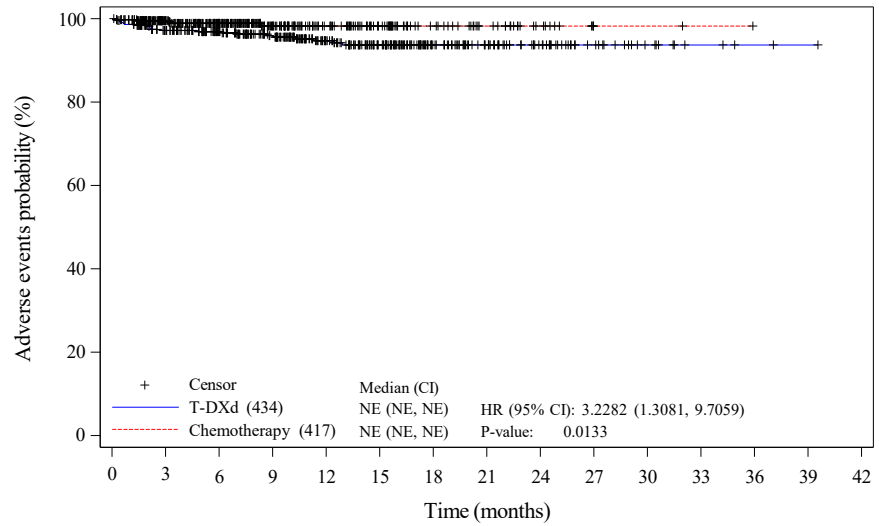
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Lymphopenia



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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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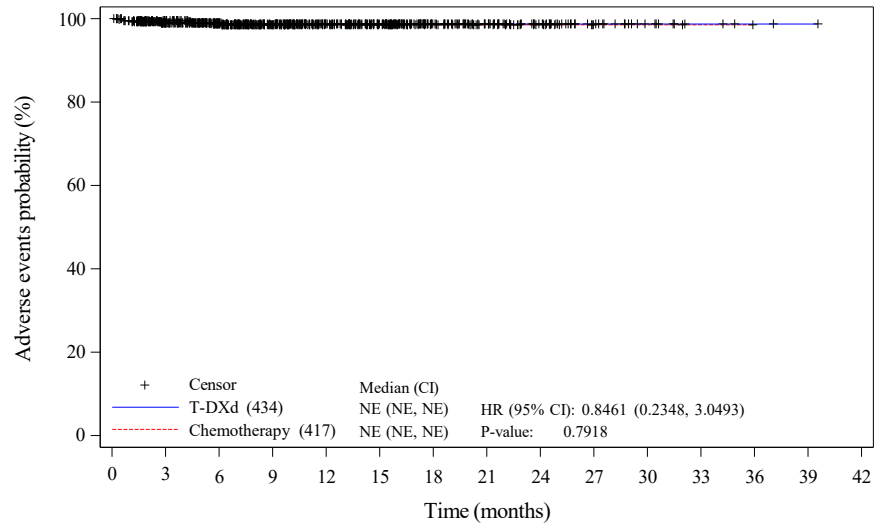
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Febrile neutropenia



Patients still at risk:

T-DXd(434)	434	394	331	277	203	154	89	61	38	21	10	4	2	1	0
Chemotherapy (417)	417	317	227	143	93	62	35	22	10	2	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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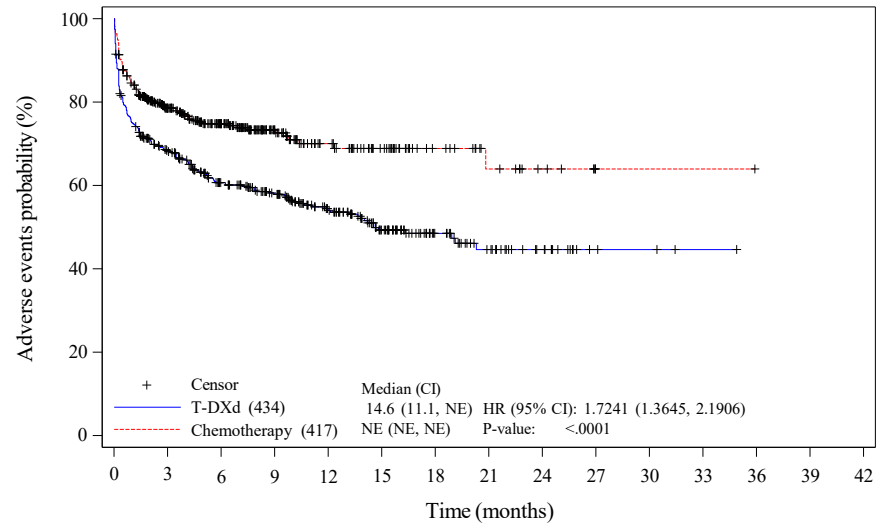
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Patients still at risk:

T-DXd(434)	434	274	208	171	125	81	45	29	16	4	3	1	0
Chemotherapy (417)	417	254	175	103	62	42	22	13	7	1	1	1	0

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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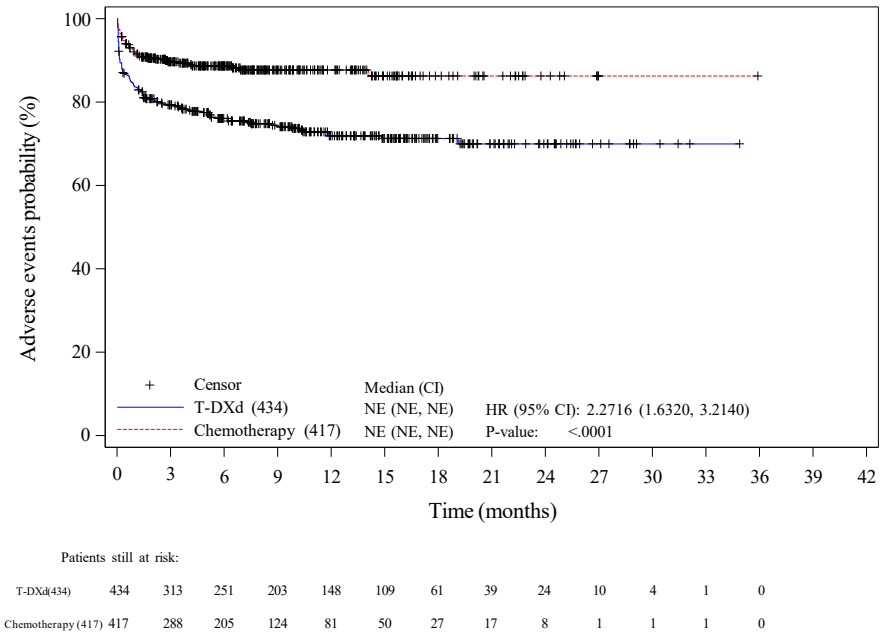
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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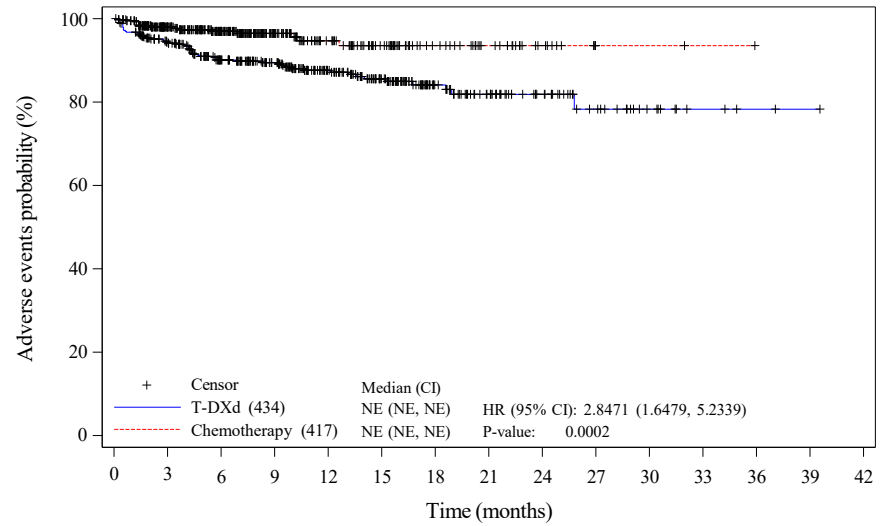
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hypokalaemia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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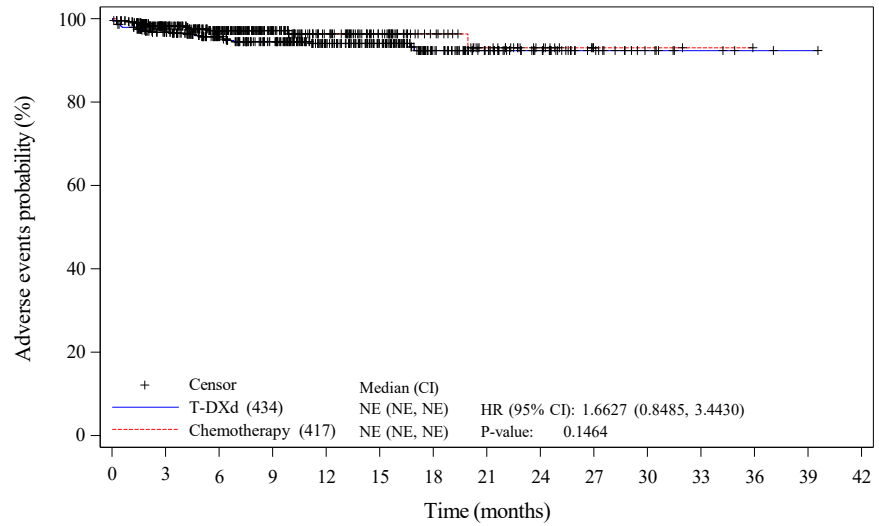
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hypoalbuminaemia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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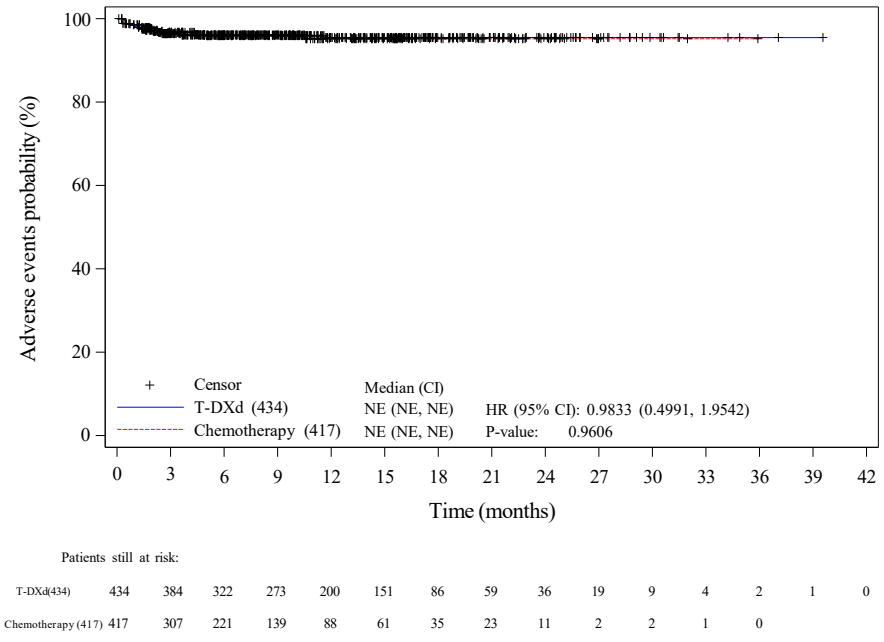
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hypocalcaemia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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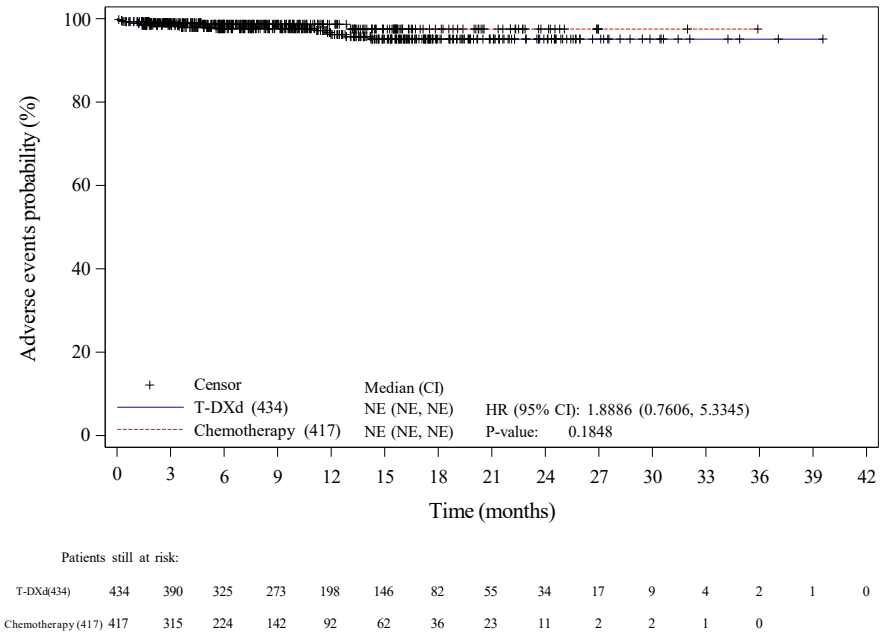
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hyperglycaemia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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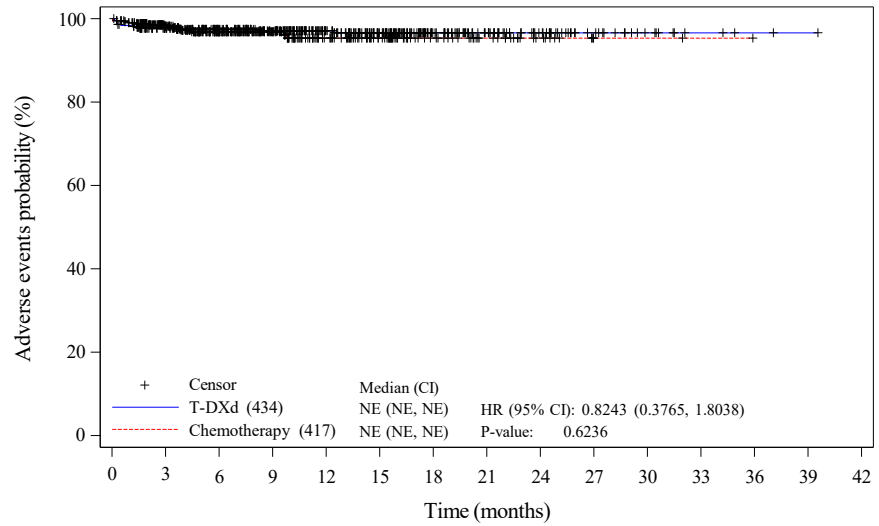
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hyponatraemia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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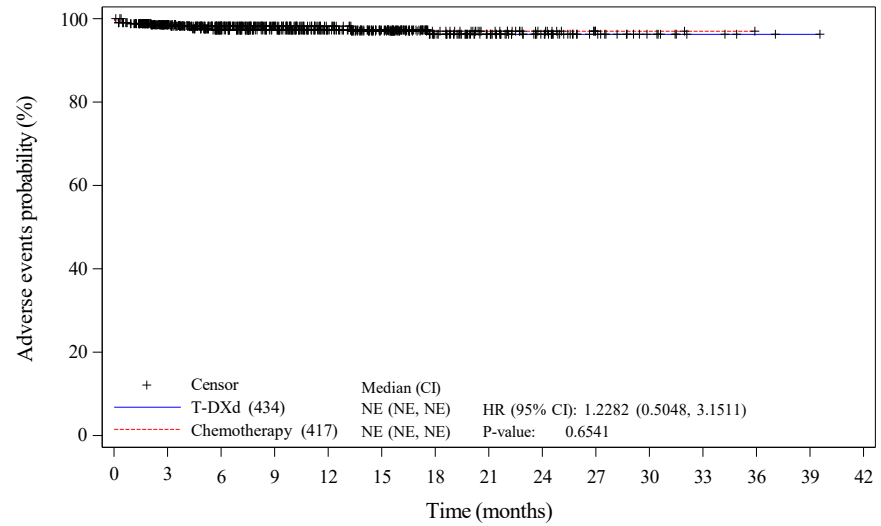
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hypomagnesaemia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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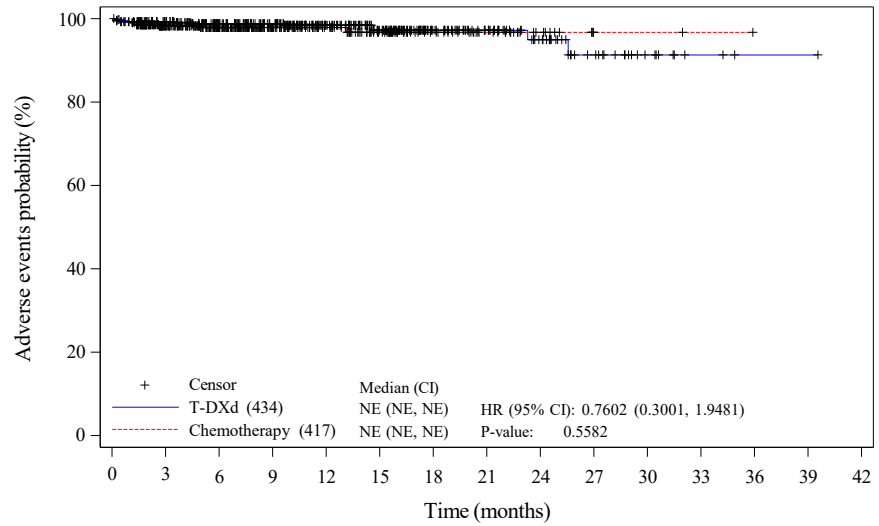
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hypercalcaemia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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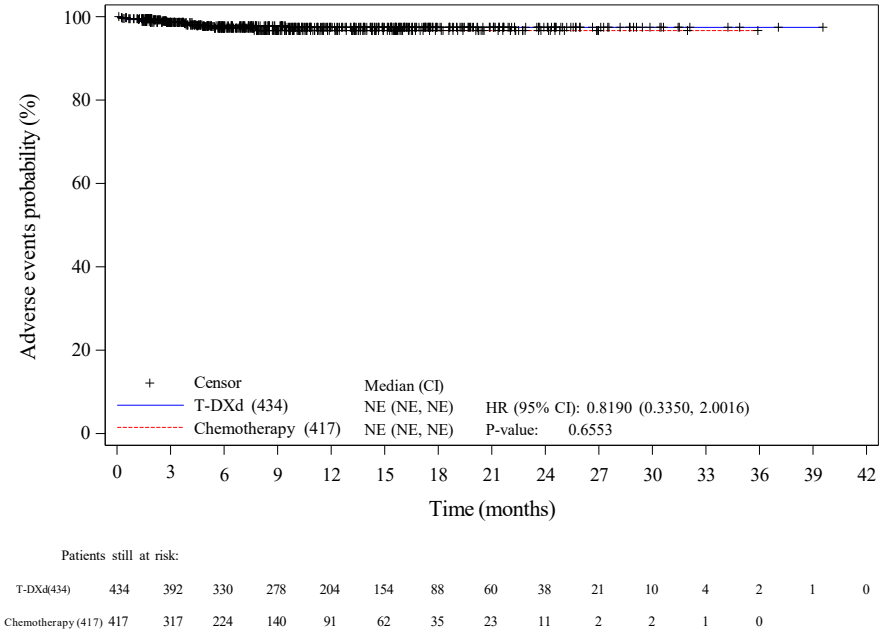
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hypophosphataemia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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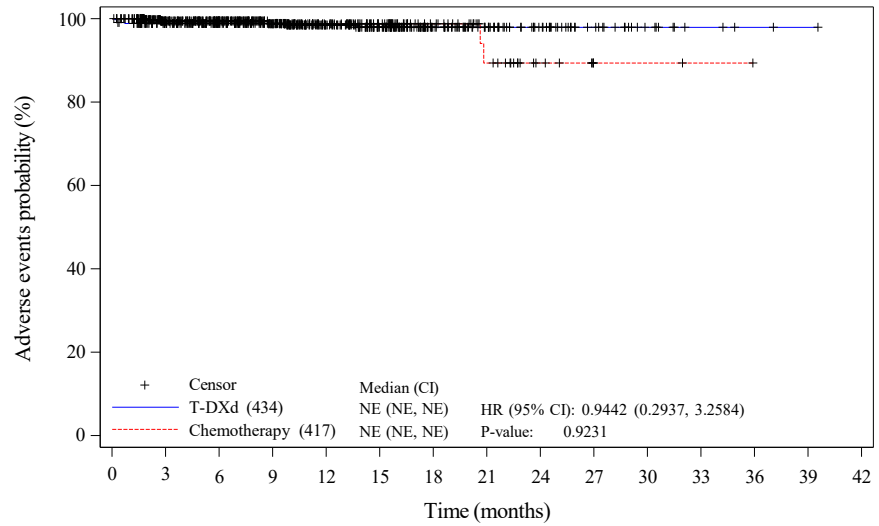
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Dehydration



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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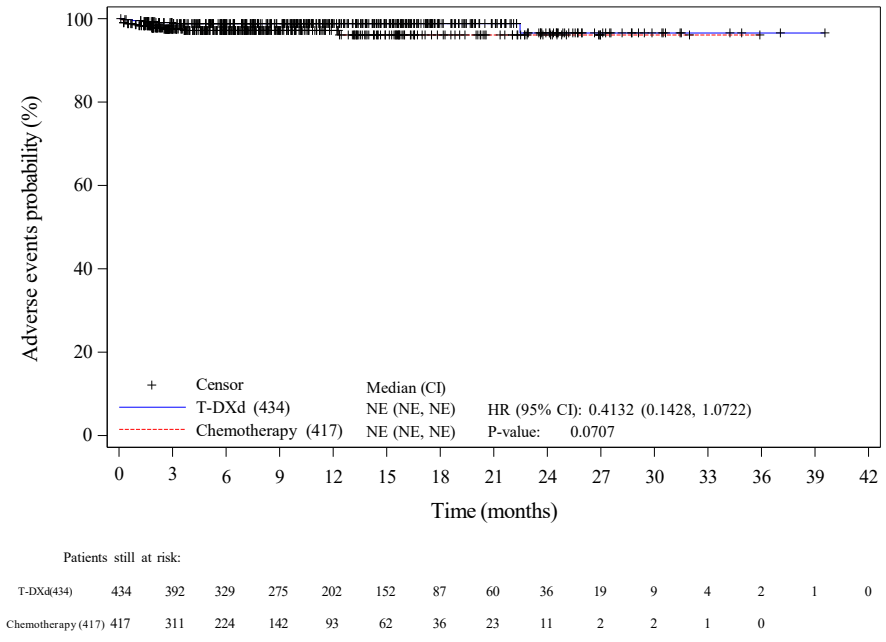
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hyperuricaemia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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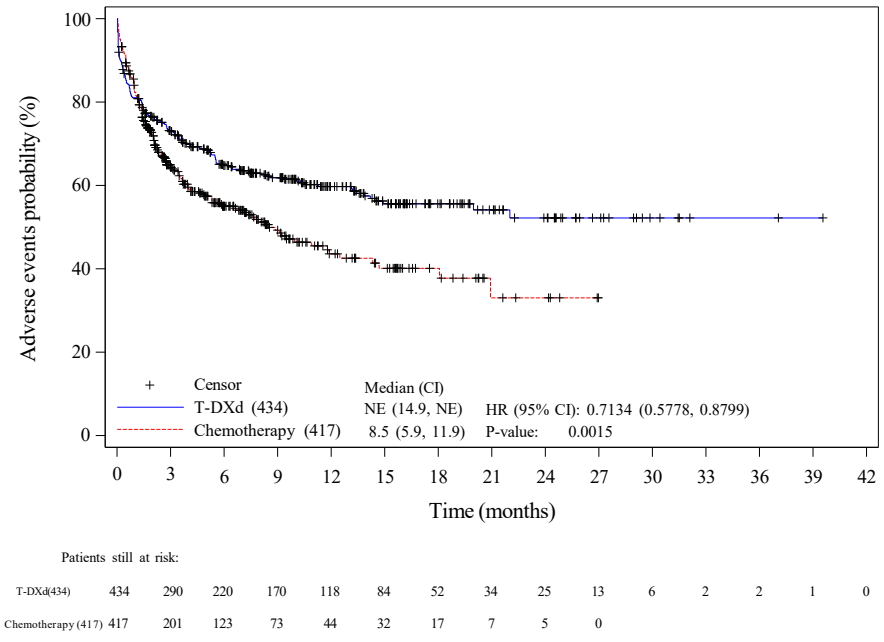
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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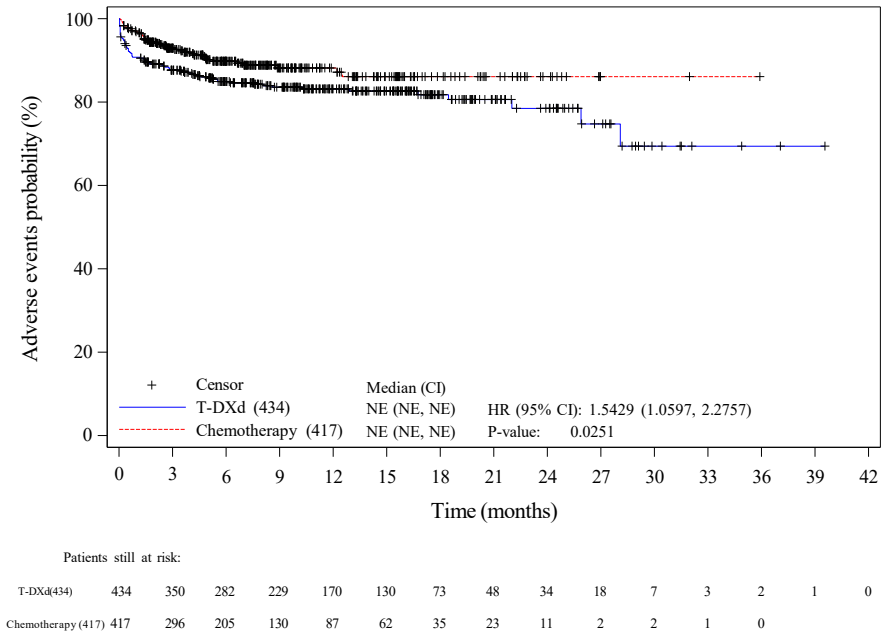
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: Headache



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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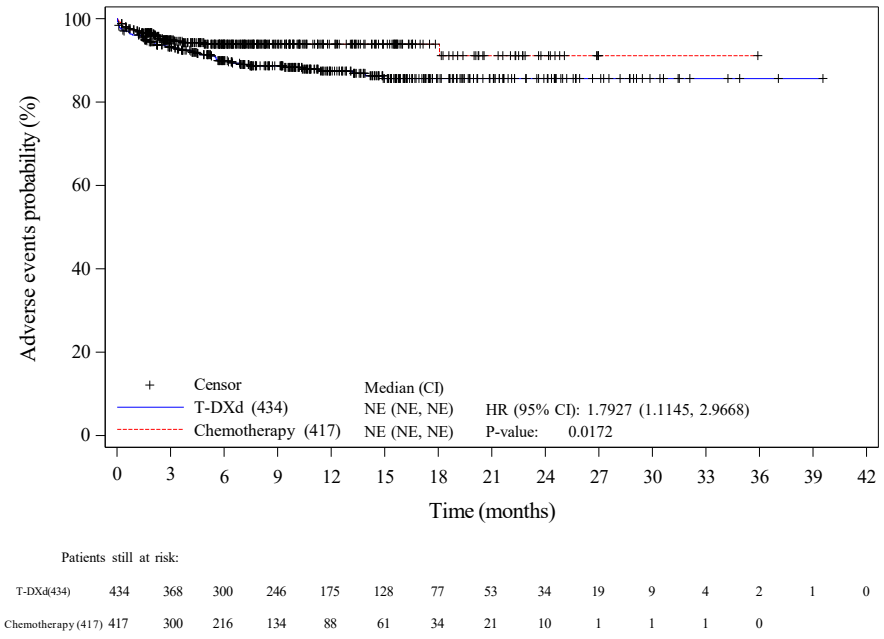
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: Dysgeusia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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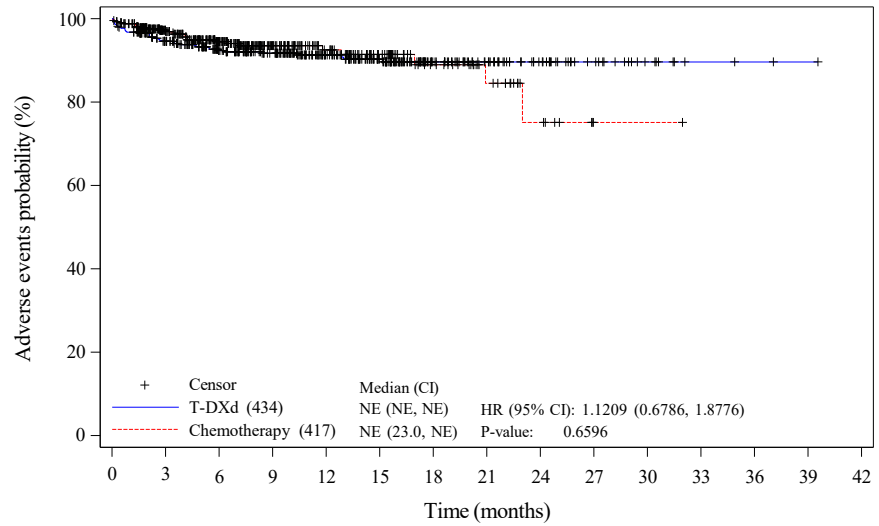
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: Dizziness



Patients still at risk:

T-DXd(434)	434	373	307	256	190	142	78	54	34	19	9	3	2	1	0
Chemotherapy (417)	417	311	218	137	89	58	32	19	8	1	1	0			

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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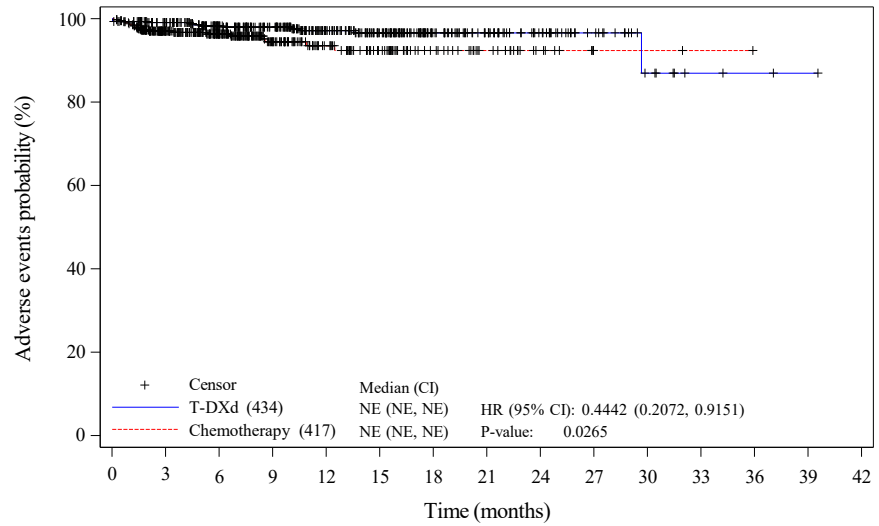
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: Paraesthesia



Patients still at risk:

T-DXd(434)	434	393	328	273	199	150	86	60	37	20	8	3	2	1	0
Chemotherapy (417)	417	310	220	132	86	60	35	22	10	2	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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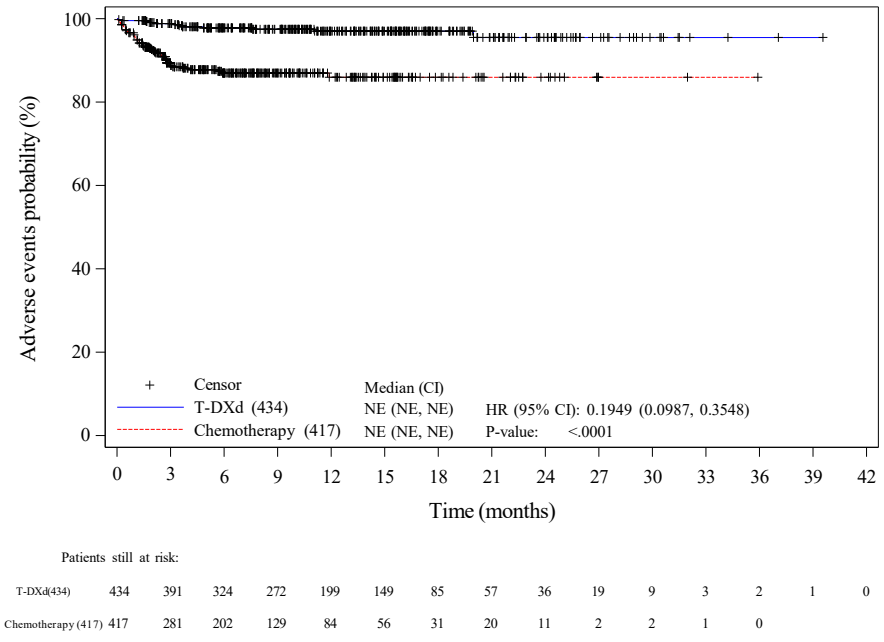
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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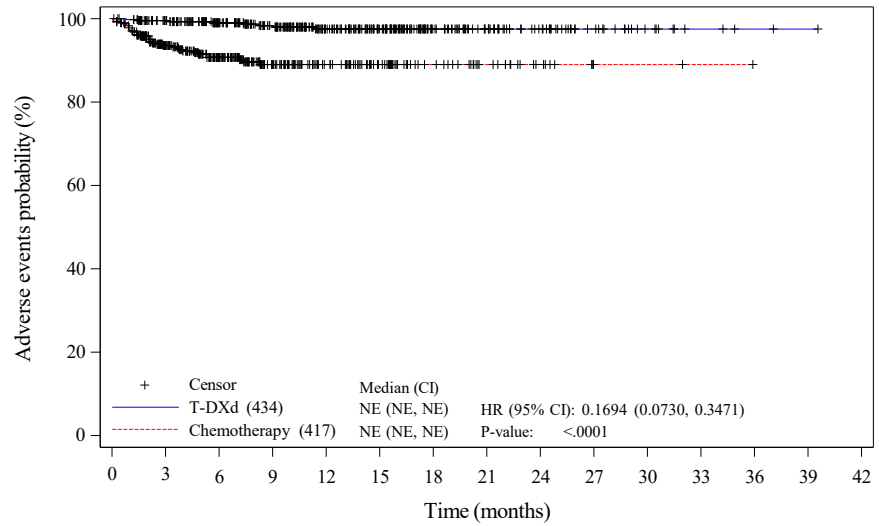
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: Neuropathy peripheral



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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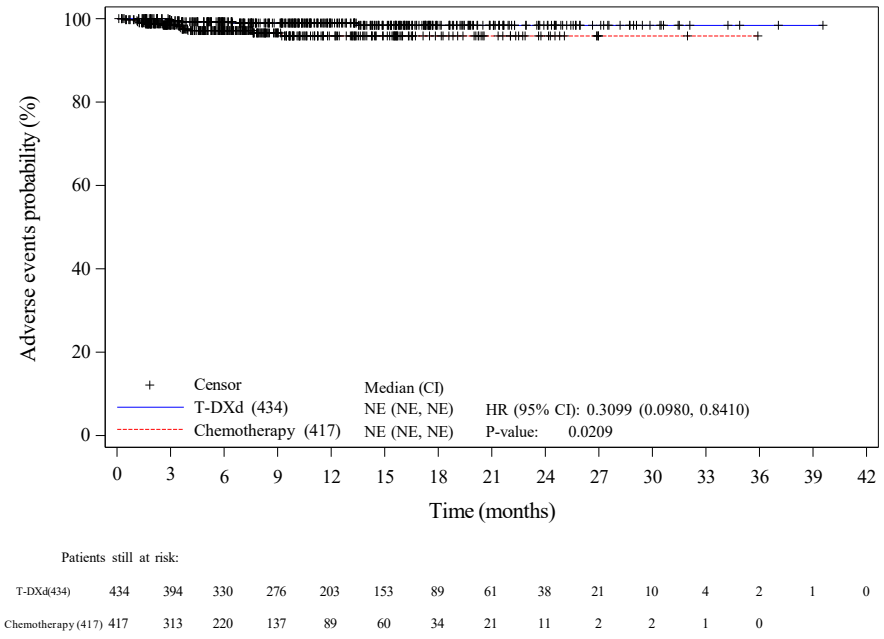
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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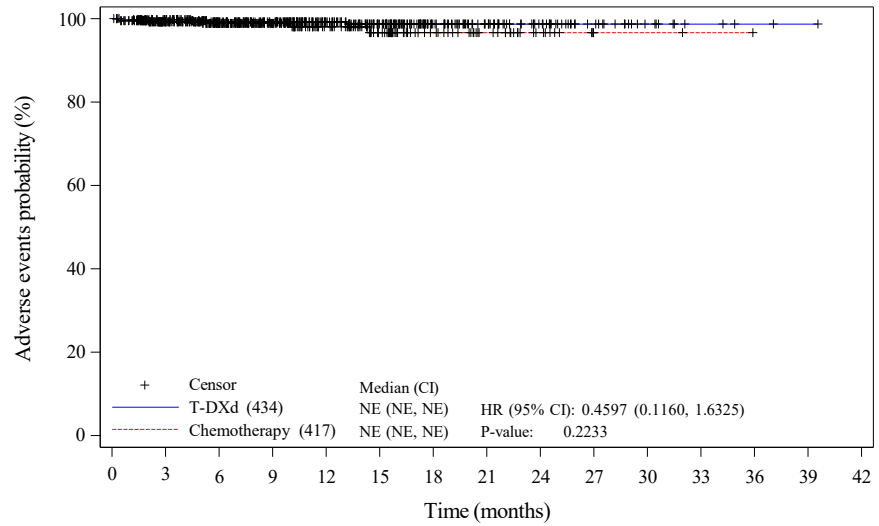
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: Somnolence



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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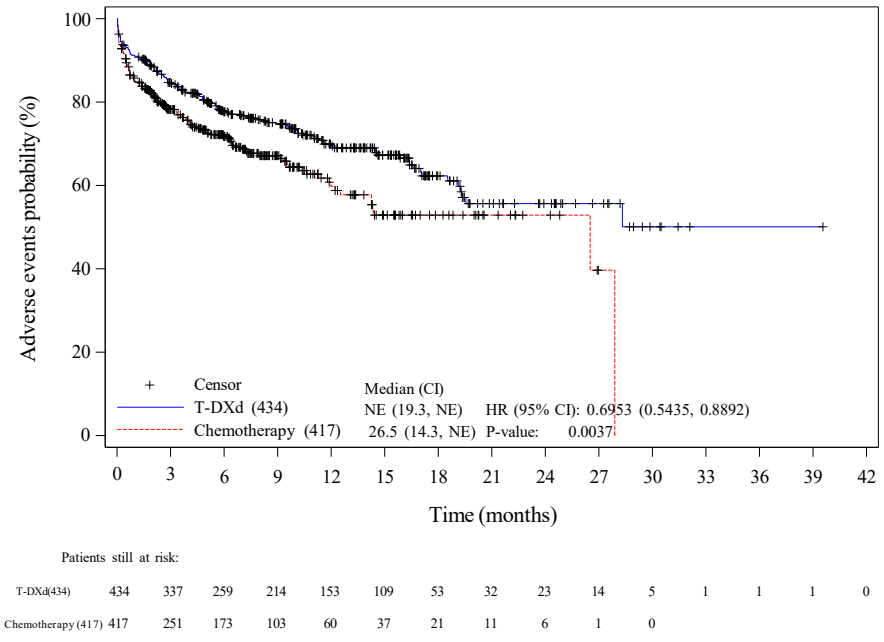
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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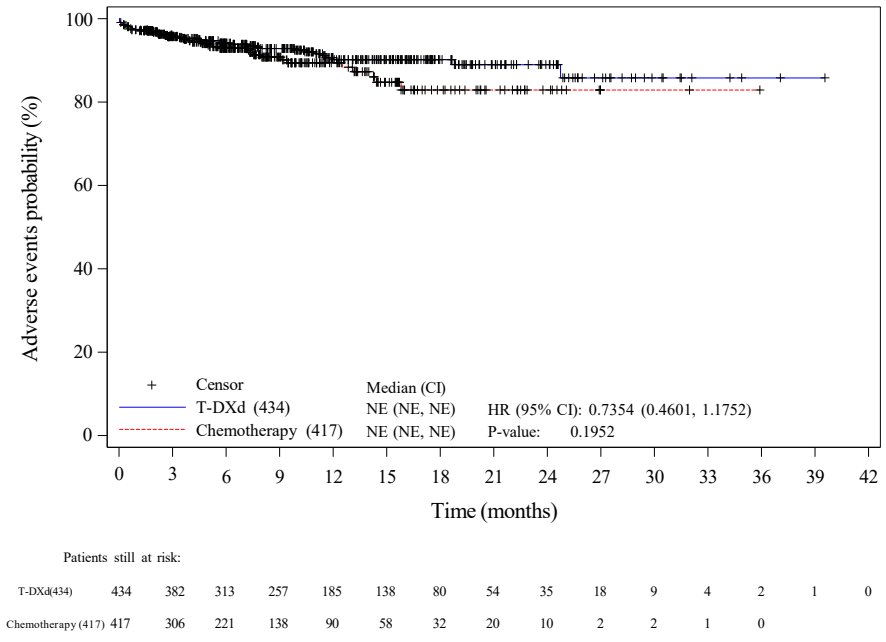
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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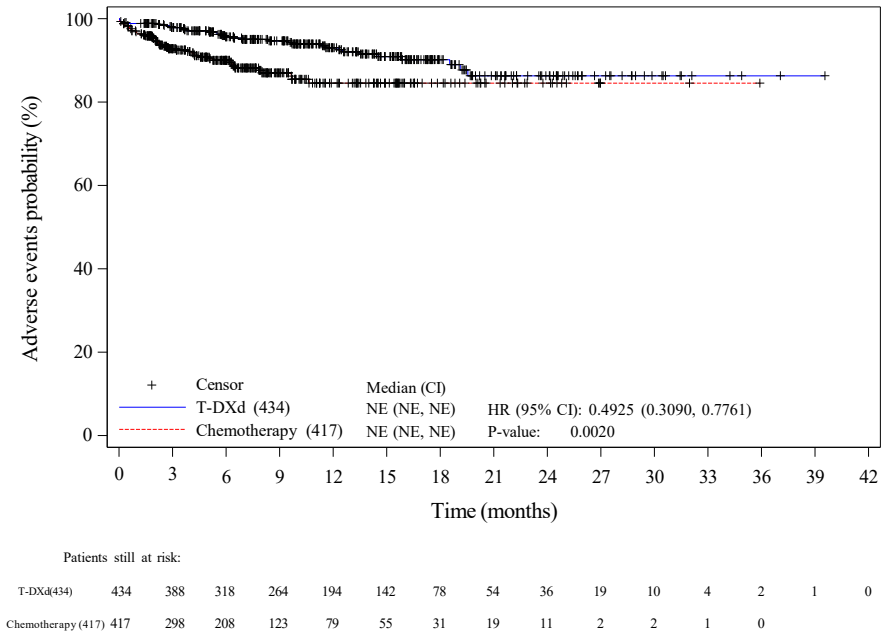
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: Arthralgia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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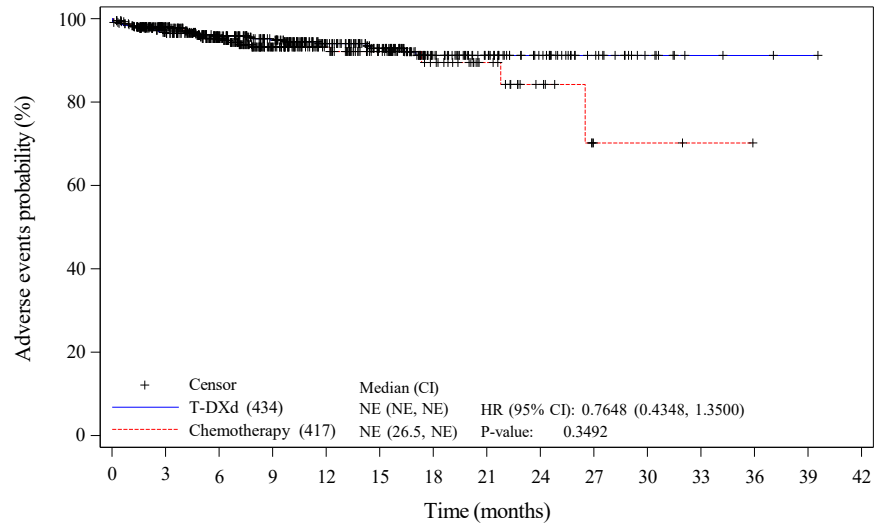
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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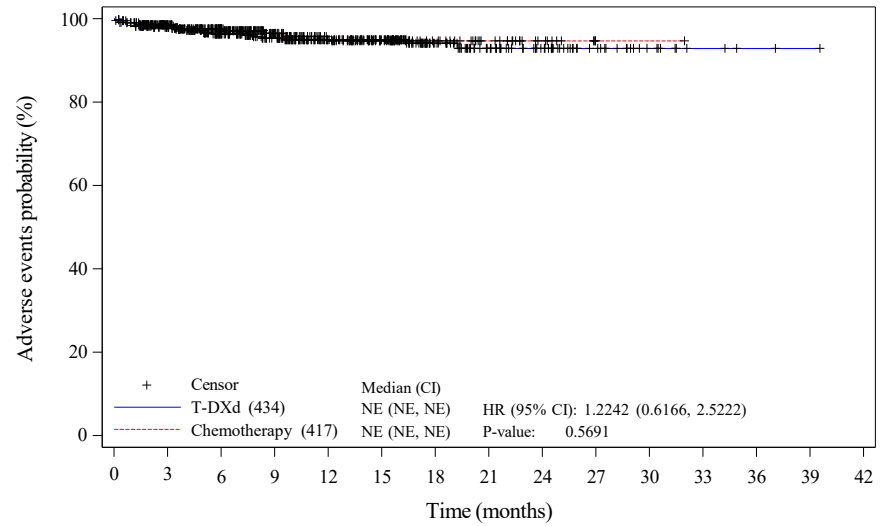
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: Musculoskeletal chest pain



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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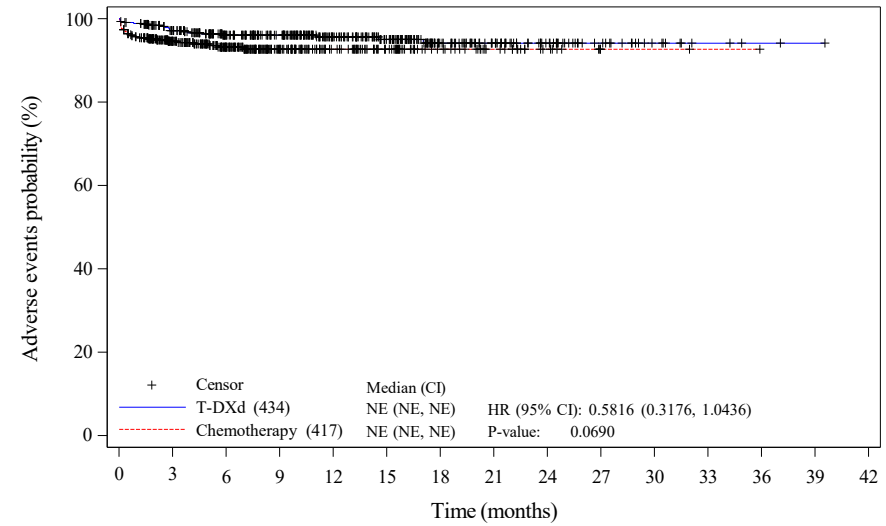
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia



Patients still at risk:

T-DXd(434)	434	384	318	271	199	150	84	59	37	21	10	4	2	1	0
Chemotherapy (417)	417	303	218	136	87	60	34	21	10	2	2	1	0		

Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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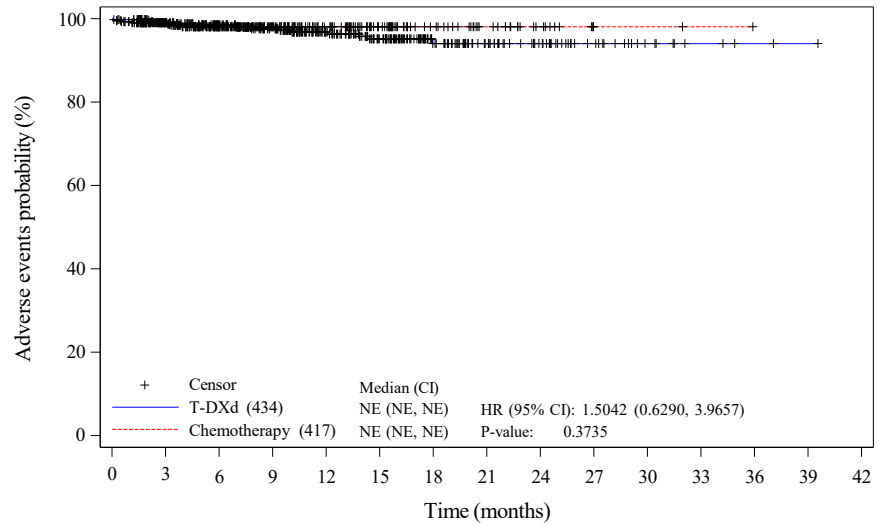
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: Muscle spasms



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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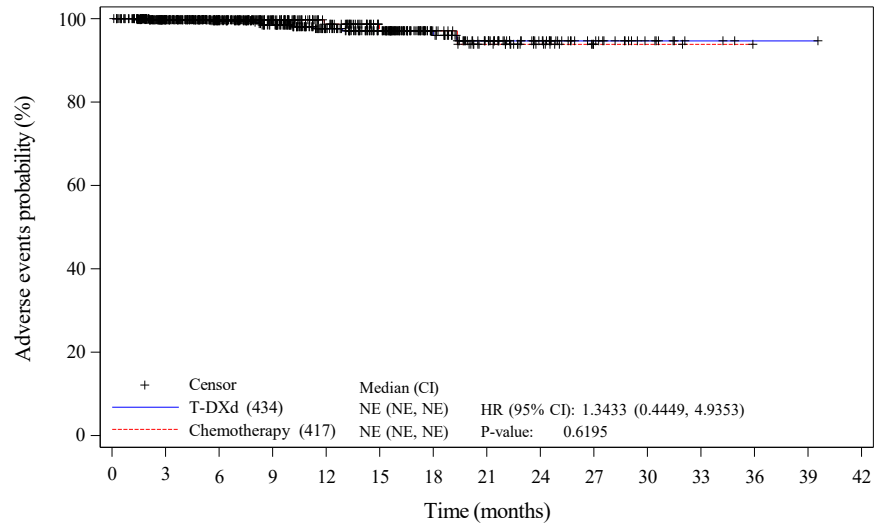
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: Musculoskeletal pain



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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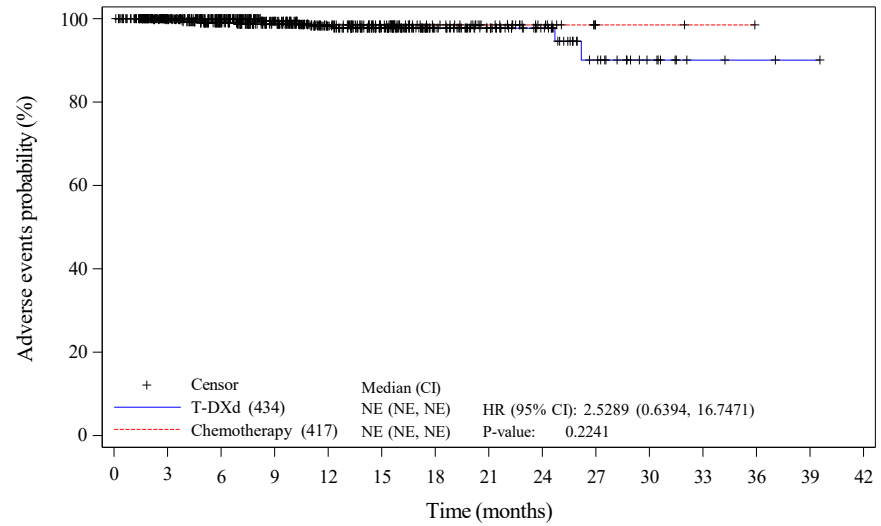
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: Neck pain



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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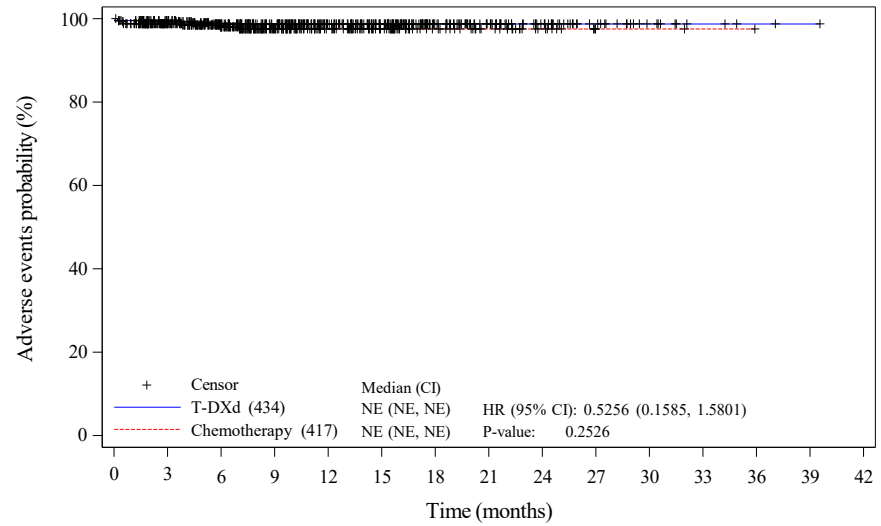
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: Bone pain



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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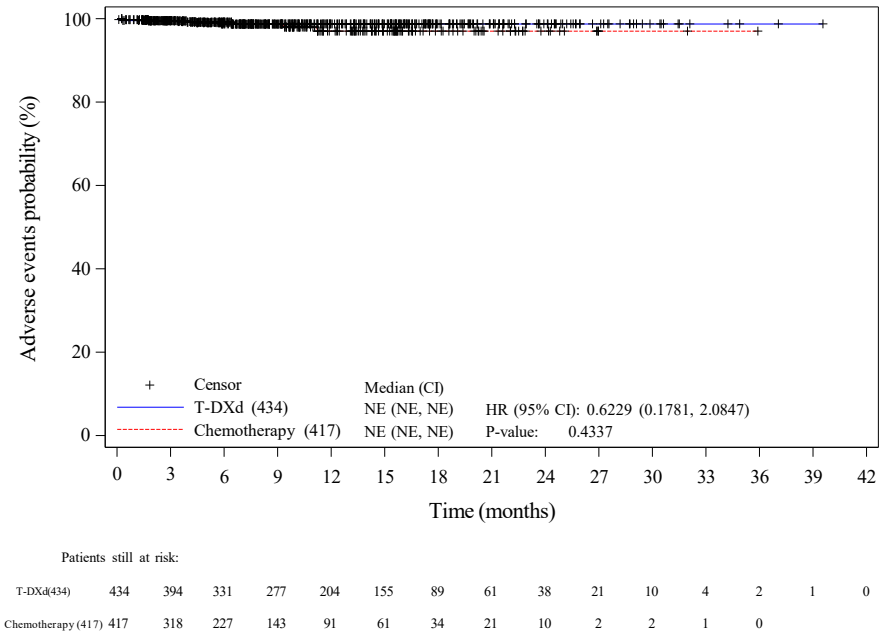
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: Muscular weakness



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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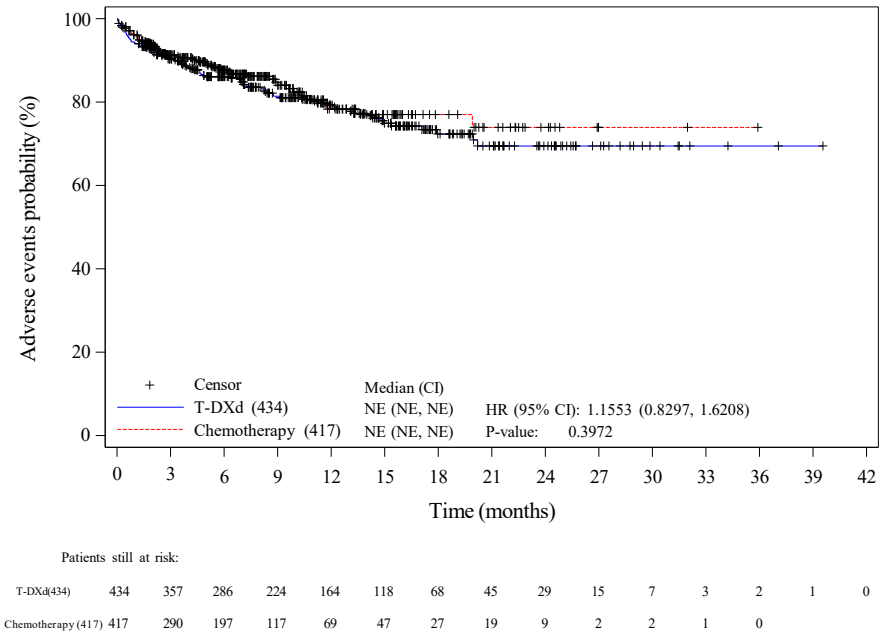
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Eye disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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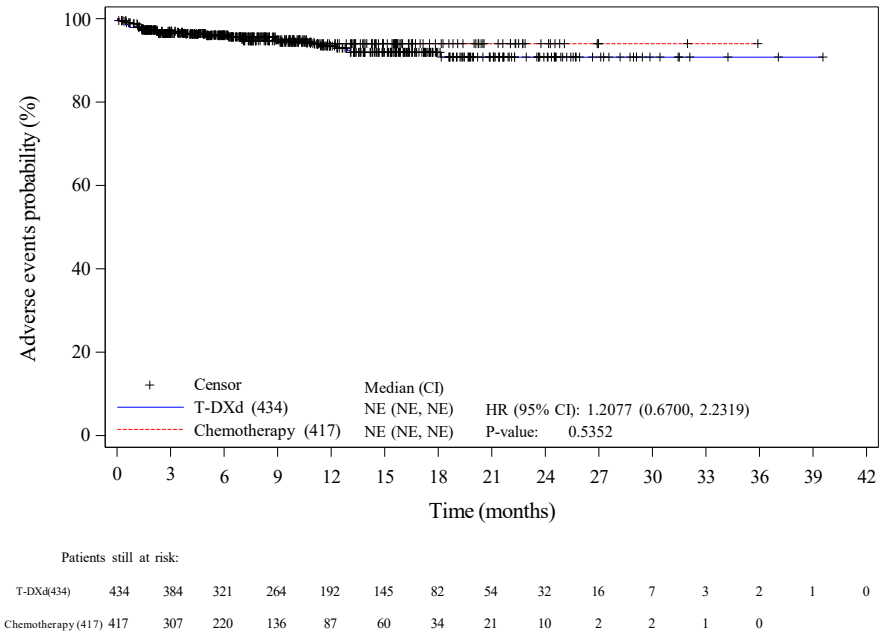
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Eye disorders; PT: Dry eye



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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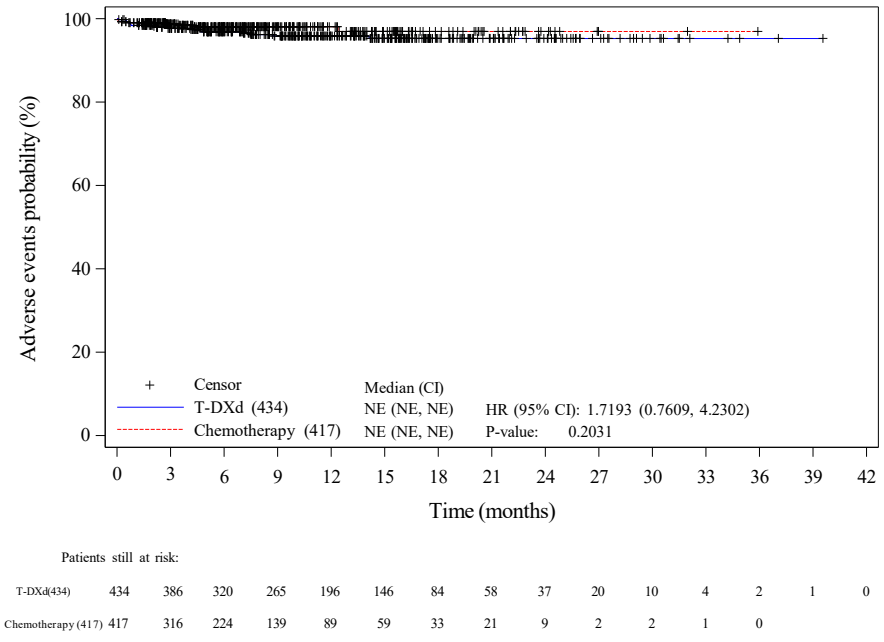
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Eye disorders; PT: Vision blurred



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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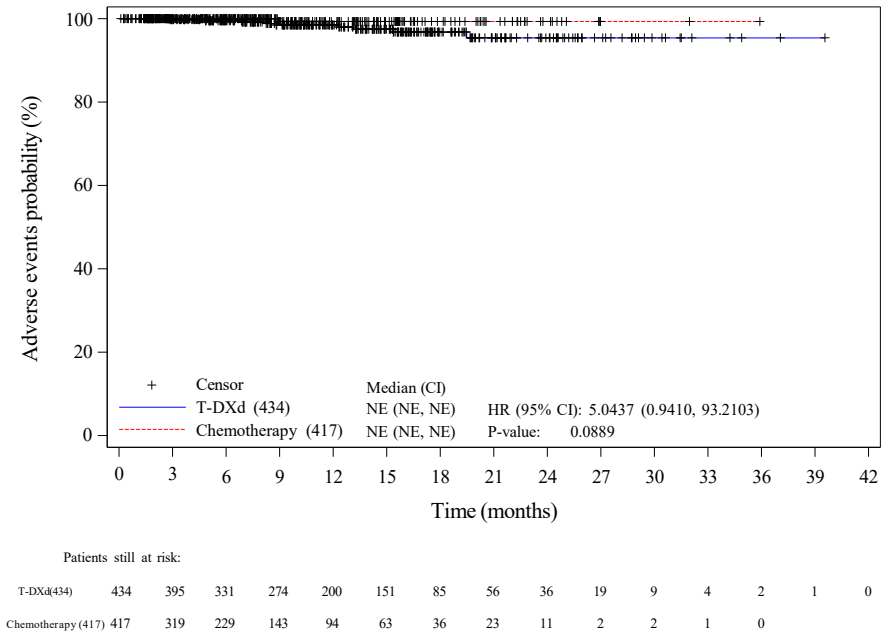
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Eye disorders; PT: Cataract



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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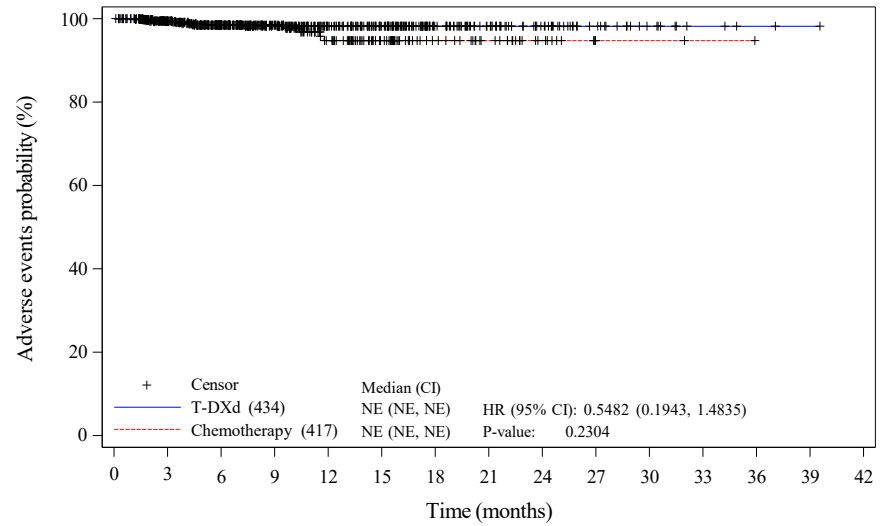
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Eye disorders; PT: Lacrimation increased



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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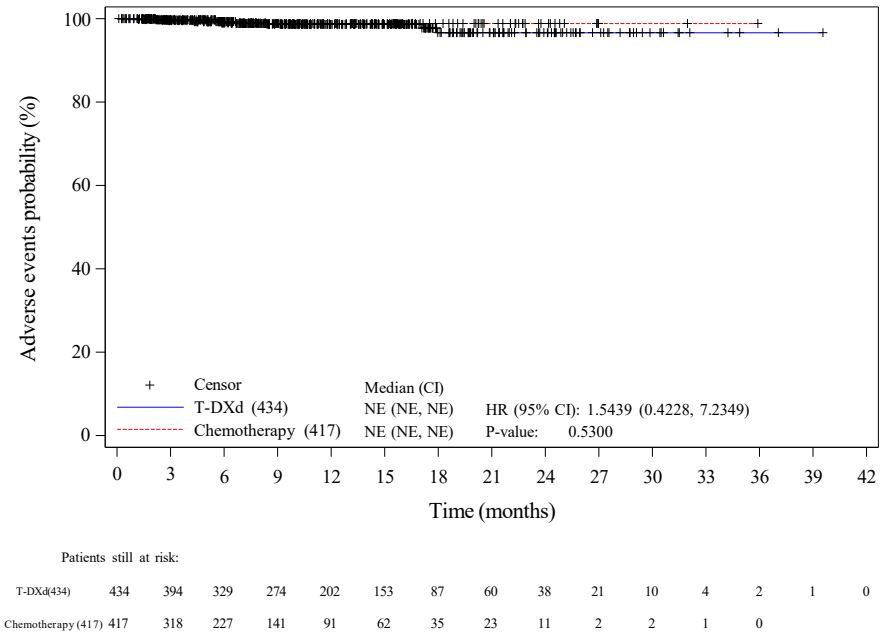
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Eye disorders; PT: Visual impairment



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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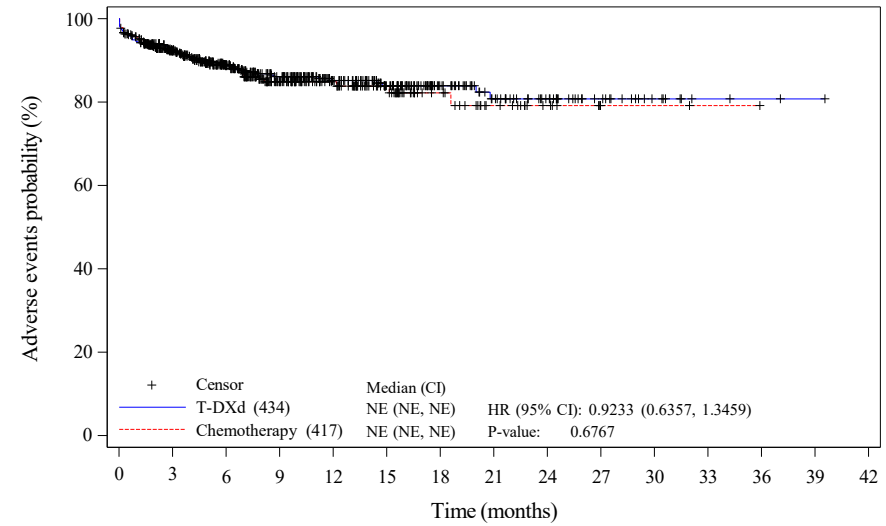
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Vascular disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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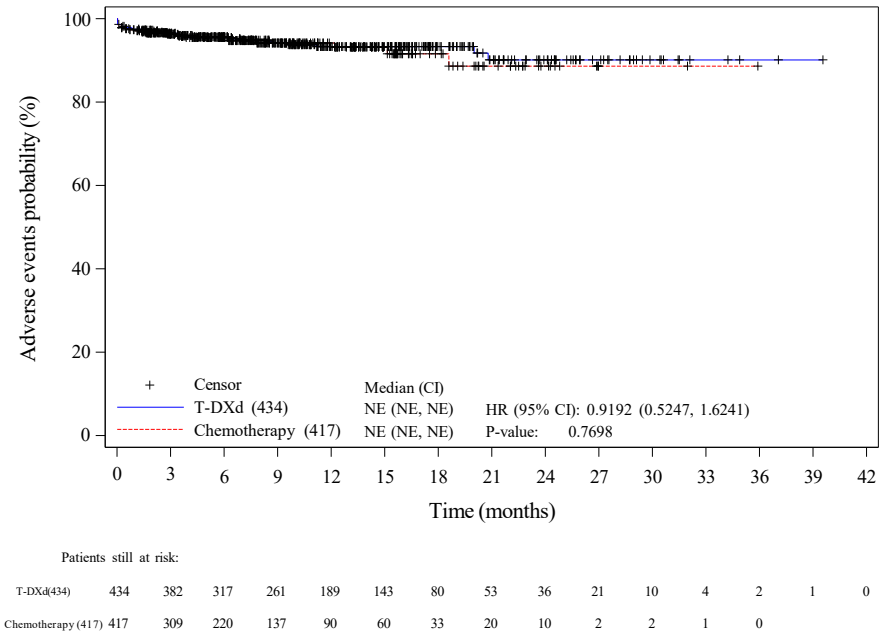
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Vascular disorders; PT: Hypertension



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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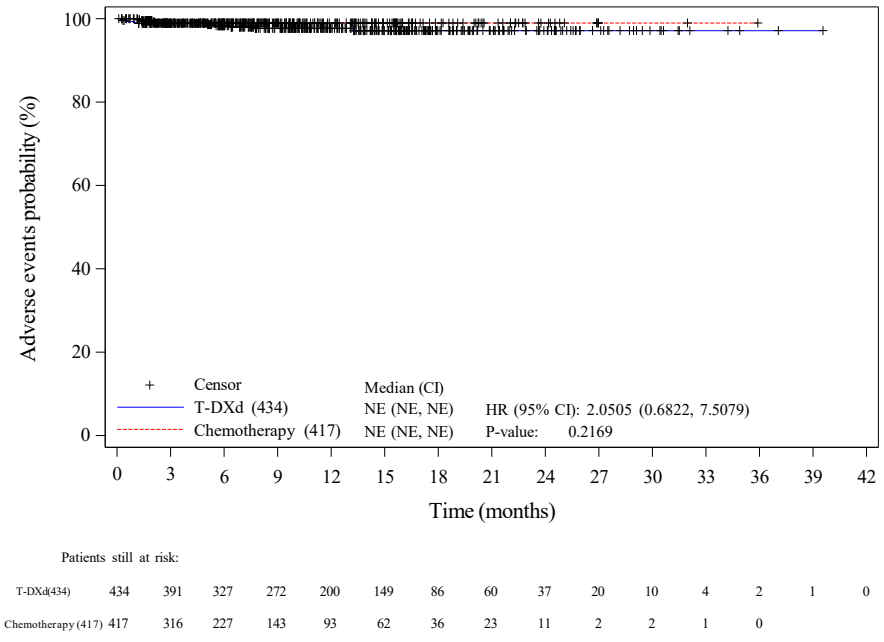
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Vascular disorders; PT: Hypotension



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
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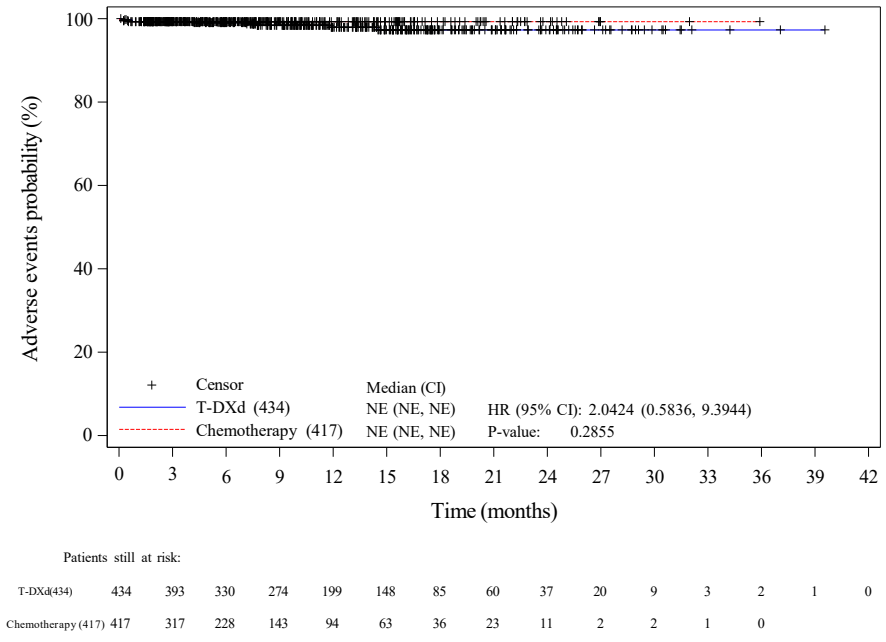
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Vascular disorders; PT: Hot flush



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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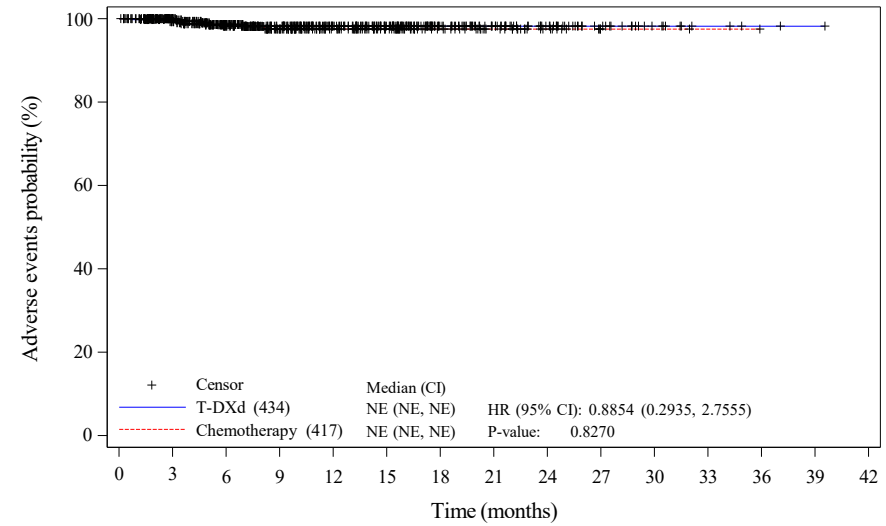
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Vascular disorders; PT: Lymphoedema



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
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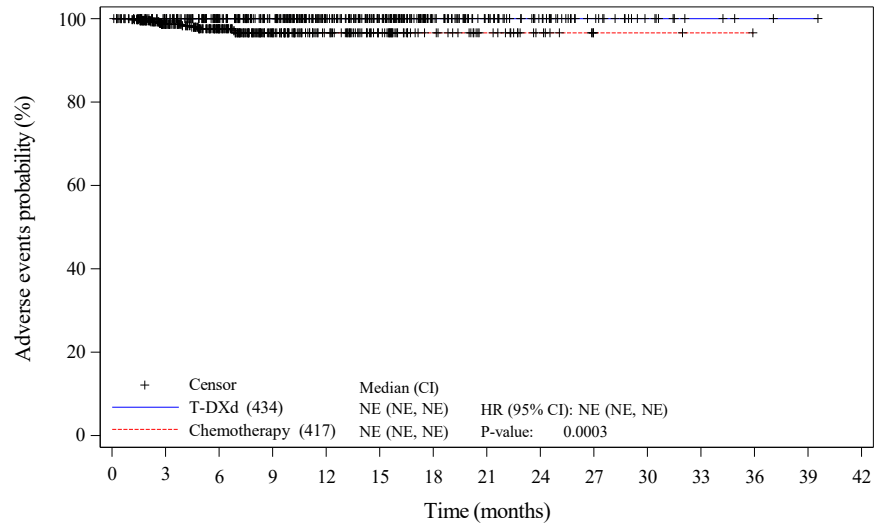
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Vascular disorders; PT: Deep vein thrombosis



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Psychiatric disorders; PT: All (any PT)

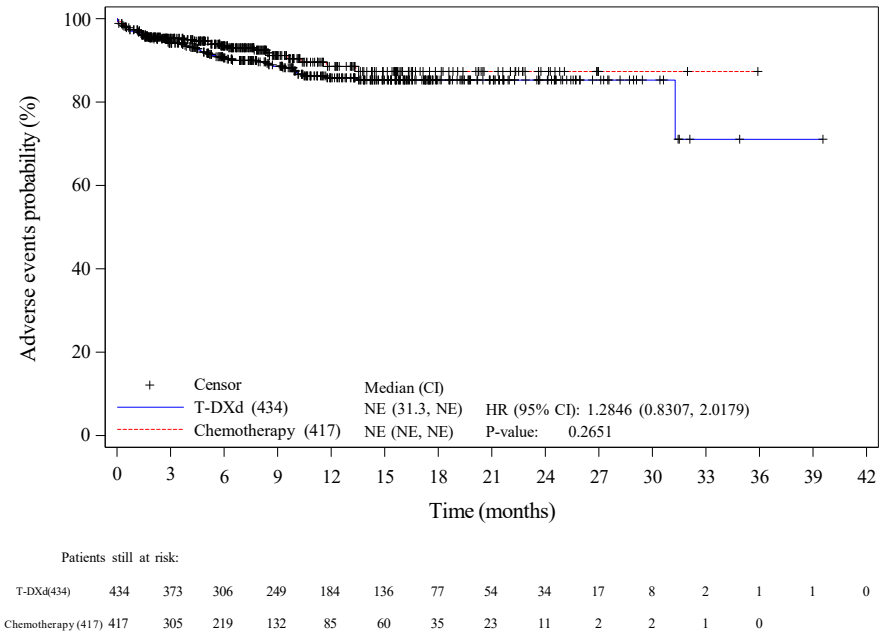

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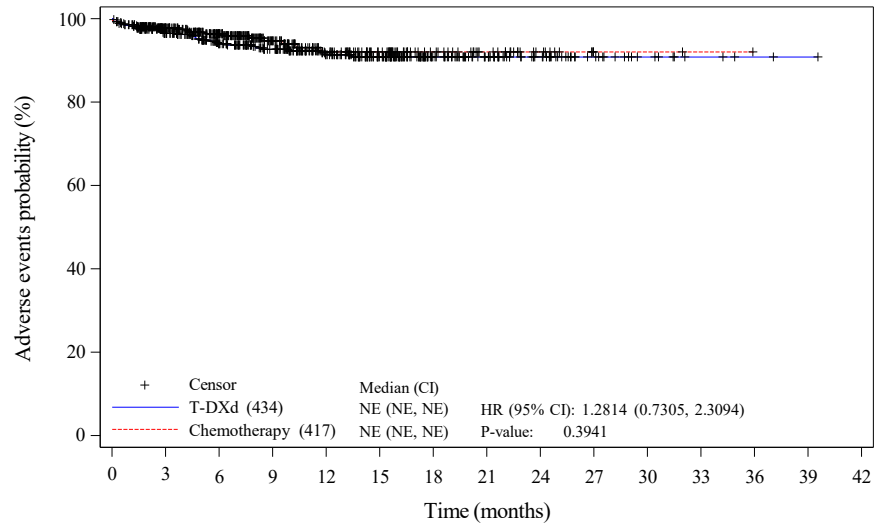
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Psychiatric disorders; PT: Insomnia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
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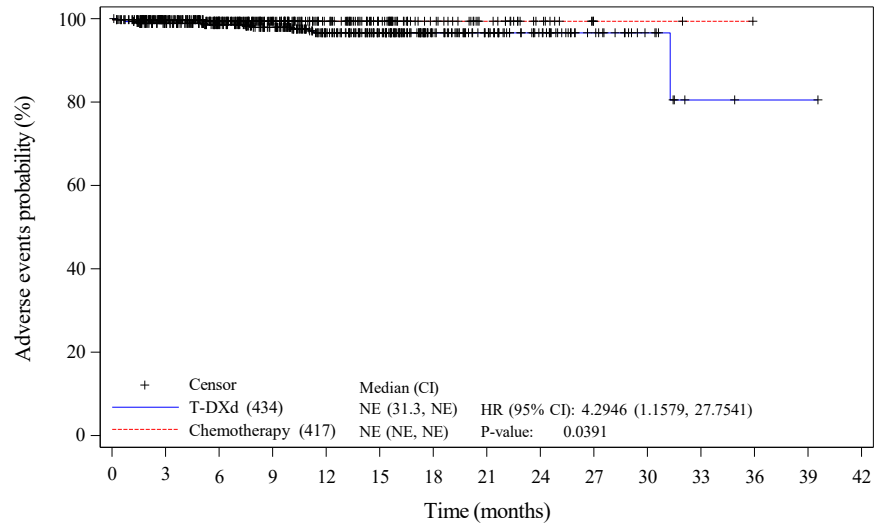
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Psychiatric disorders; PT: Anxiety



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Psychiatric disorders; PT: Depression

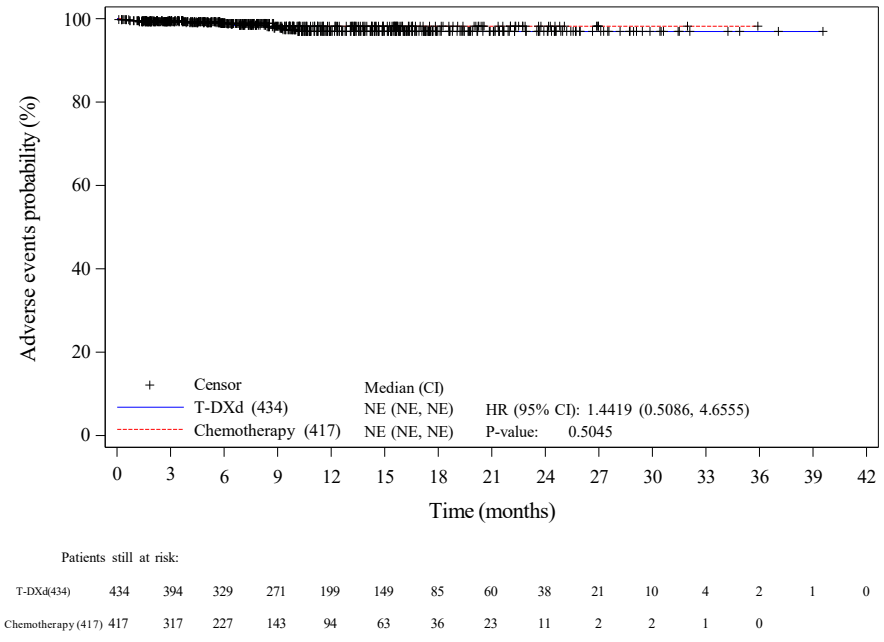

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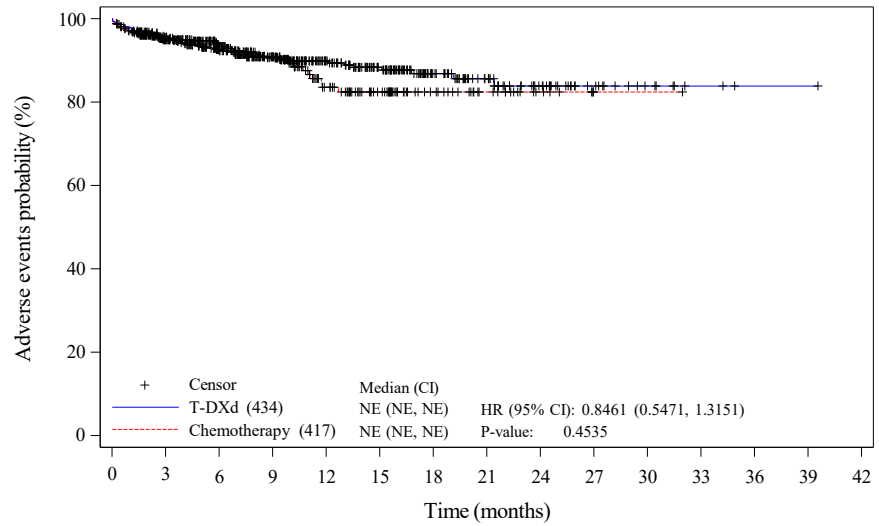
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Injury, poisoning and procedural complications; PT: All (any PT)



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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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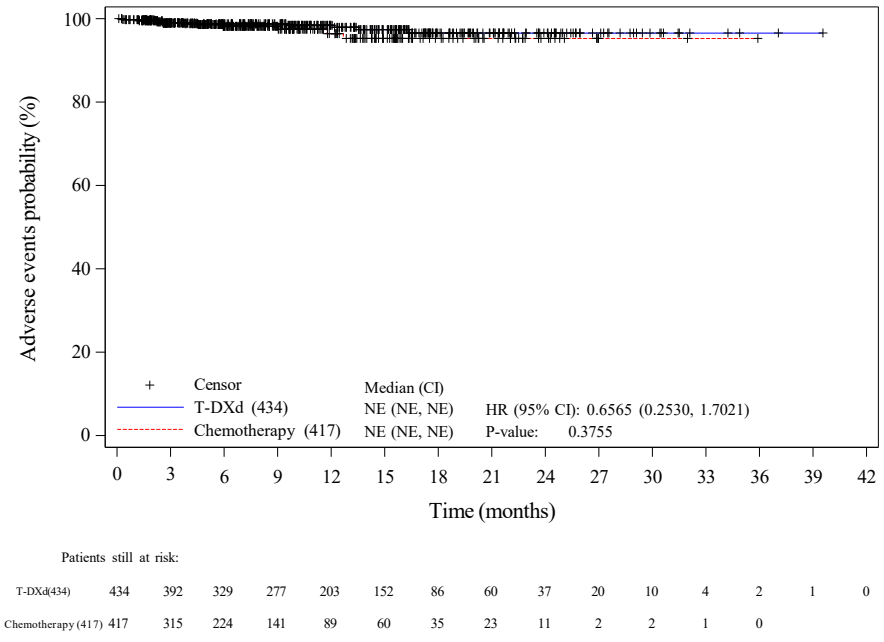
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Injury, poisoning and procedural complications; PT: Fall



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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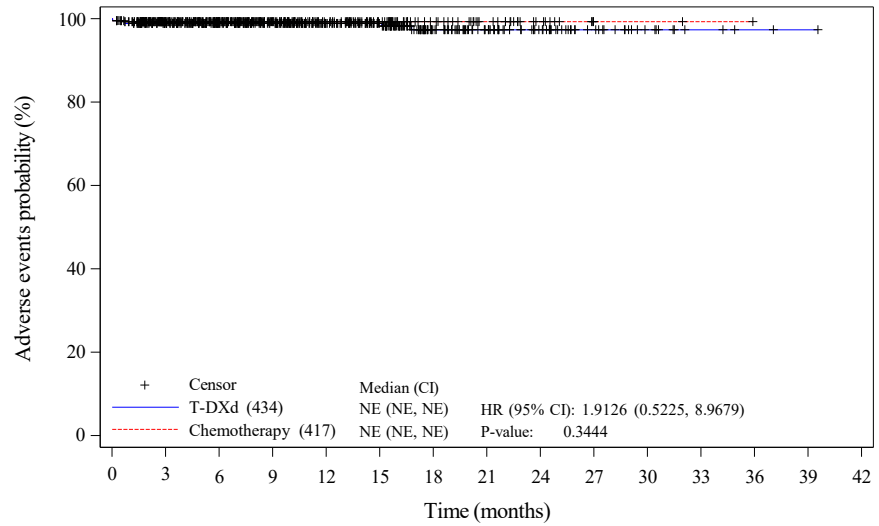
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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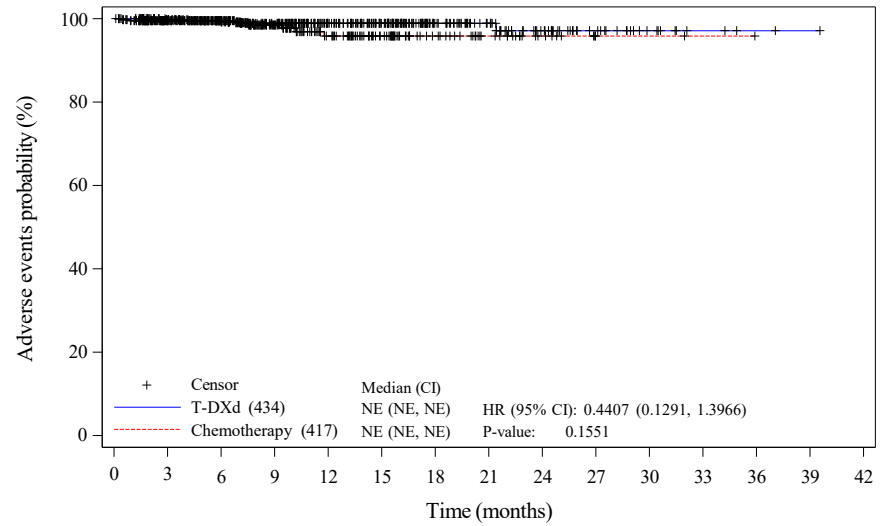
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Injury, poisoning and procedural complications; PT: Contusion



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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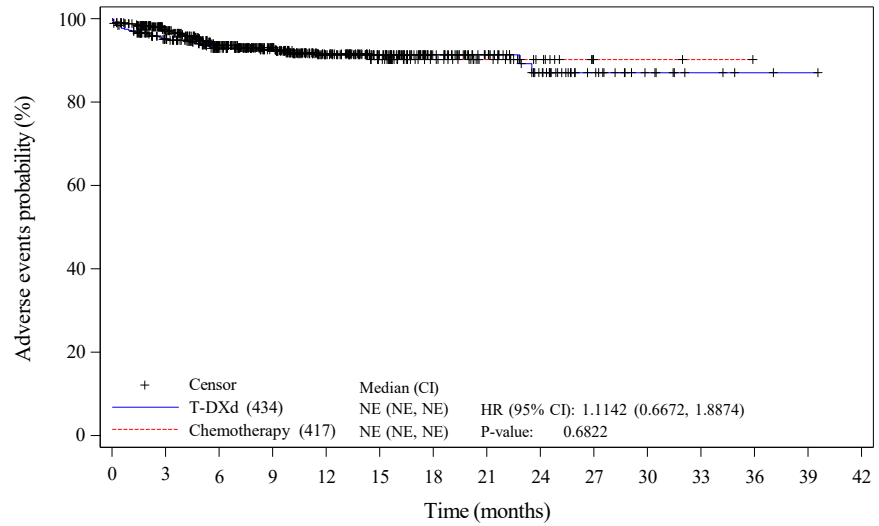
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Cardiac disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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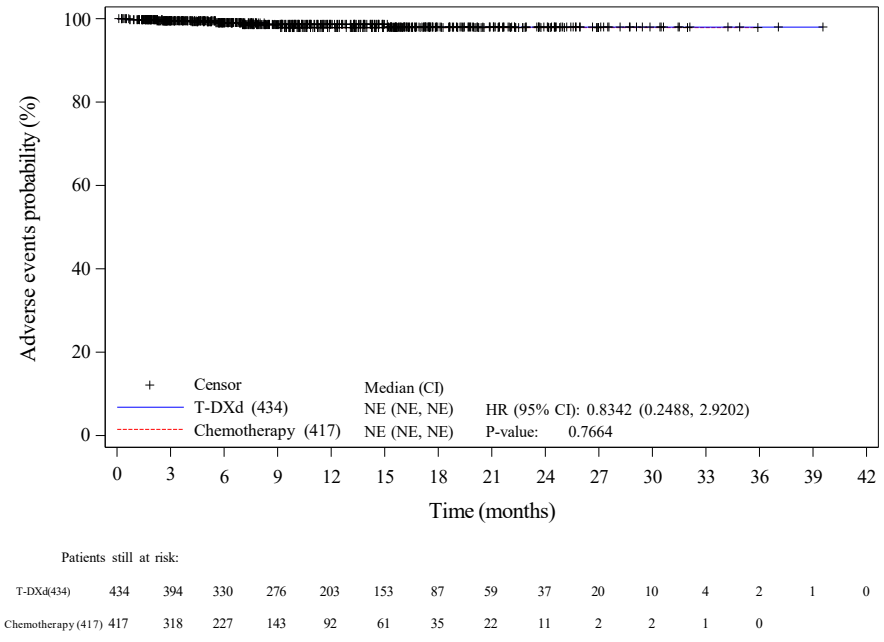
Run date: 16DEC2024 7:30; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Cardiac disorders; PT: Tachycardia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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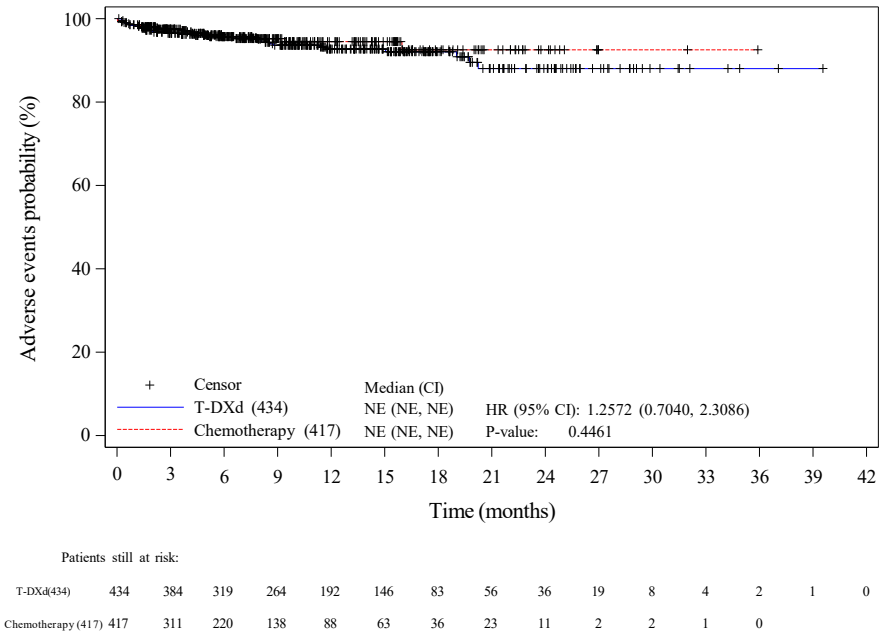
Run date: 16DEC2024 7:31; Program name: F.2.29.1_10TEAE_SAF.sas; Output name: F.2.29.1_10TEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Renal and urinary disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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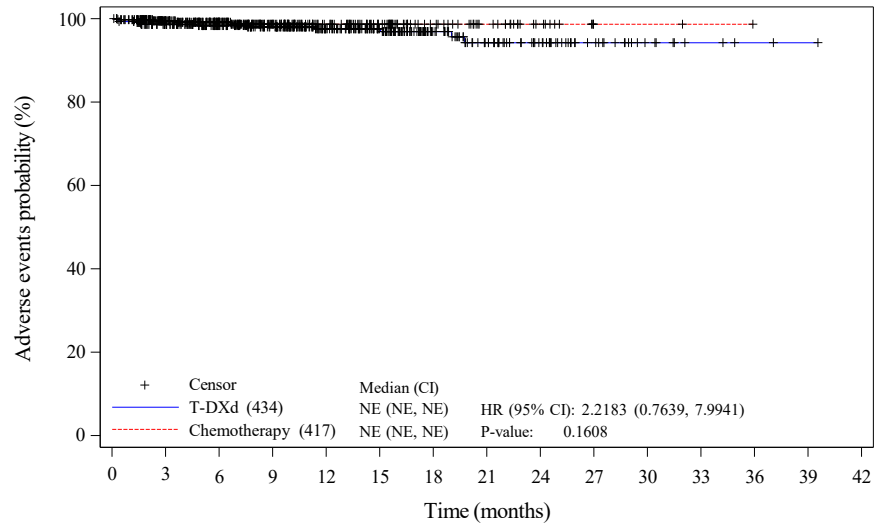
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Renal and urinary disorders; PT: Dysuria



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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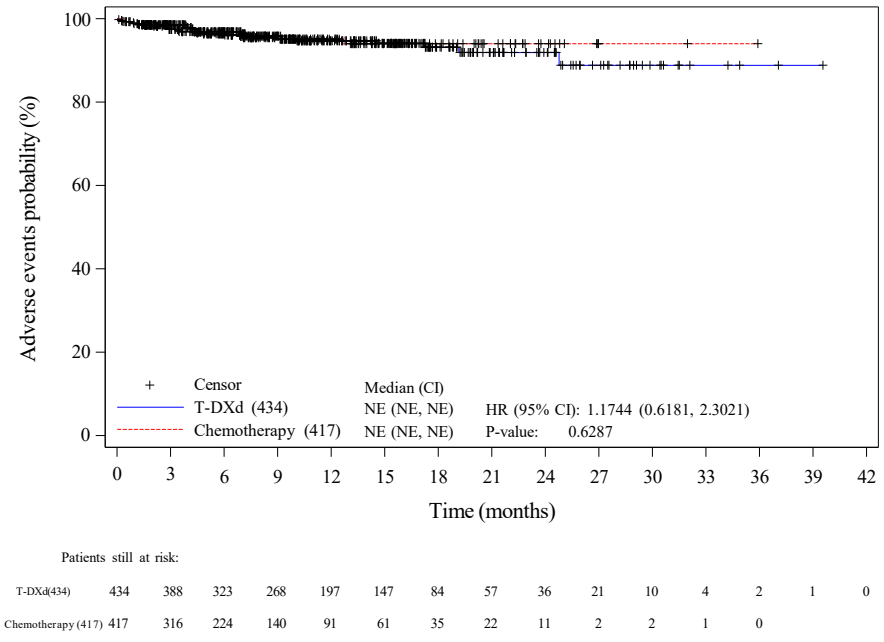
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Hepatobiliary disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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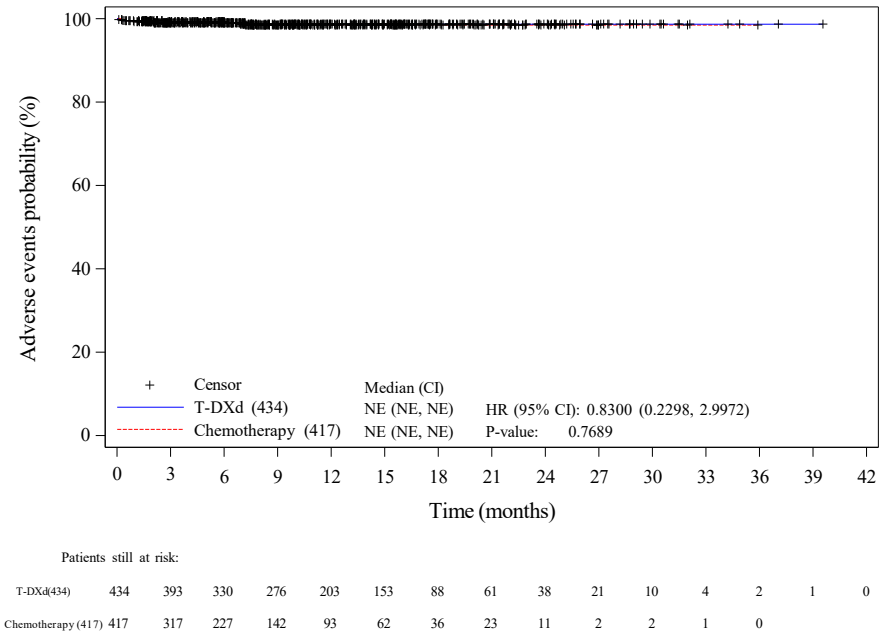
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Hepatobiliary disorders; PT: Hypertransaminasaemia



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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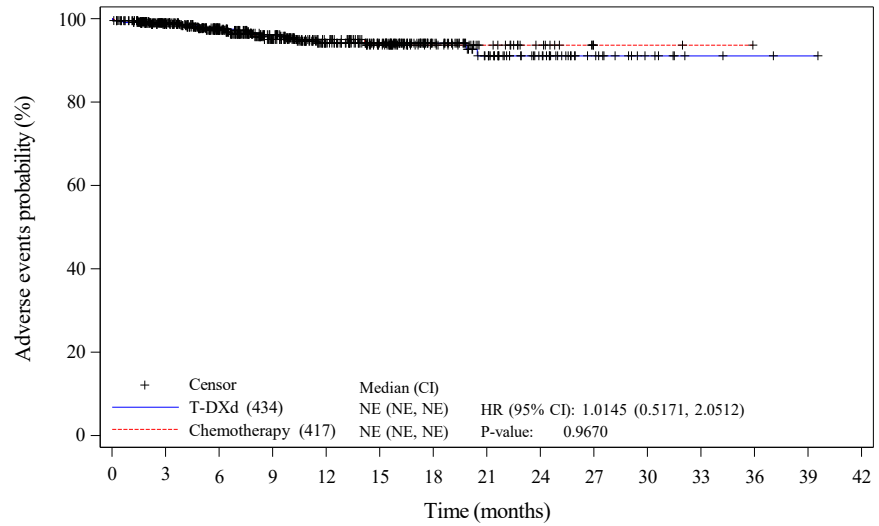
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Reproductive system and breast disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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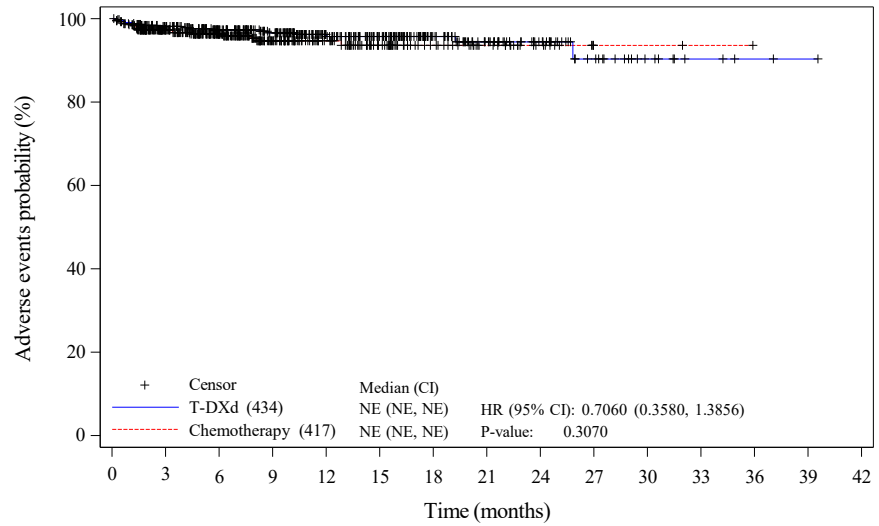
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Ear and labyrinth disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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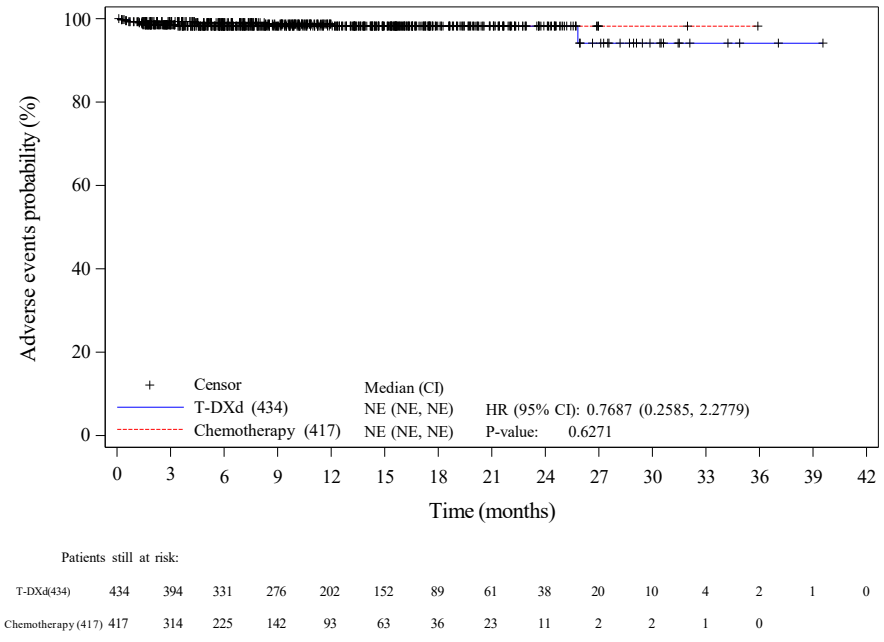
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Ear and labyrinth disorders; PT: Vertigo



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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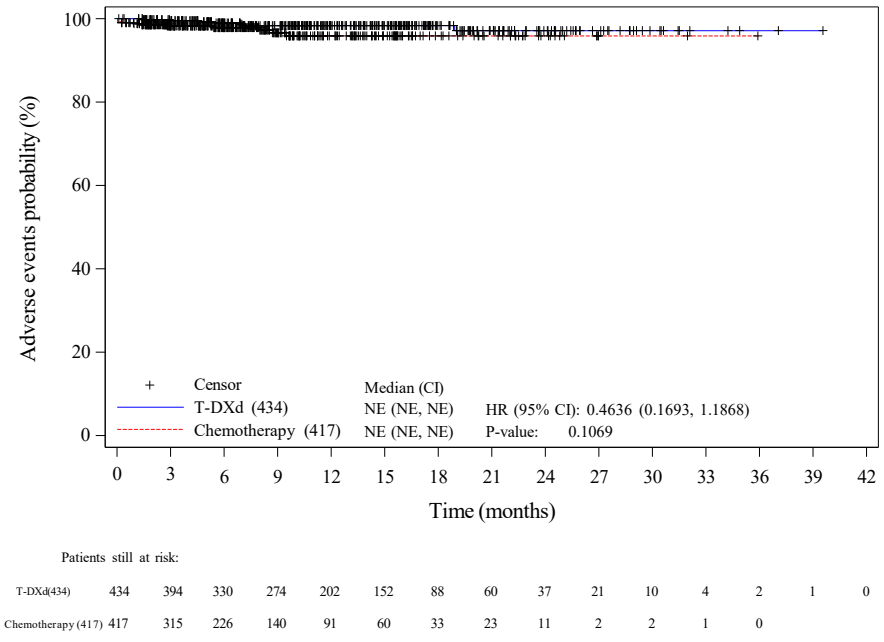
Figure 2.29.1 Adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Immune system disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from Cox proportional hazards model and two-sided p-value is based on log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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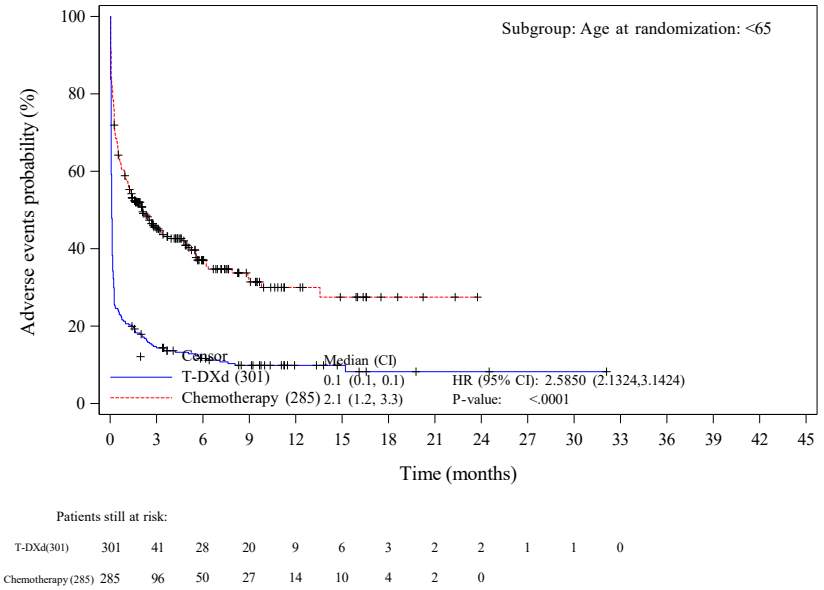
Abbildung 2.29.2 Unerwünschte Ereignisse nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Kaplan-Meier-Plot – Analyse nach Subgruppe – SAF

Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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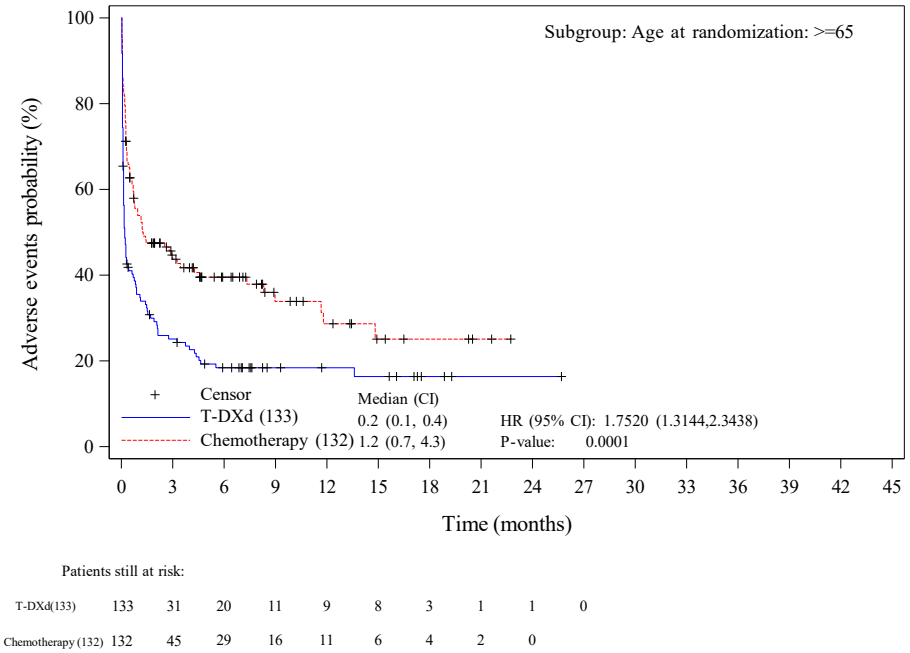
Run date: 11DEC2024 16:19; Program name: F.2.29.2_10TEAE_SAF_SUB.sas; Output name: F.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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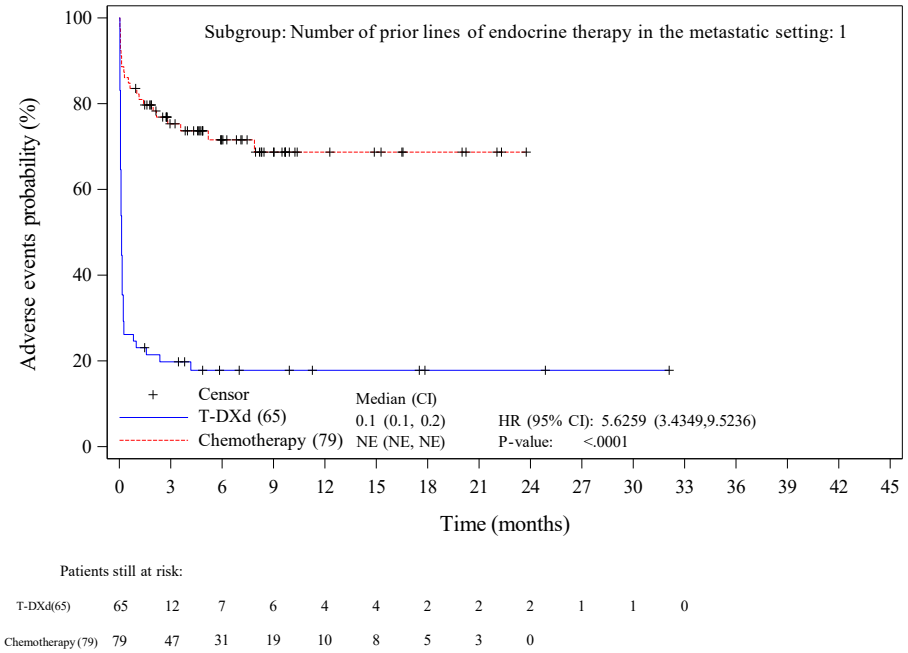
Run date: 11DEC2024 16:19; Program name: F.2.29.2_10TEAE_SAF_SUB.sas; Output name: F.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Nausea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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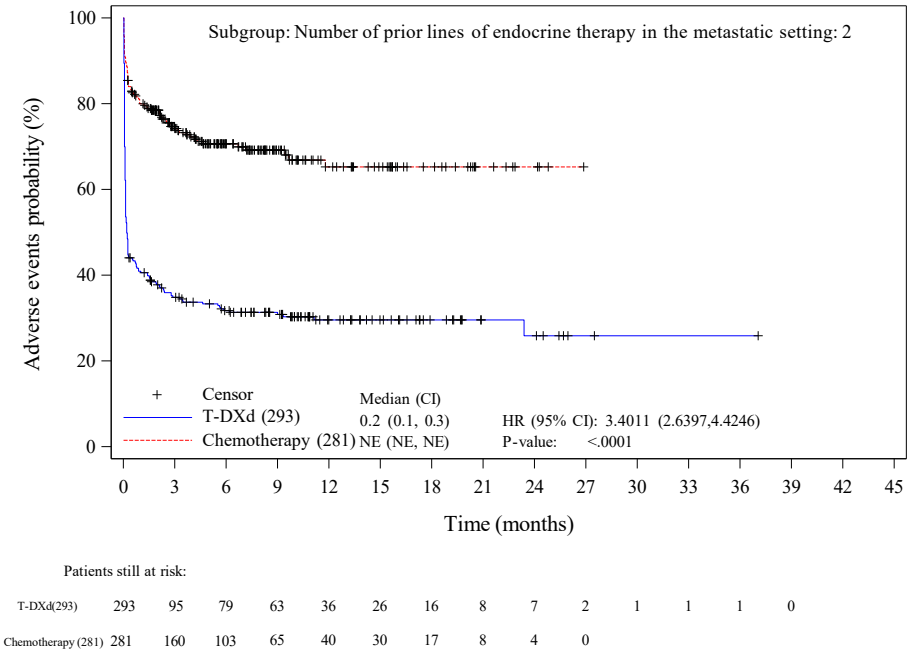
Run date: 11DEC2024 16:19; Program name: F.2.29.2_10TEAE_SAF_SUB.sas; Output name: F.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Nausea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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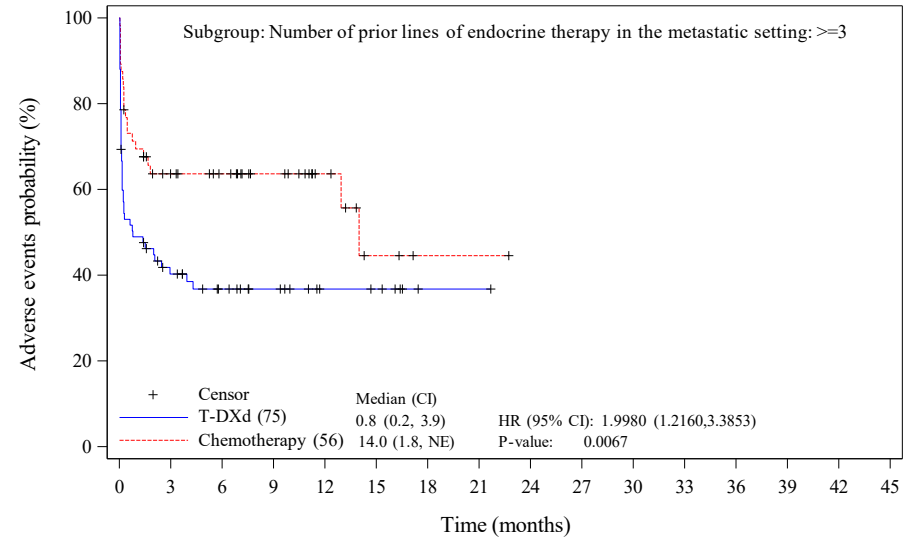
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Nausea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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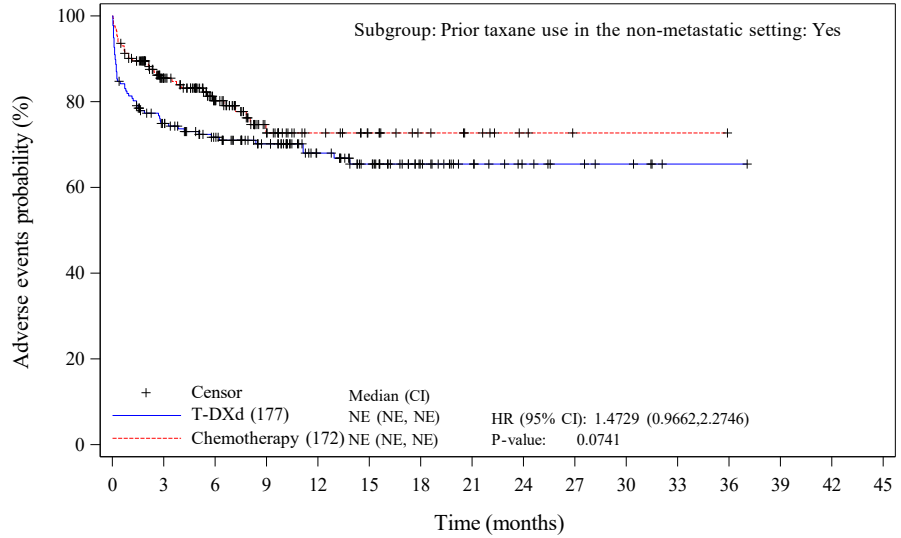
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Constipation



Patients still at risk:

T-DXd(177)	177	123	104	82	58	43	25	16	10	7	5	1	1	0
Chemotherapy (172)	172	115	74	37	23	16	10	7	3	1	1	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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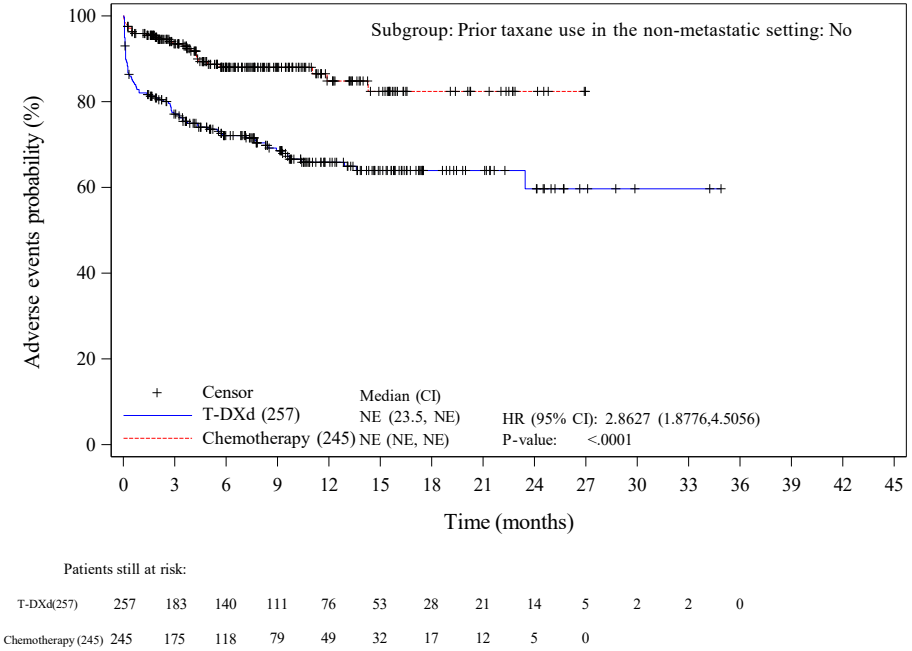
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Constipation



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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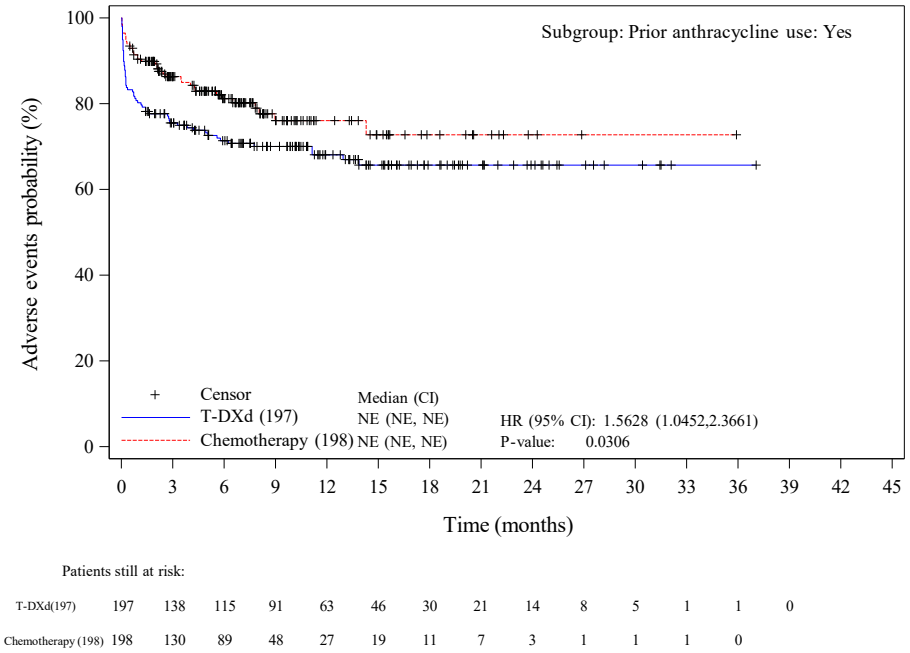
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Constipation



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Constipation

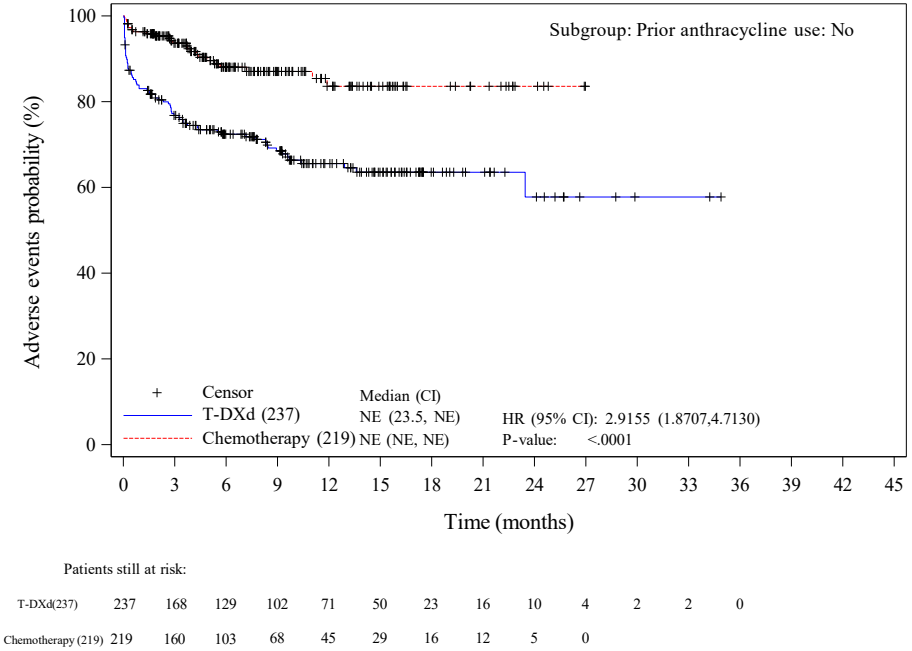

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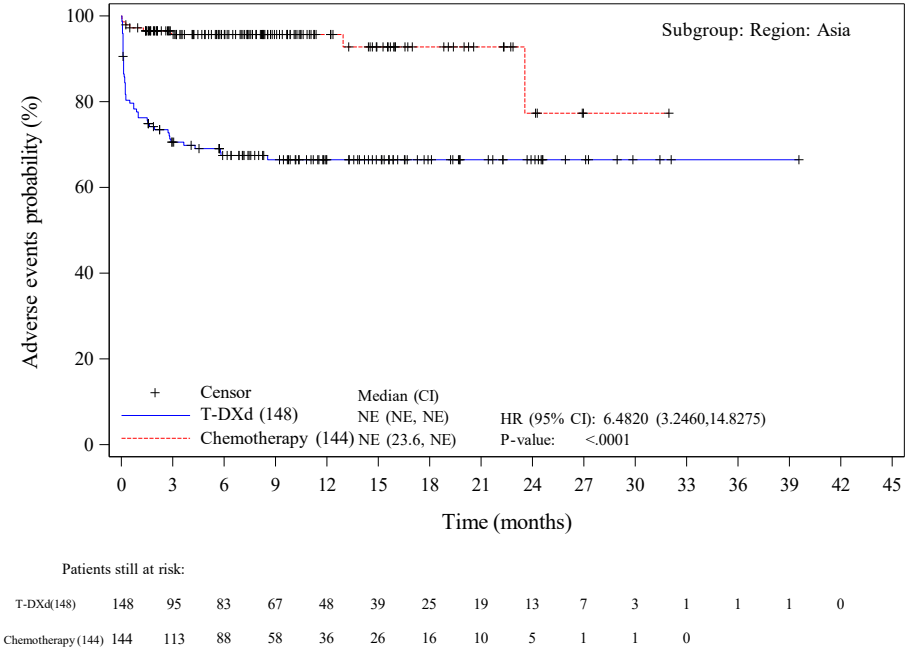
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Vomiting



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Vomiting

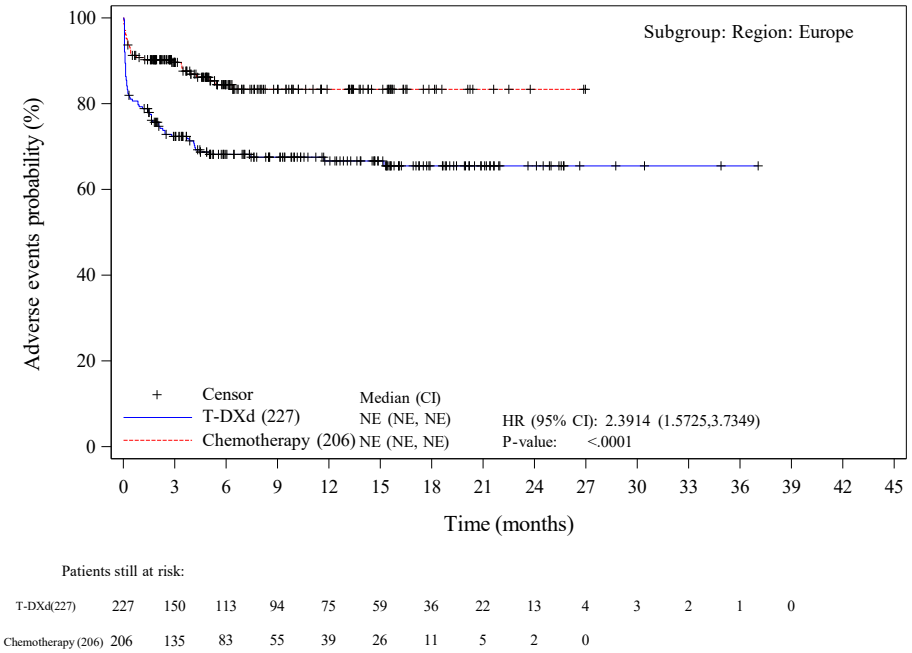

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Vomiting

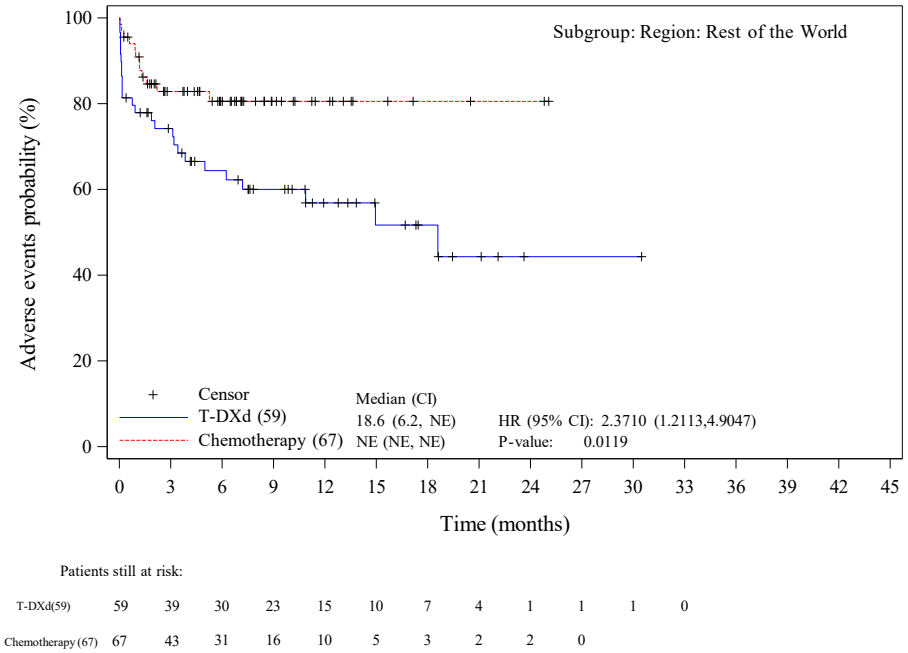

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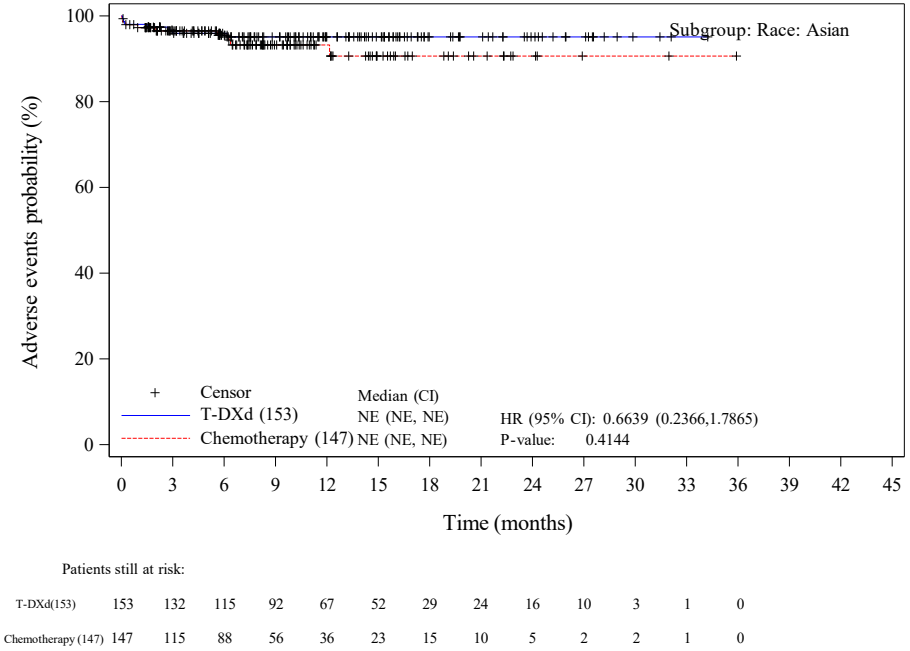
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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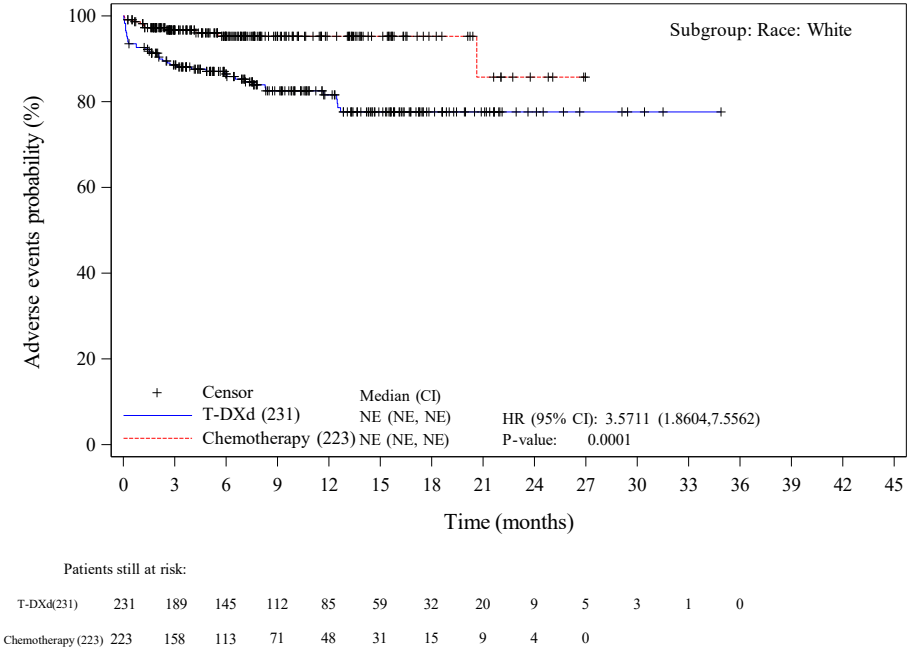
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia



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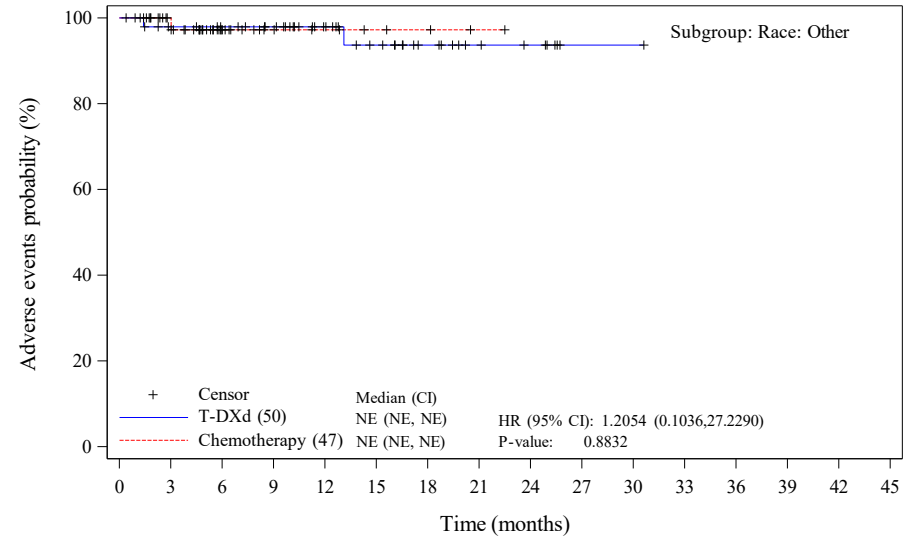
Run date: 11DEC2024 16:19; Program name: F.2.29.2_10TEAE_SAF_SUB.sas; Output name: F.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia

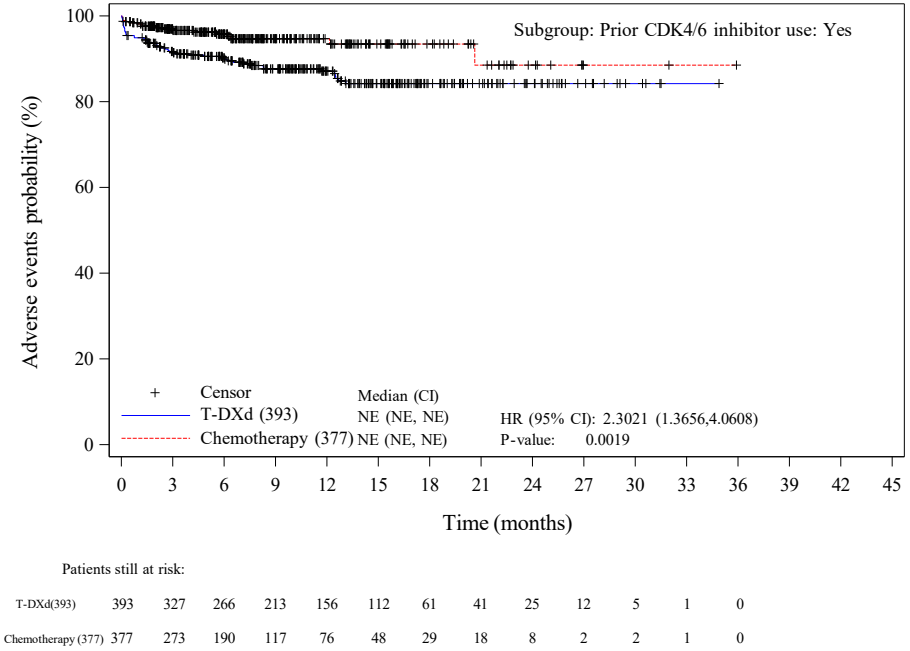

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Dyspepsia

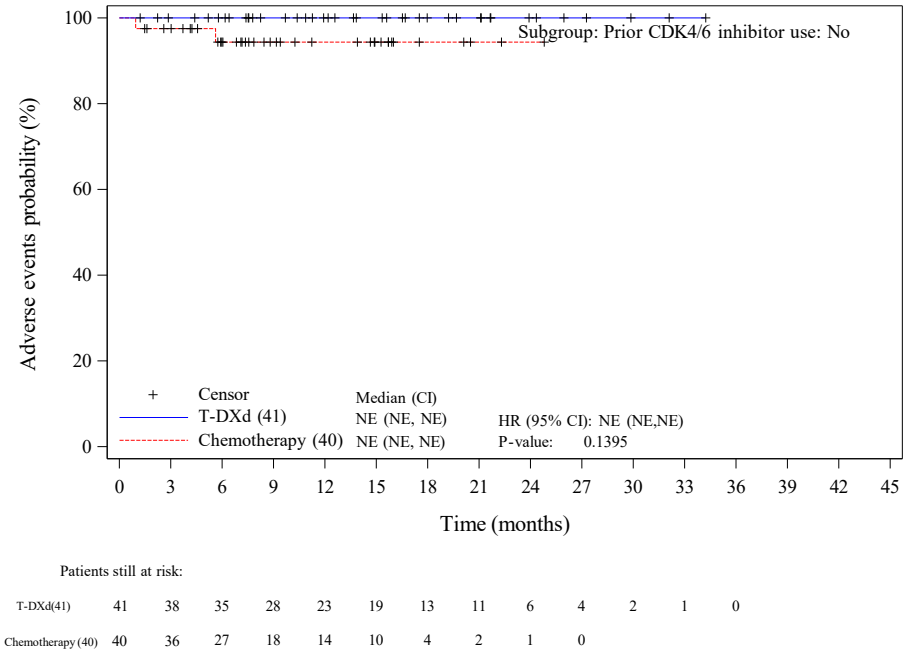

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)

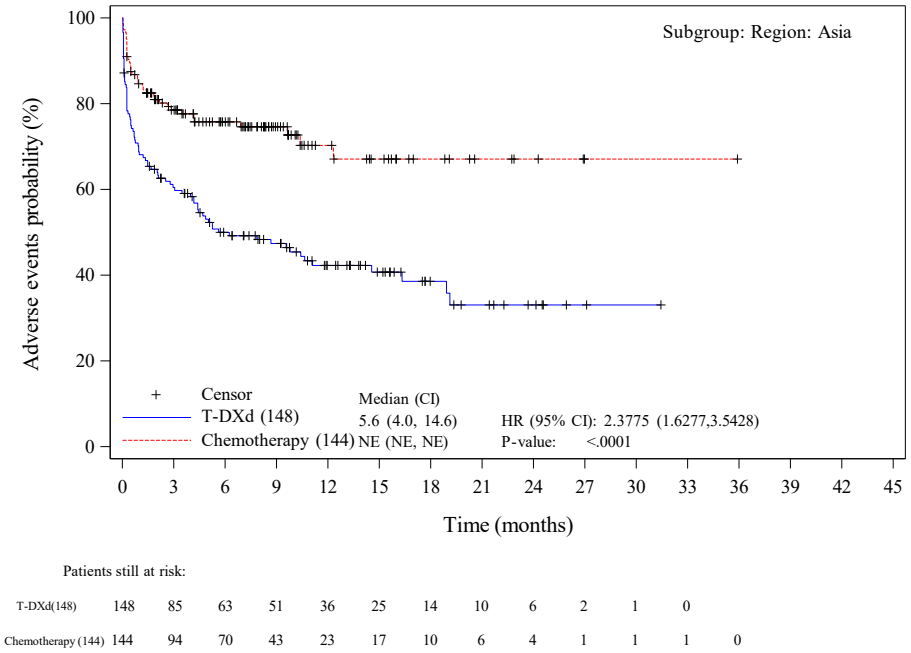

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)

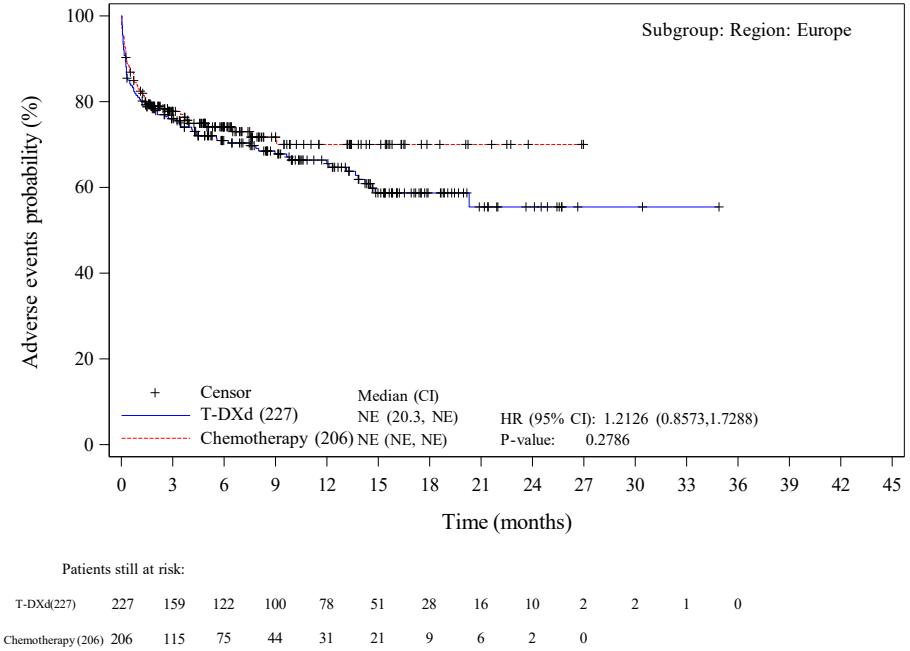

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)

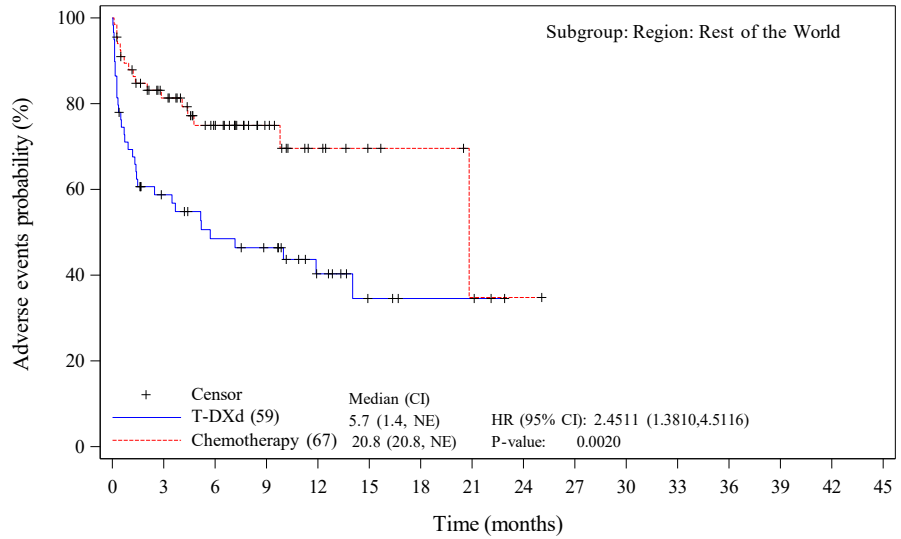

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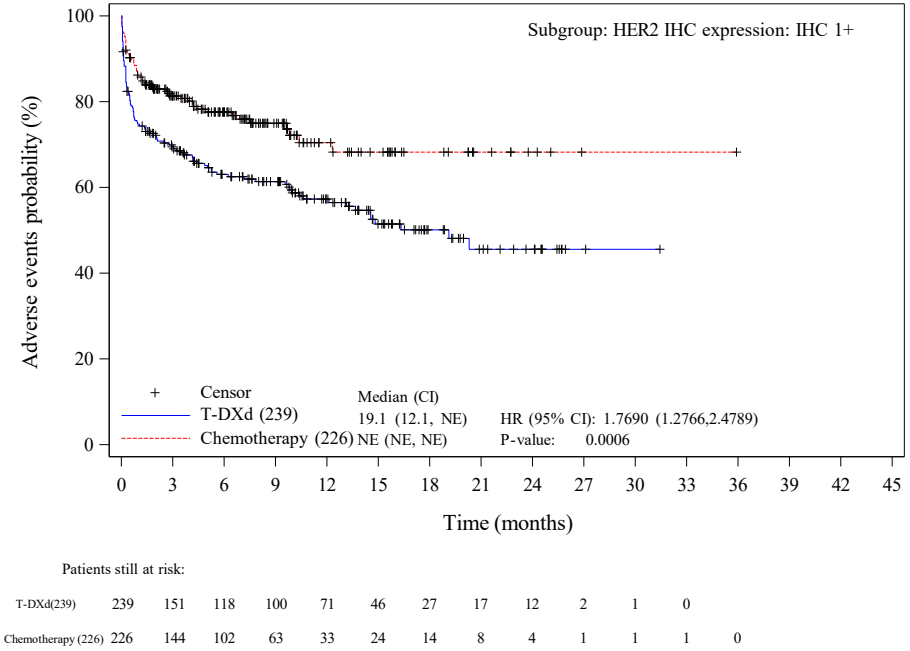
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)

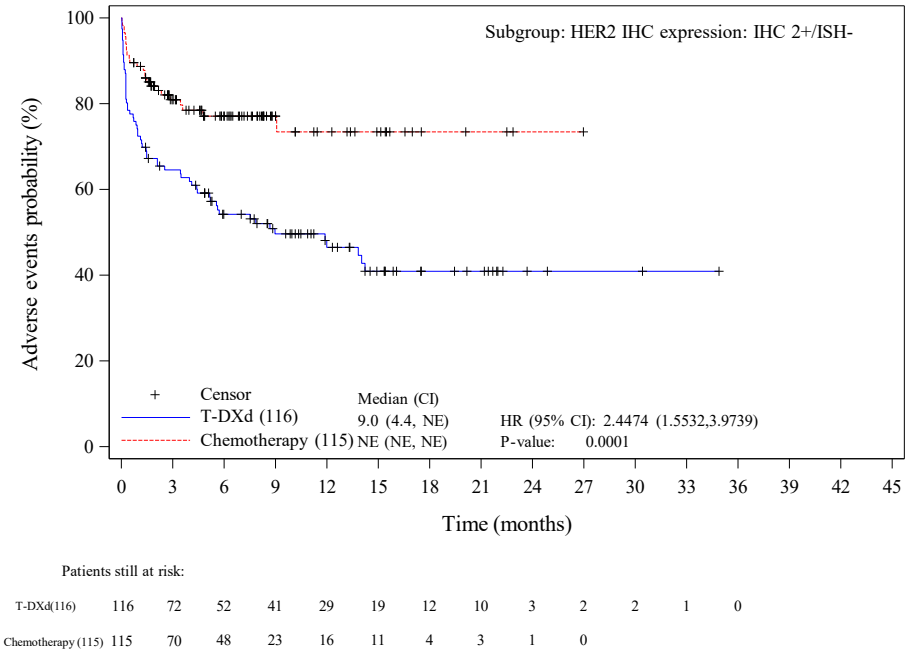

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)

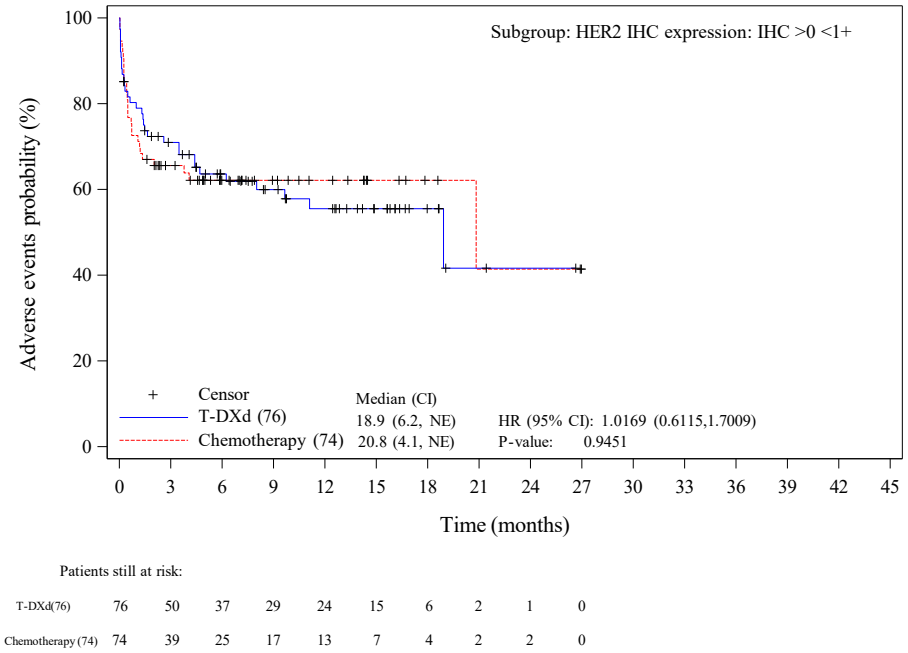

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)

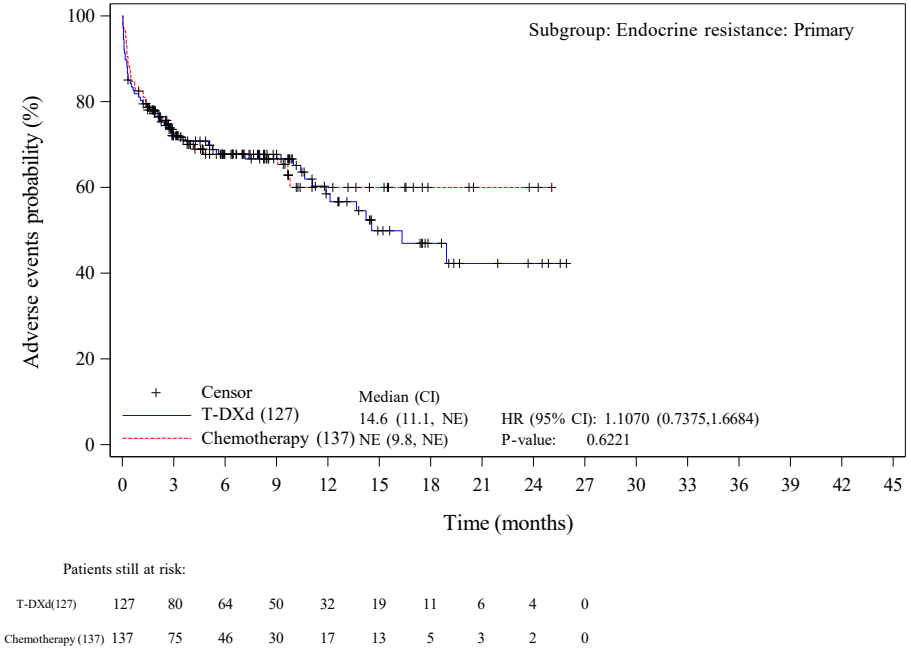

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)

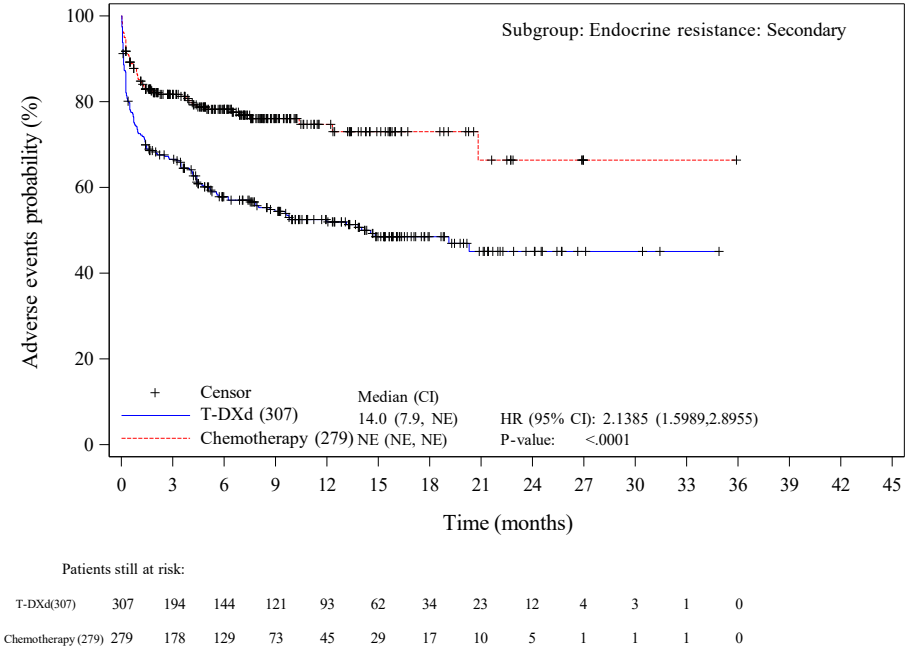

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)

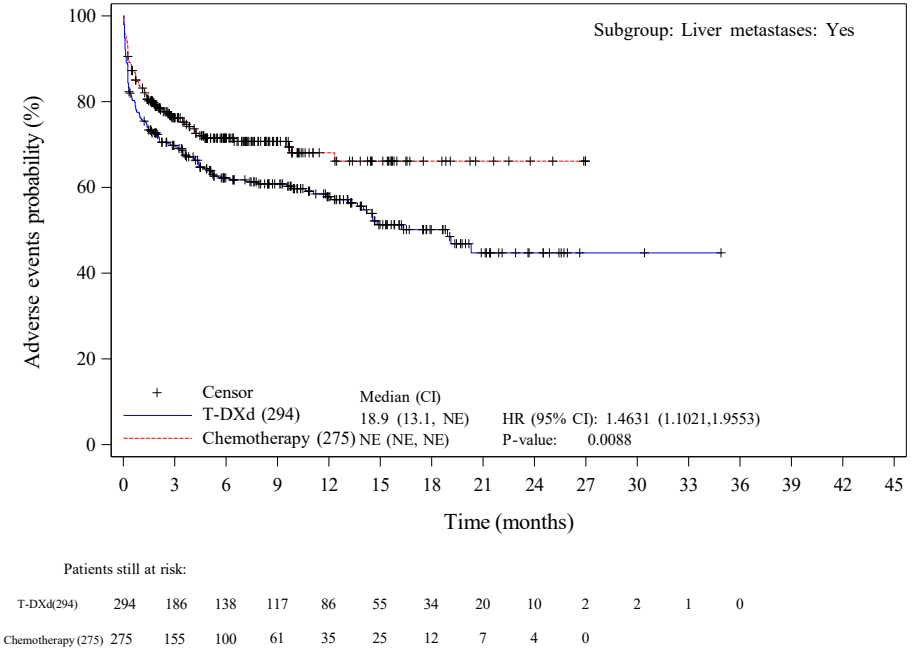

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)

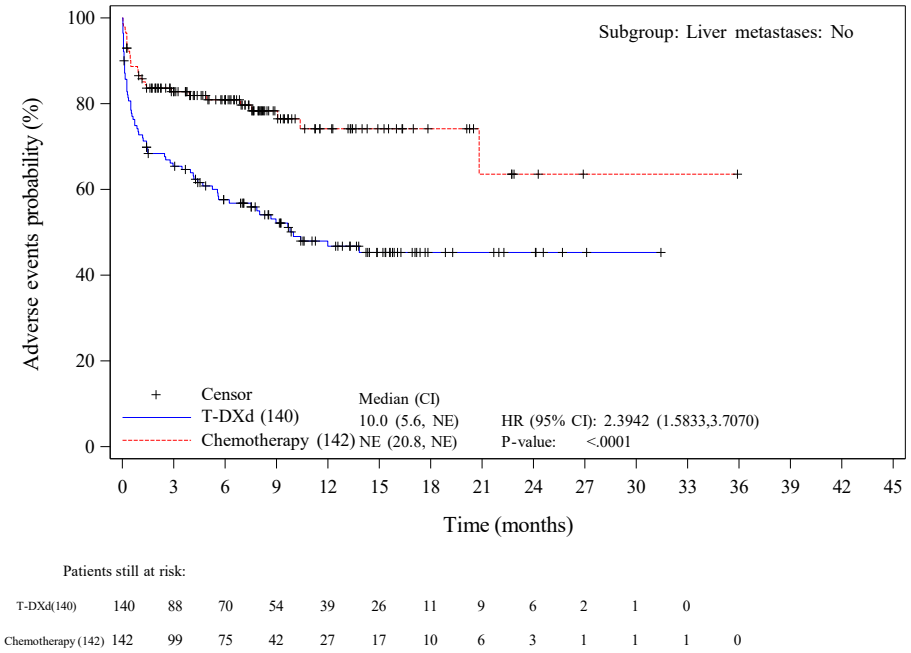

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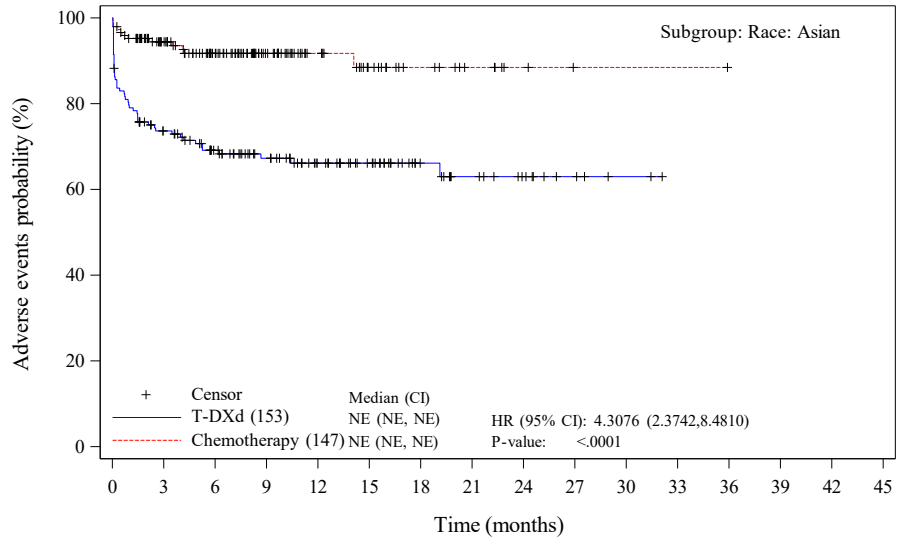
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite

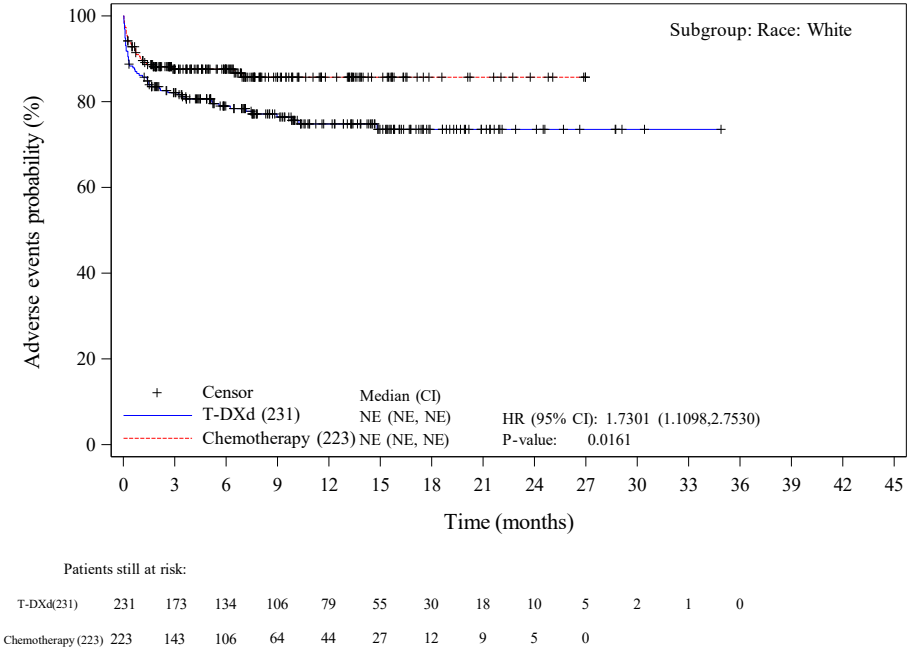

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite

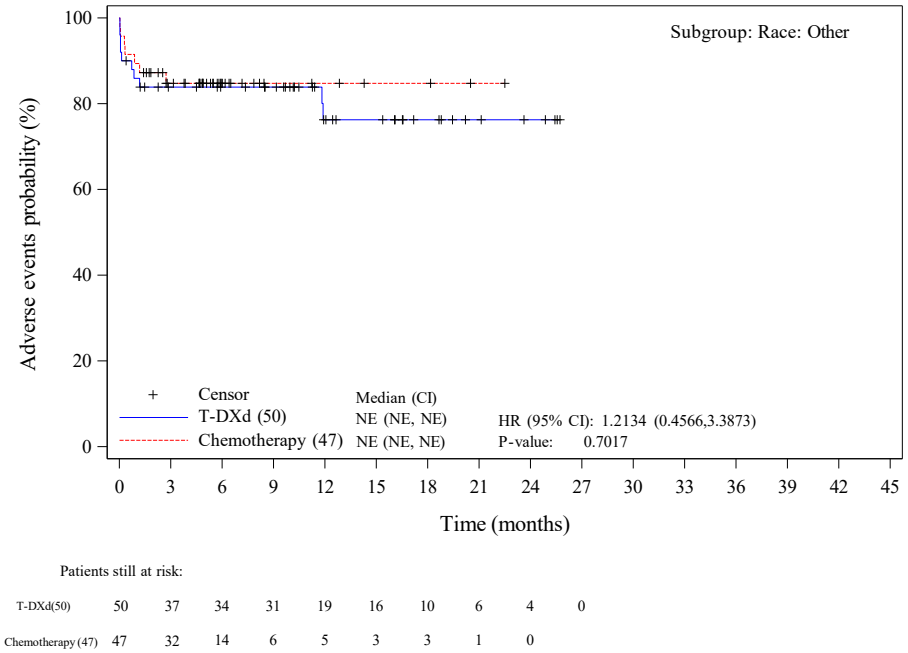

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite

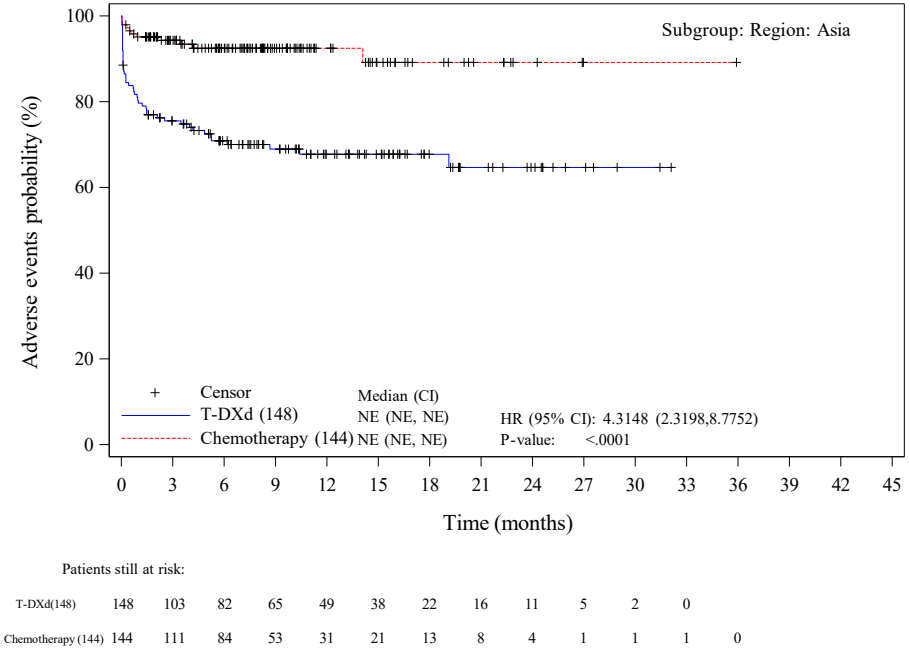

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite

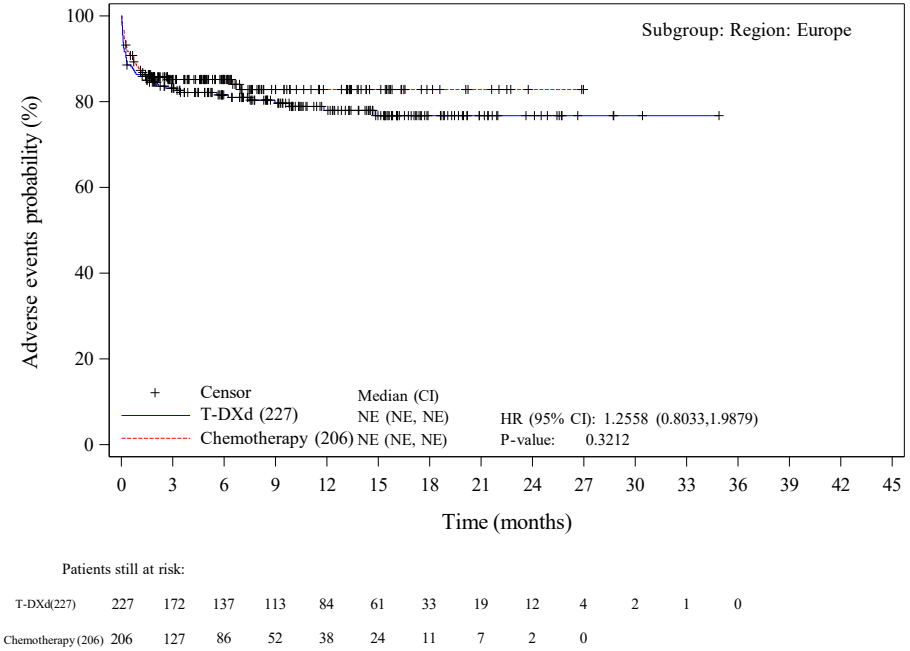

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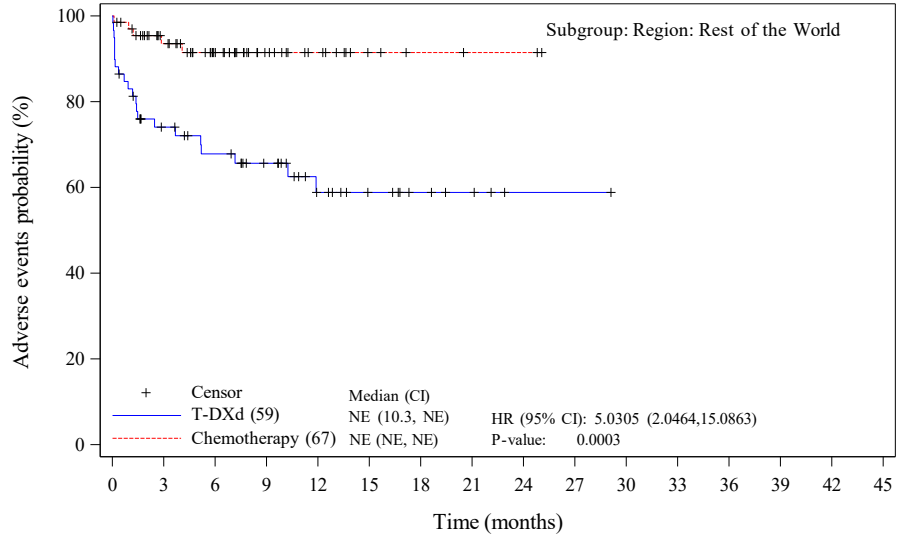
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



Patients still at risk:

T-DXd(59)	59	38	32	25	15	10	6	4	1	1	0
Chemotherapy (67)	67	50	35	19	12	5	3	2	2	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite

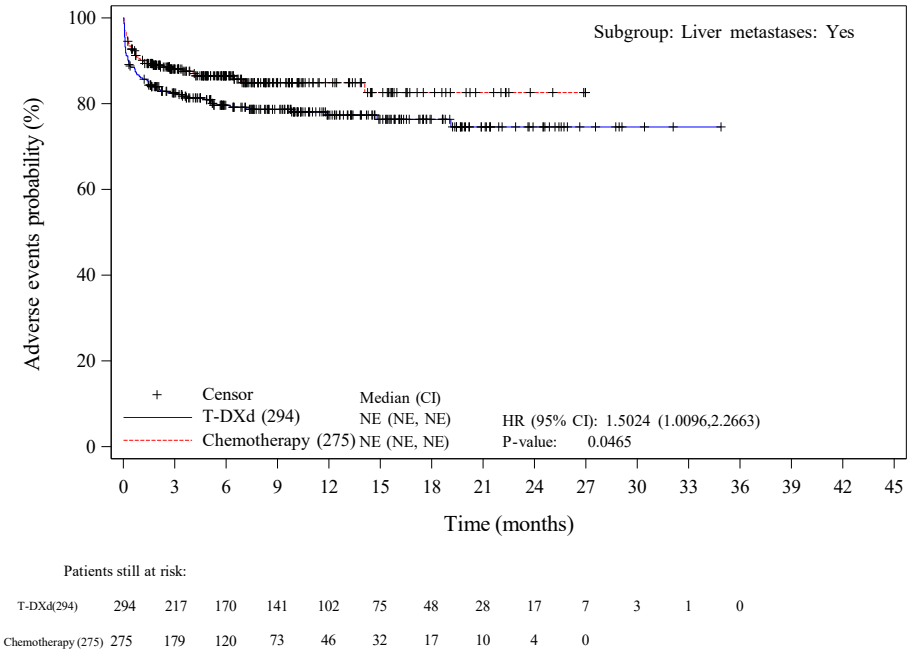

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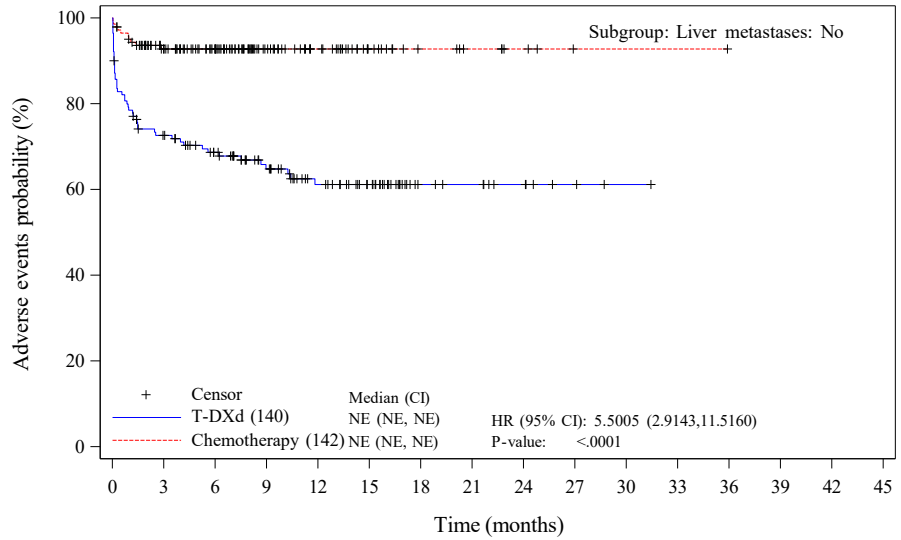
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Decreased appetite



Patients still at risk:

T-DXd(140)	140	96	81	62	46	34	13	11	7	3	1	0
Chemotherapy (142)	142	109	85	51	35	18	10	7	4	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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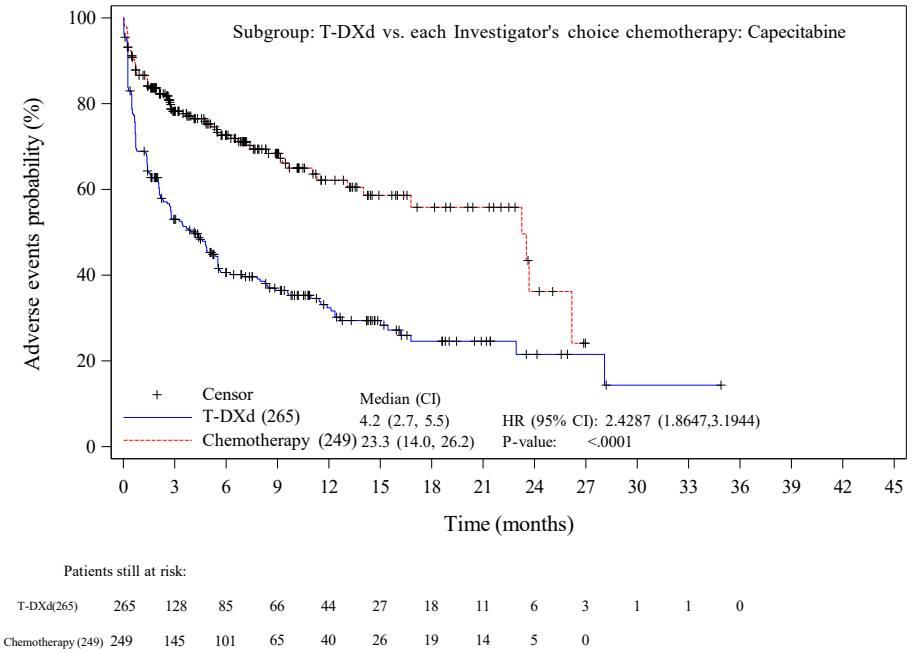
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)

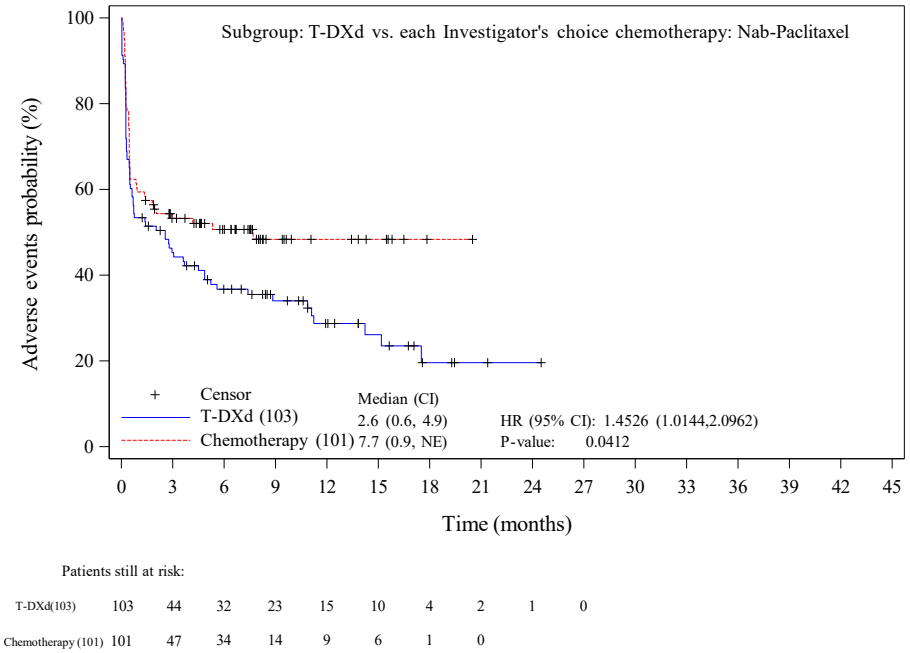

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)

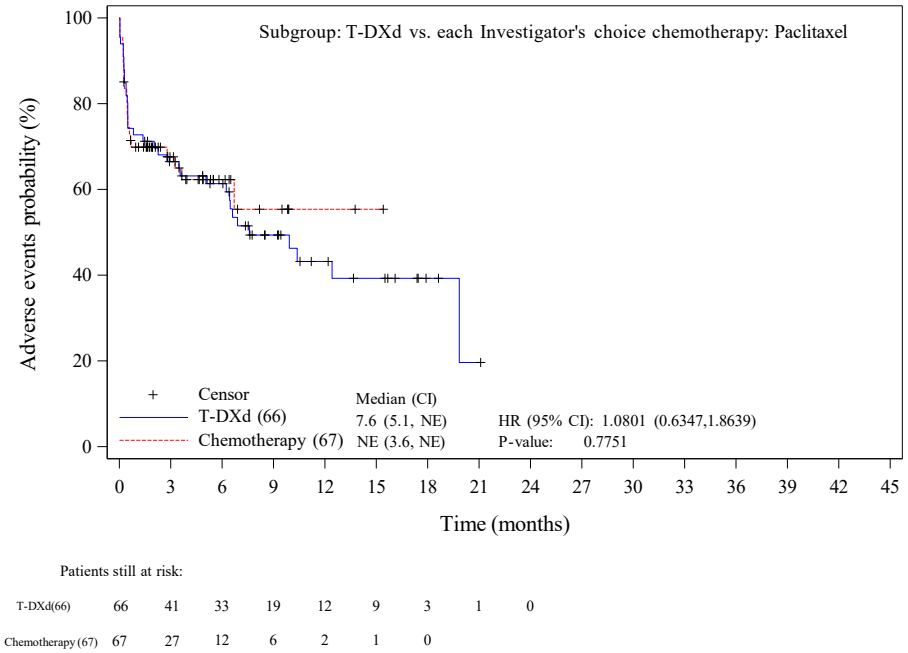

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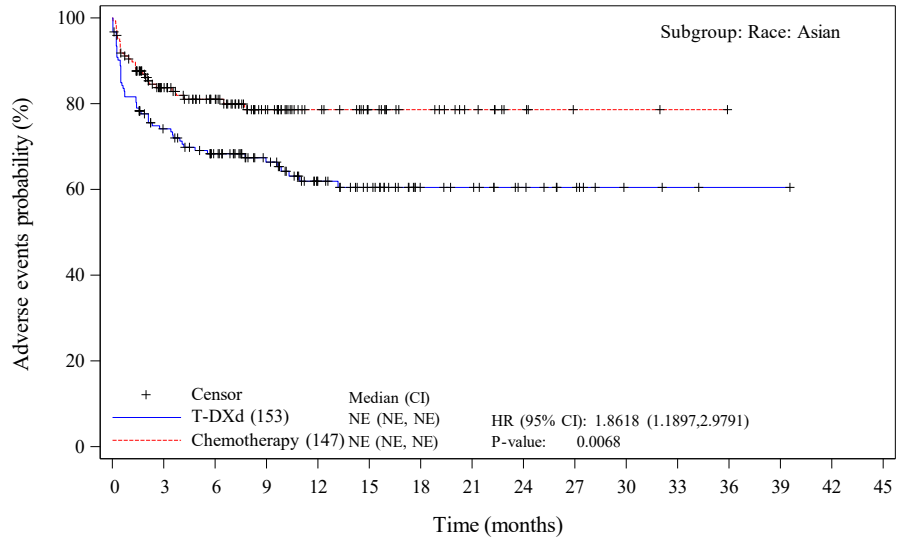
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Patients still at risk:

T-DXd(153)	153	104	86	65	45	35	20	18	12	8	3	2	1	1	0
Chemotherapy (147)	147	99	77	50	33	23	16	10	5	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased

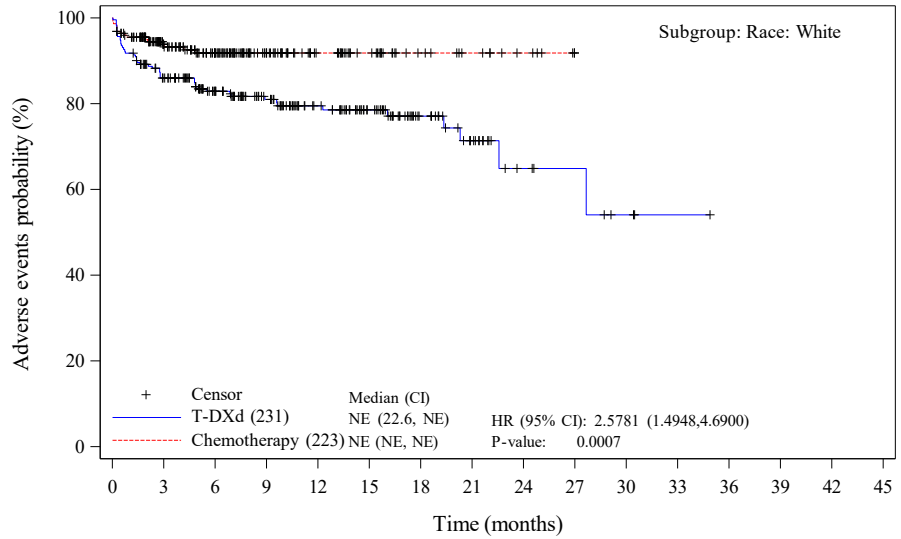

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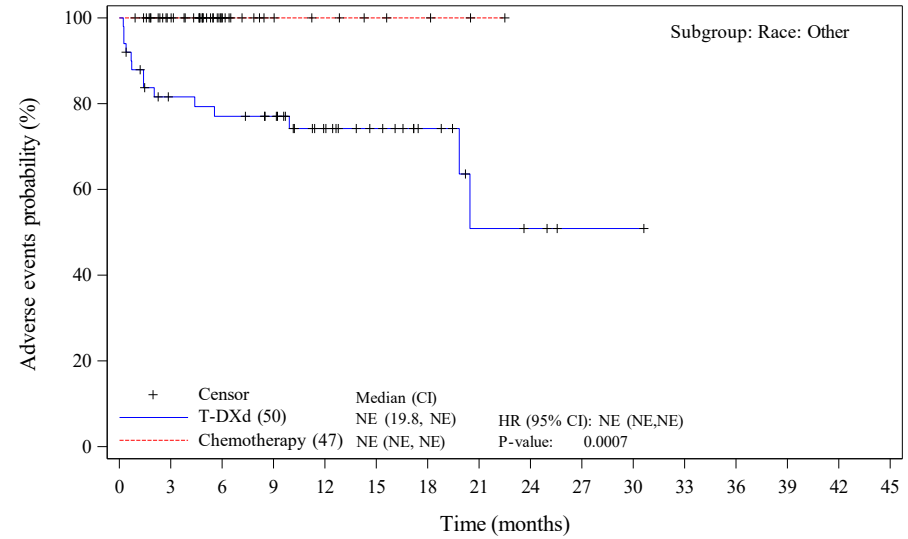
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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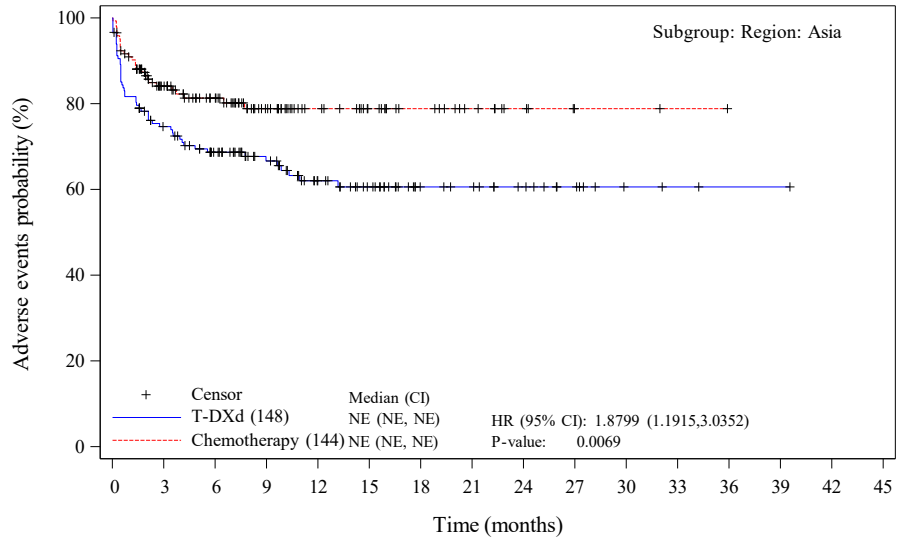
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Patients still at risk:

T-DXd(148)	148	102	83	63	45	35	20	18	13	8	3	2	1	1	0
Chemotherapy (144)	144	98	76	50	33	24	17	11	6	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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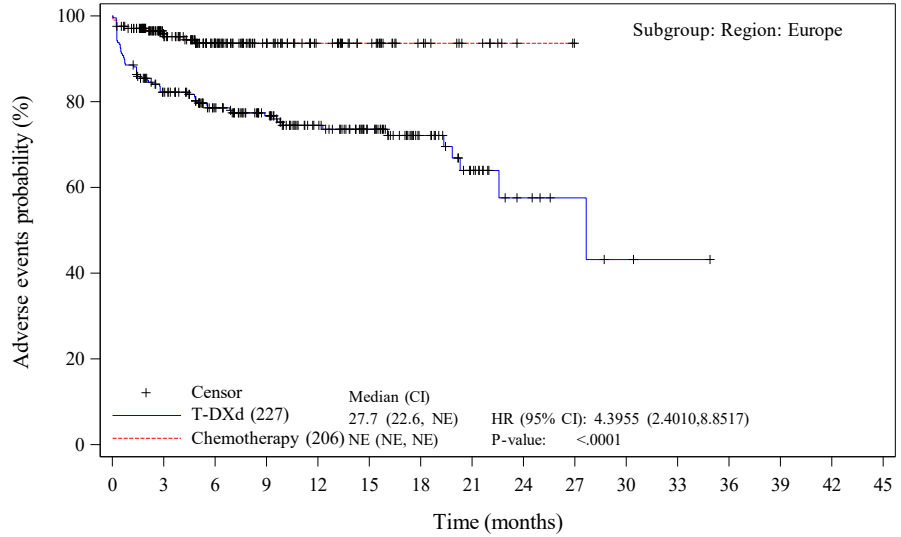
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased



Patients still at risk:

T-DXd(227)	227	174	138	111	83	60	34	18	7	4	2	1	0
Chemotherapy (206)	206	141	92	59	39	27	14	8	2	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Aspartate aminotransferase increased

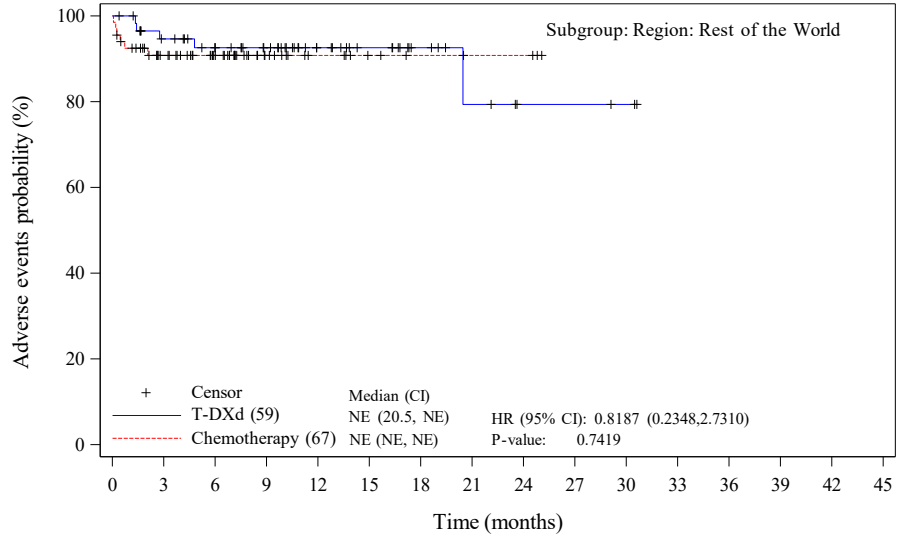

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Alanine aminotransferase increased

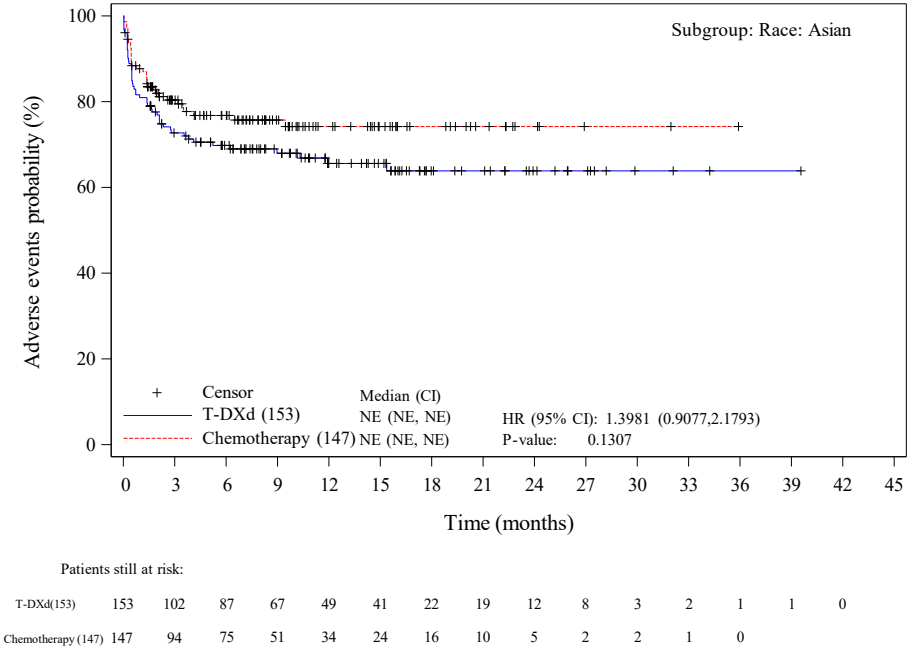

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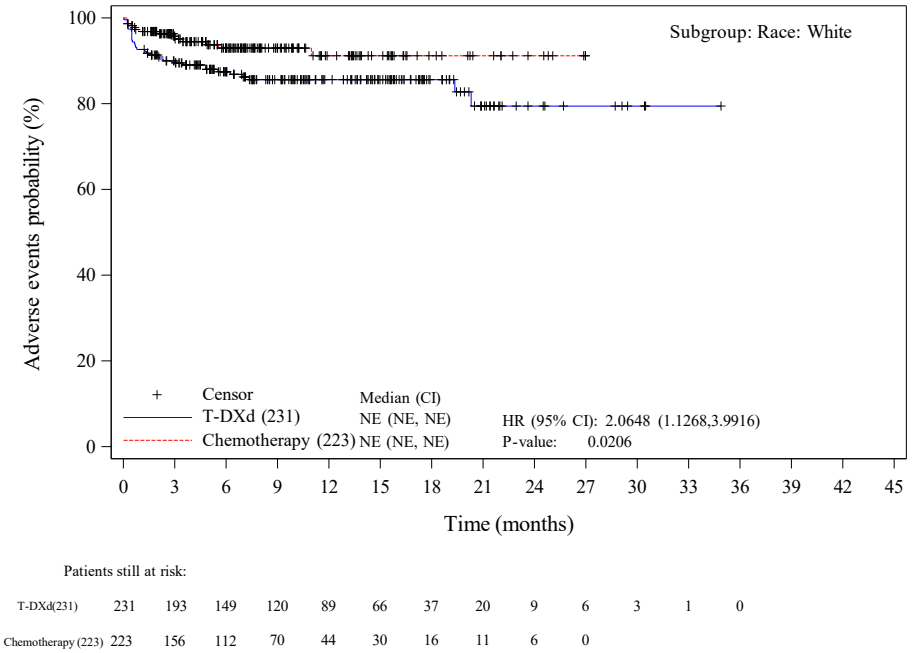
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Alanine aminotransferase increased



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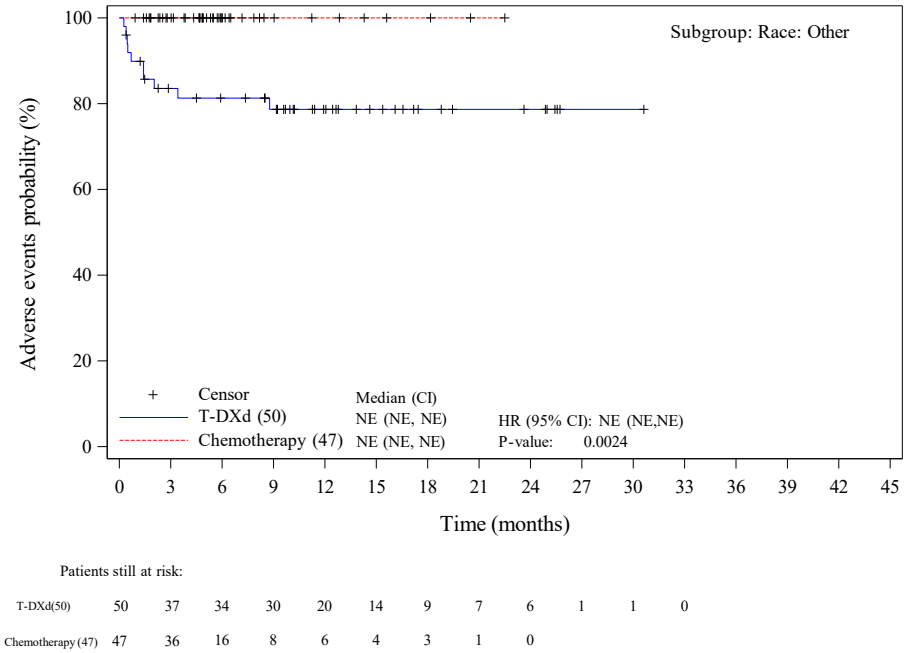

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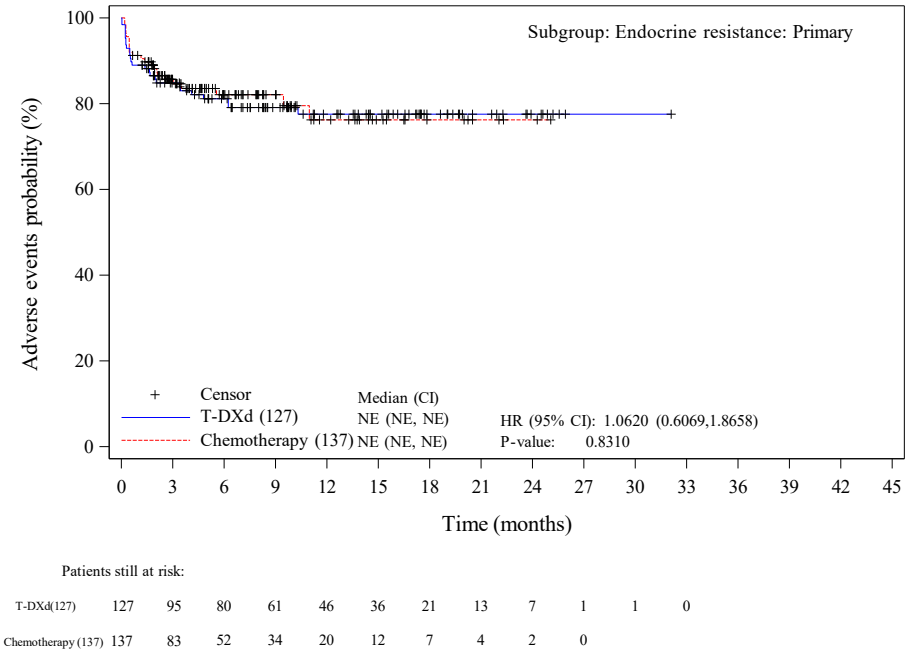

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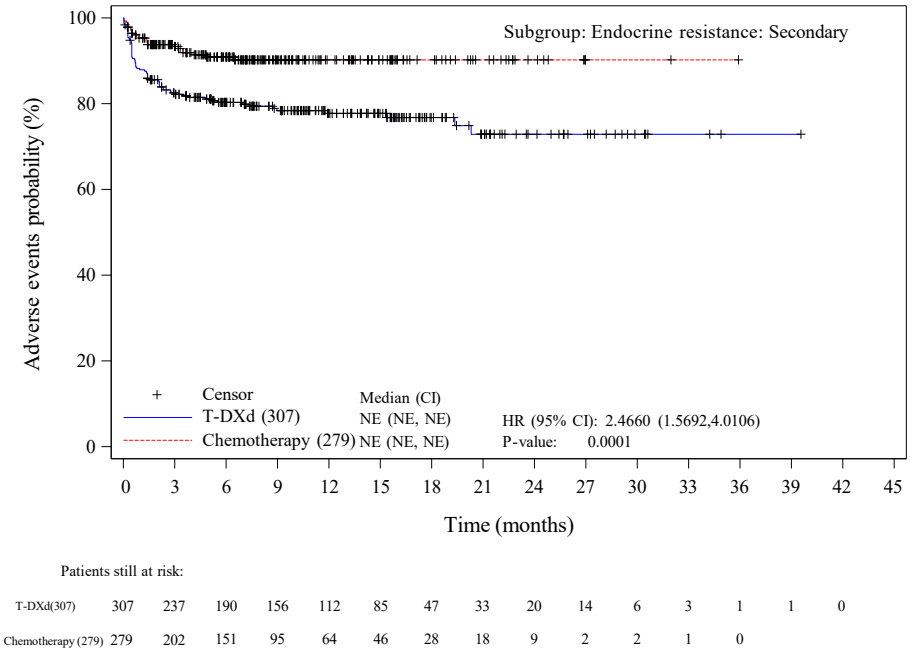

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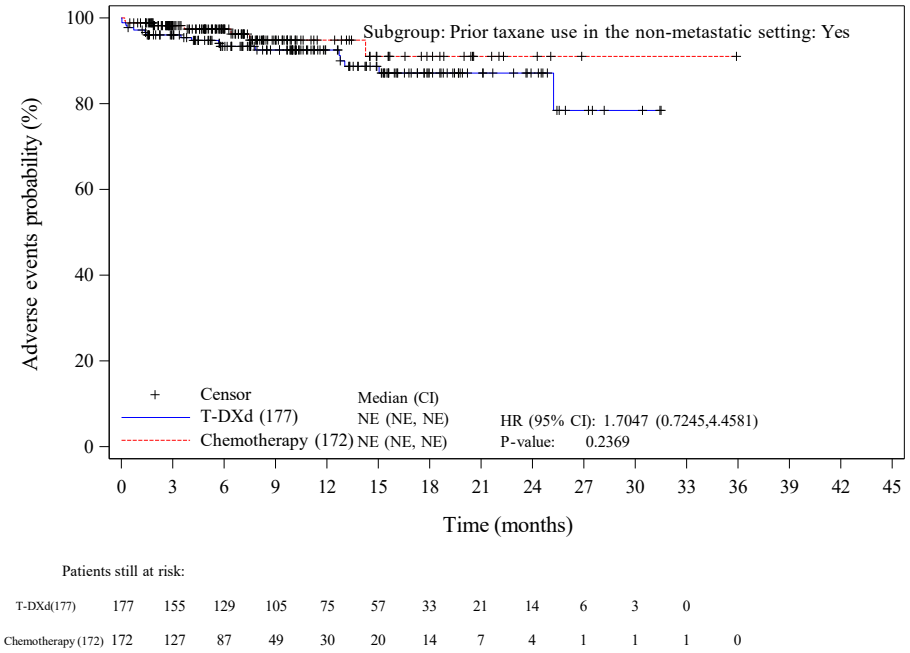
SOC: Investigations; PT: Gamma-glutamyltransferase increased



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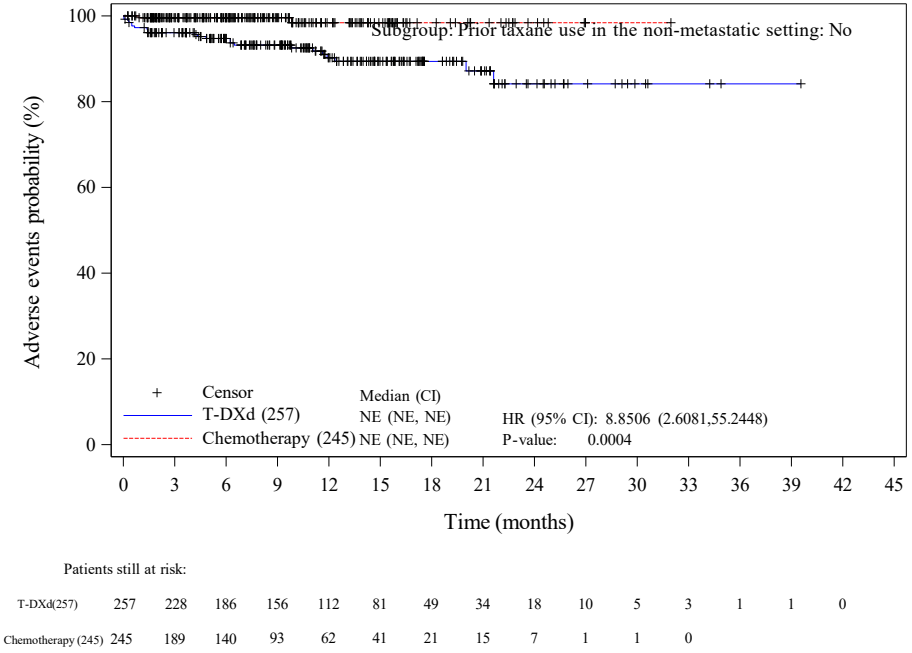
SOC: Investigations; PT: Gamma-glutamyltransferase increased



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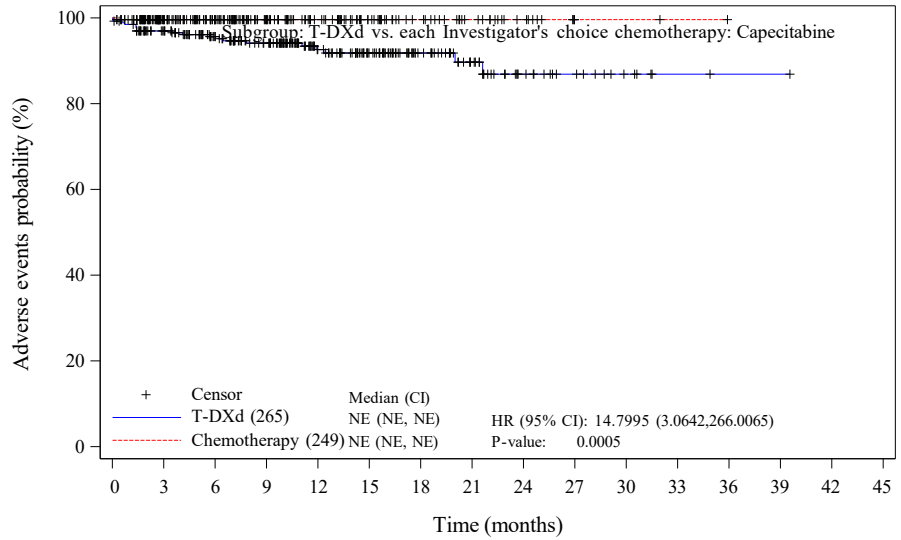
SOC: Investigations; PT: Gamma-glutamyltransferase increased



Patients still at risk:

T-DXd(265)	265	236	197	168	116	86	55	36	19	12	6	2	1	1	0
Chemotherapy (249)	249	186	140	97	69	47	31	20	11	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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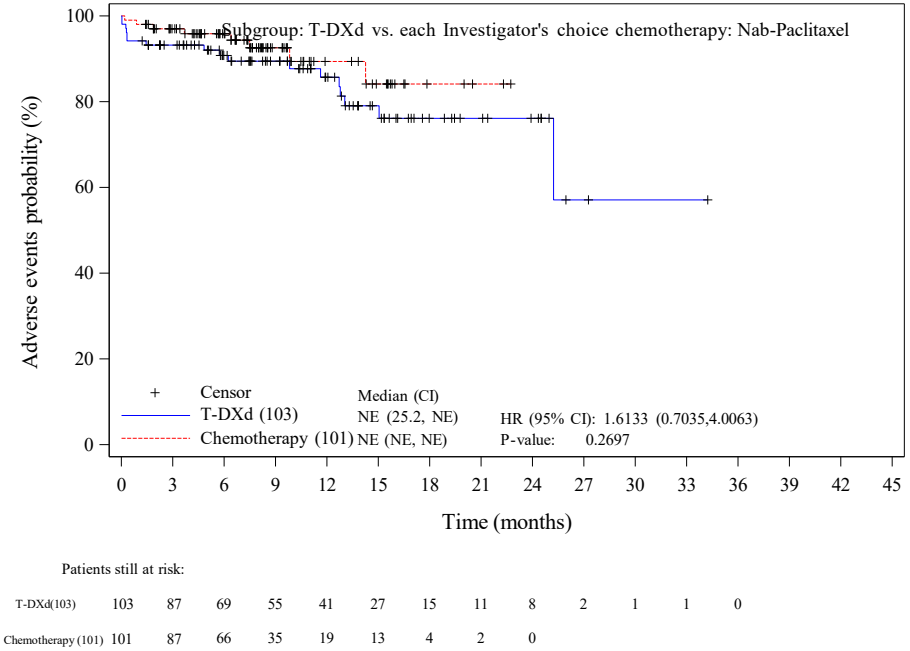
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Gamma-glutamyltransferase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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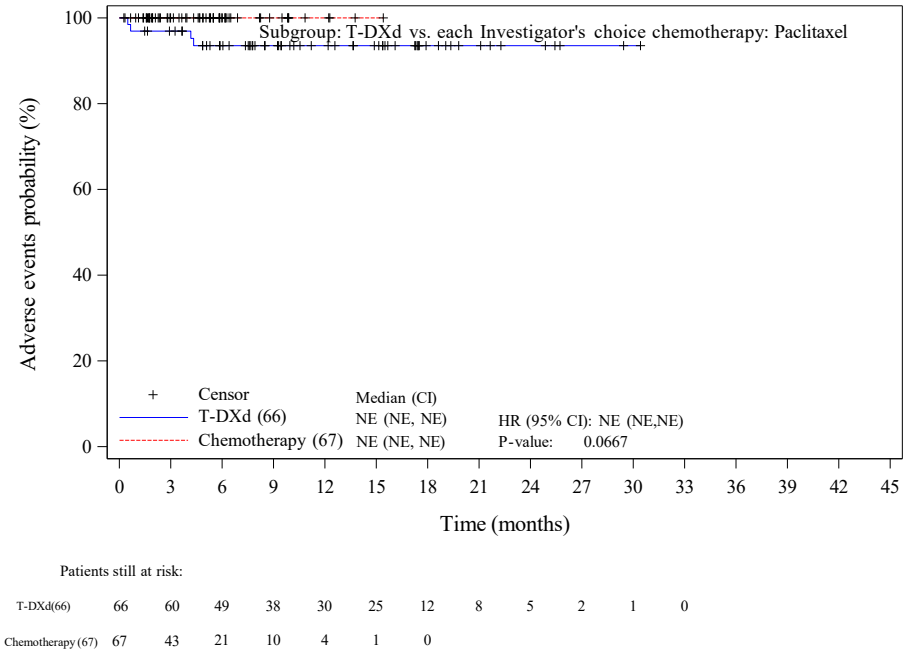
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Gamma-glutamyltransferase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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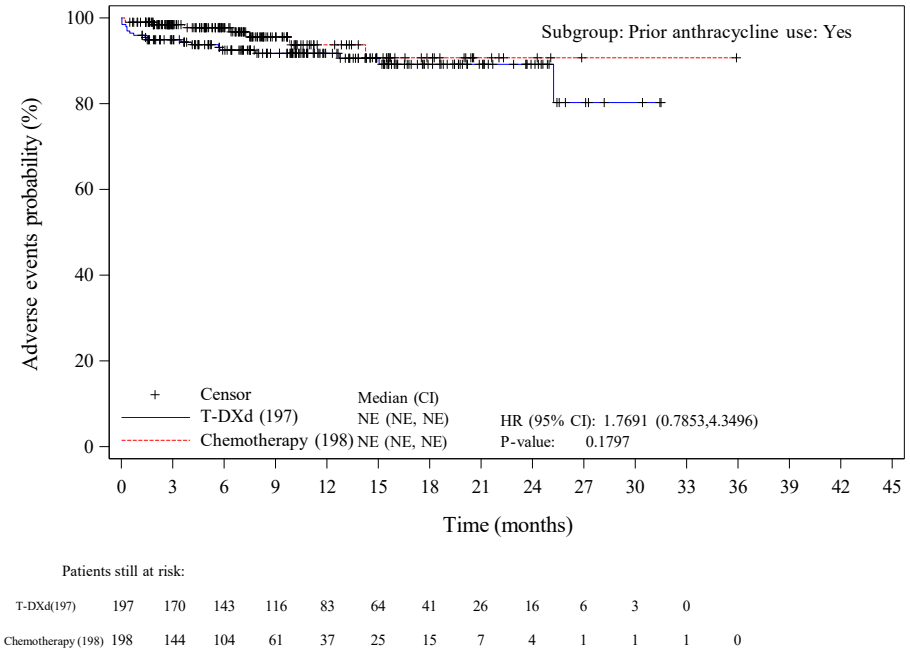
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Gamma-glutamyltransferase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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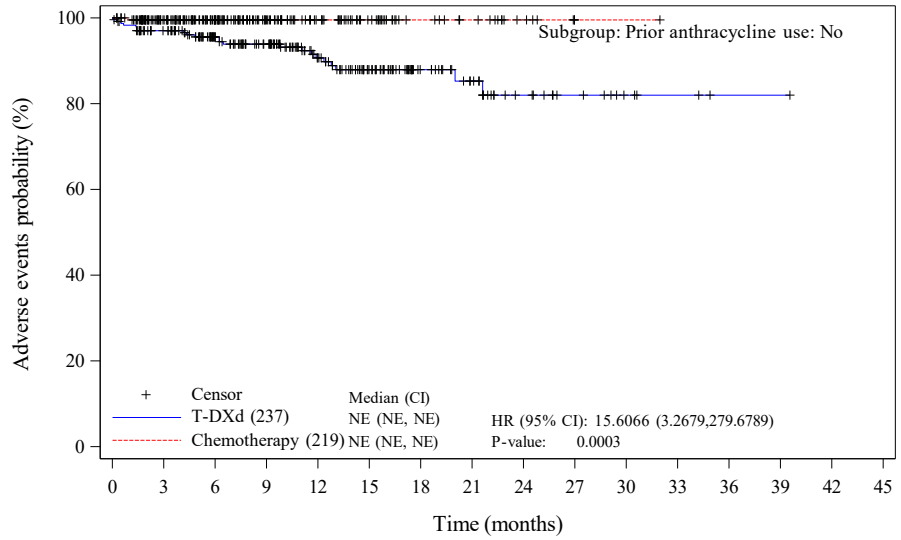
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Gamma-glutamyltransferase increased



Patients still at risk:

T-DXd(237)	237	213	172	145	104	74	41	29	16	10	5	3	1	1	0
Chemotherapy (219)	219	172	123	81	55	36	20	15	7	1	1	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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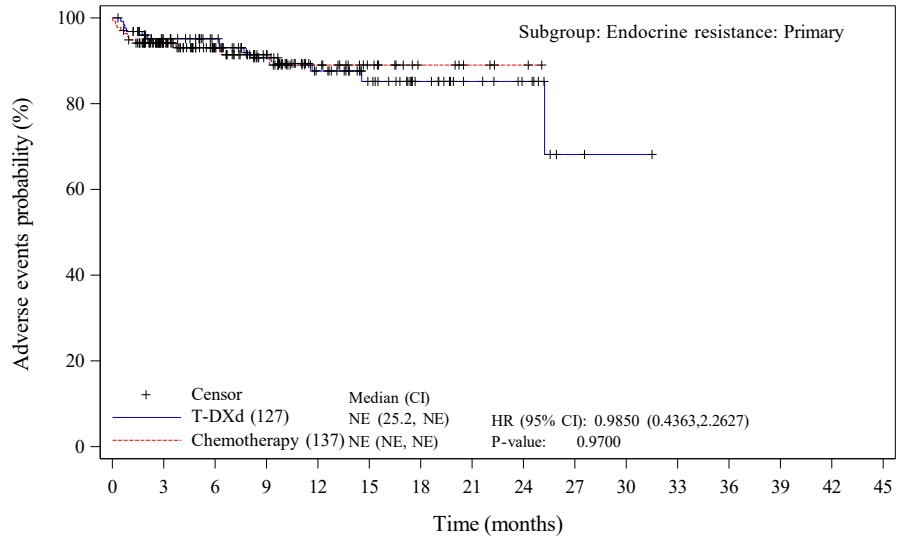
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Blood alkaline phosphatase increased



Patients still at risk:

T-DXd(127)	127	105	92	71	48	34	21	13	9	2	1	0
Chemotherapy (137)	137	93	60	40	24	15	7	4	2	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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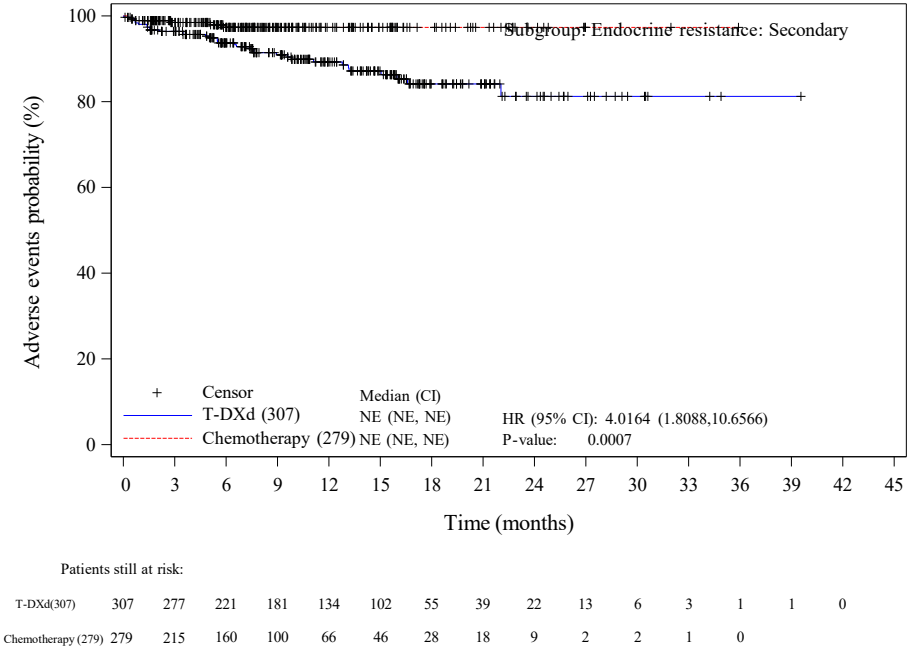
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Blood alkaline phosphatase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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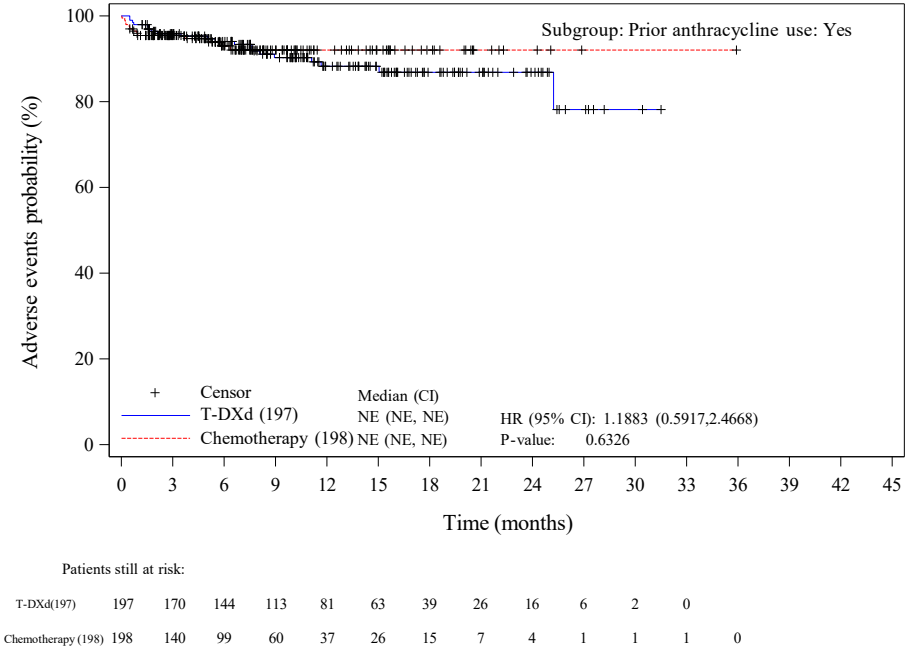
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Blood alkaline phosphatase increased



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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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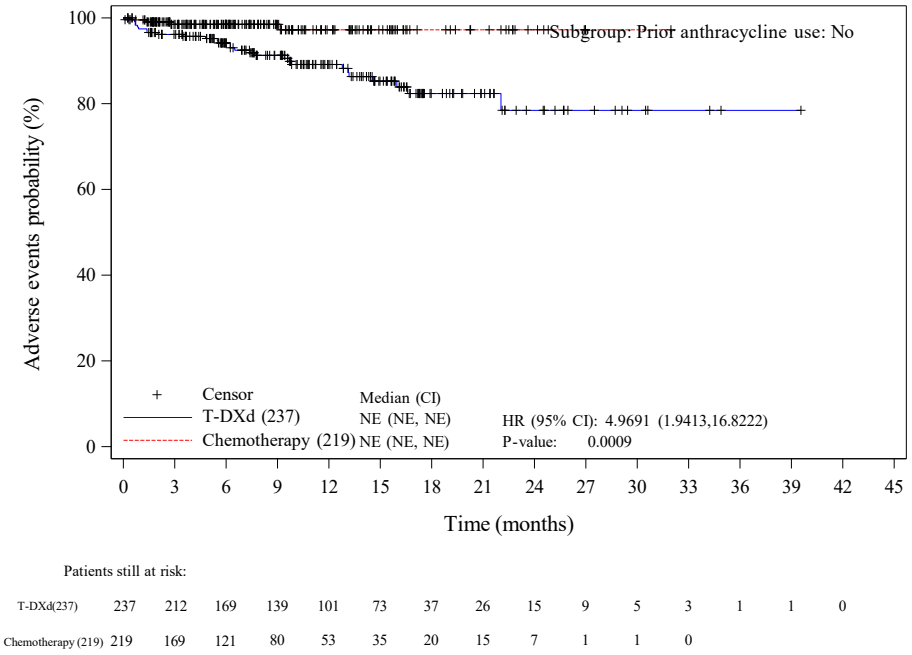
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Blood alkaline phosphatase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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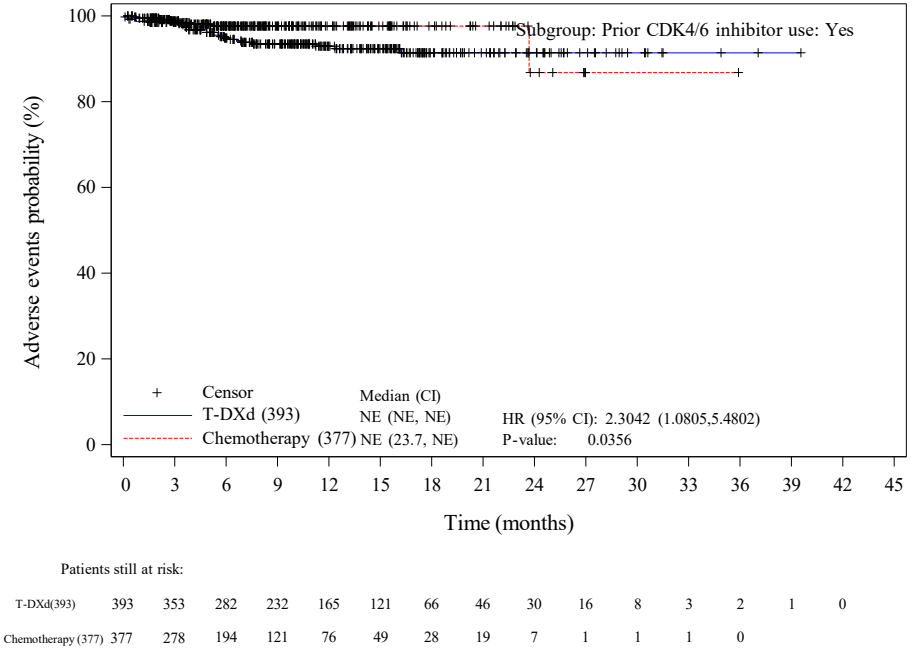
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Weight decreased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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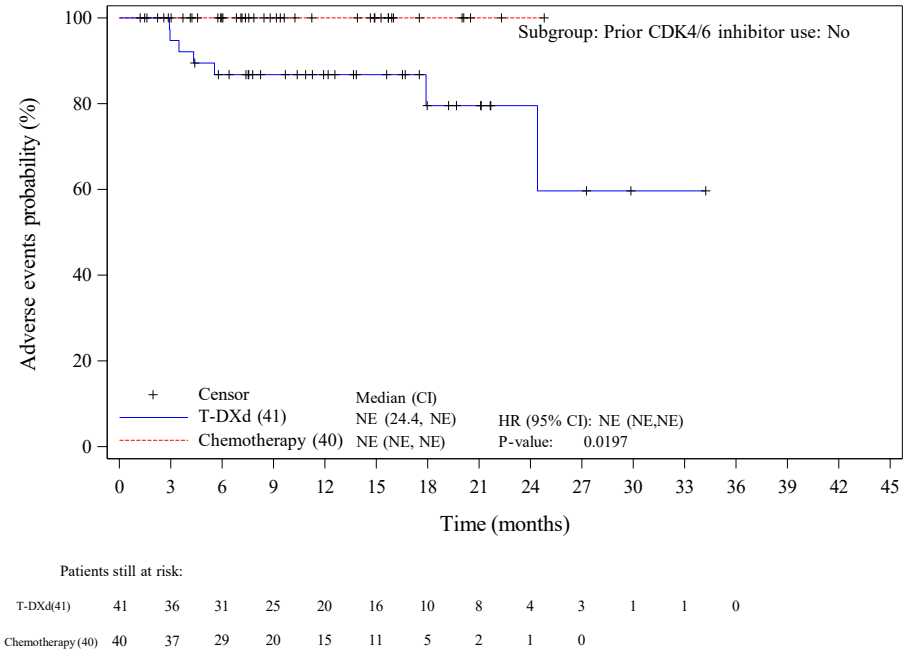
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Weight decreased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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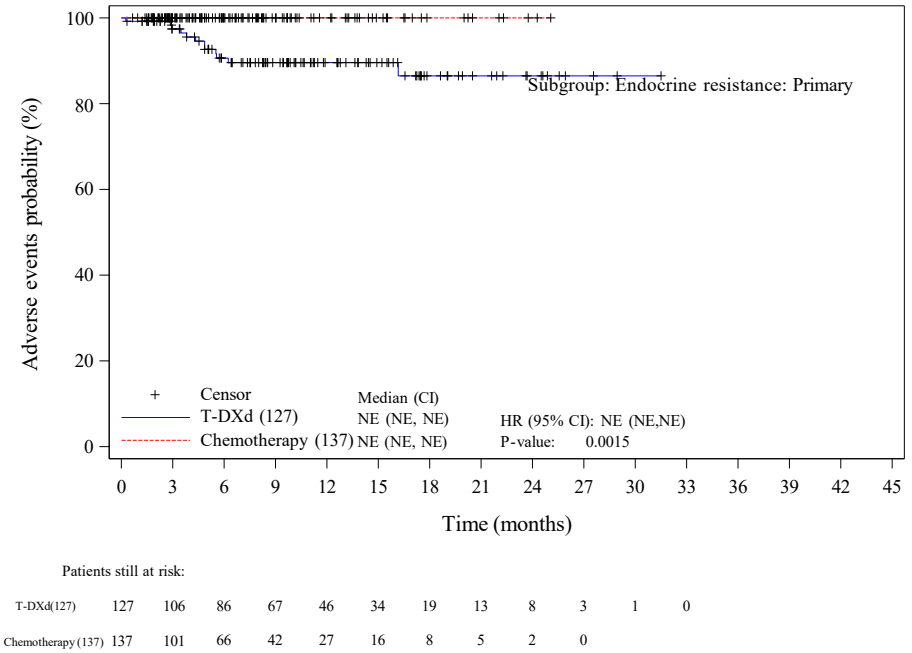
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: Weight decreased



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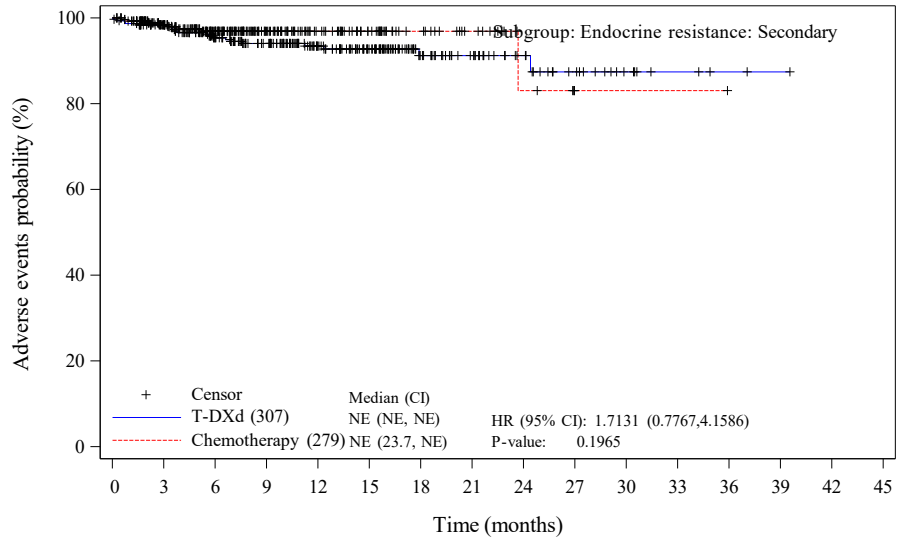
SOC: Investigations; PT: Weight decreased



Patients still at risk:

T-DXd(307)	307	283	227	190	139	103	57	41	26	16	8	4	2	1	0
Chemotherapy (279)	279	213	157	99	64	44	25	16	6	1	1	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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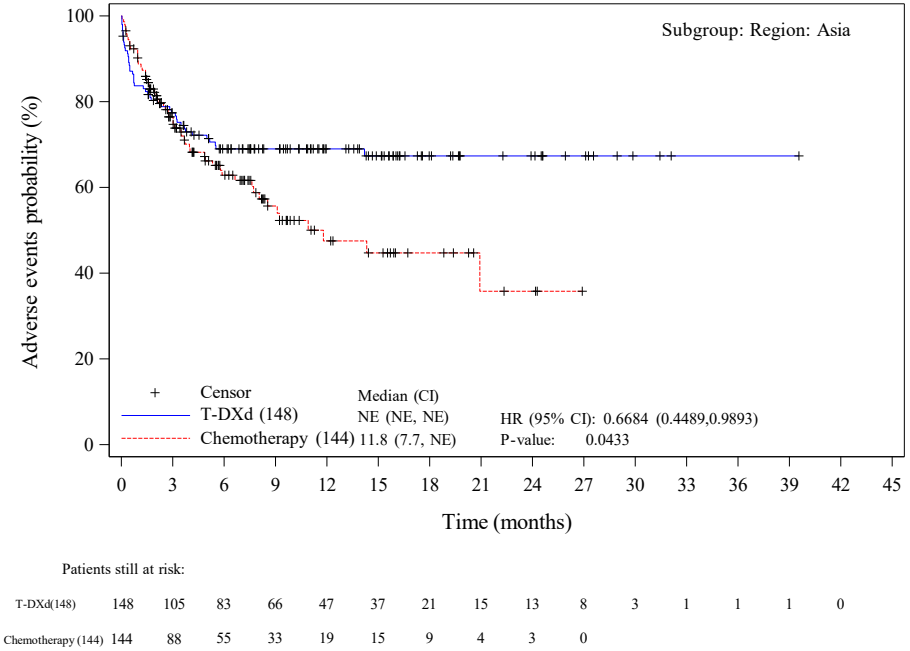
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)

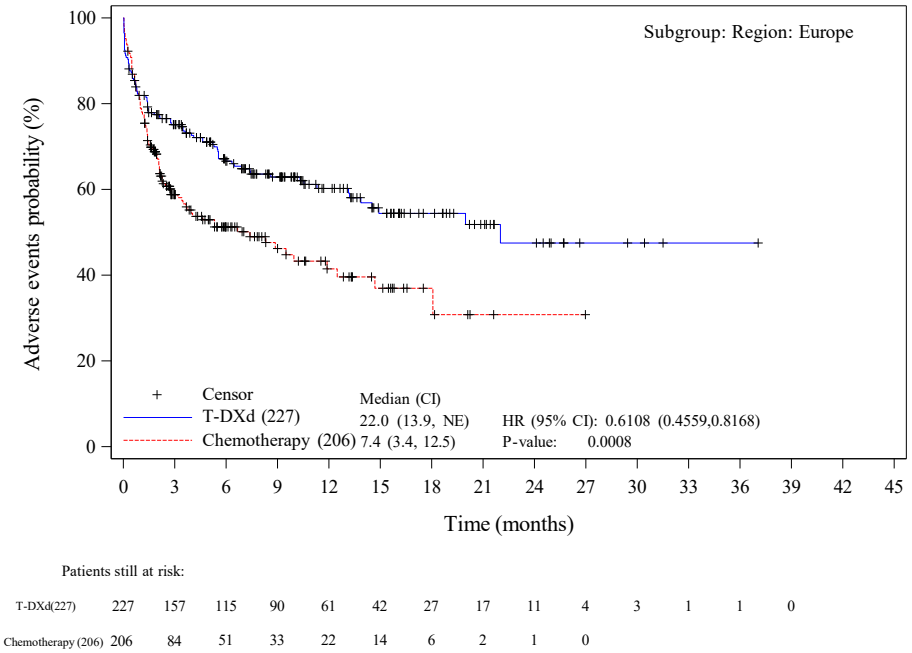

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)

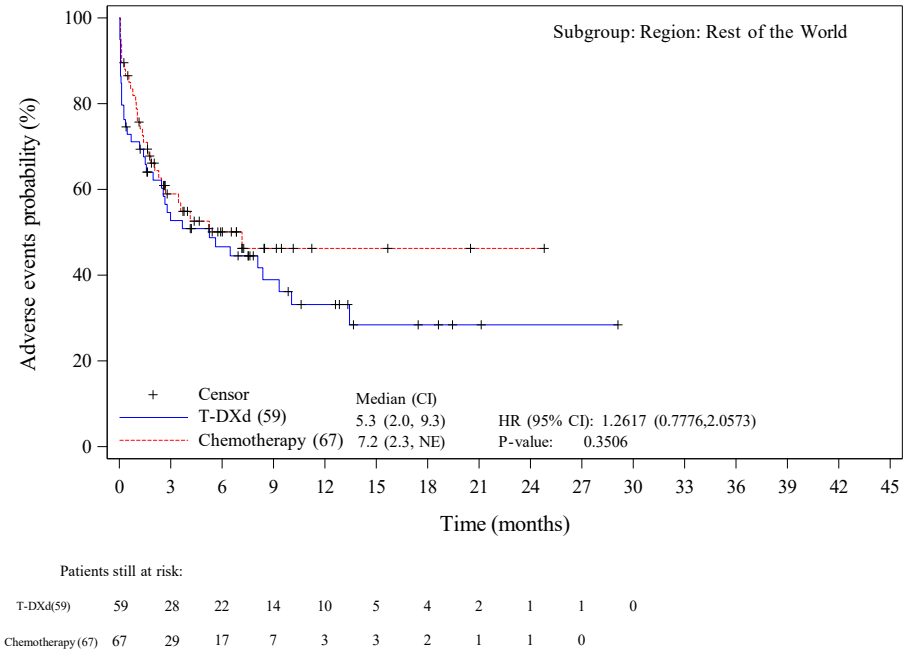

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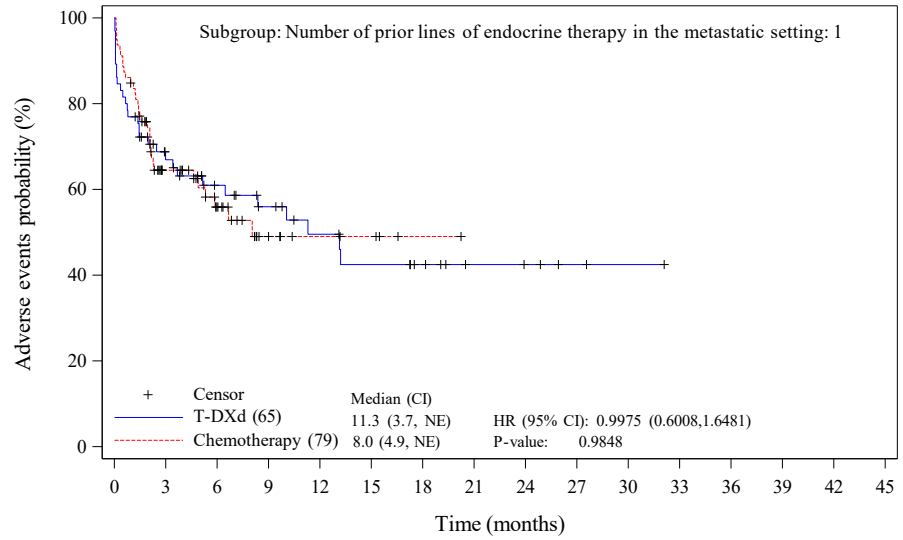
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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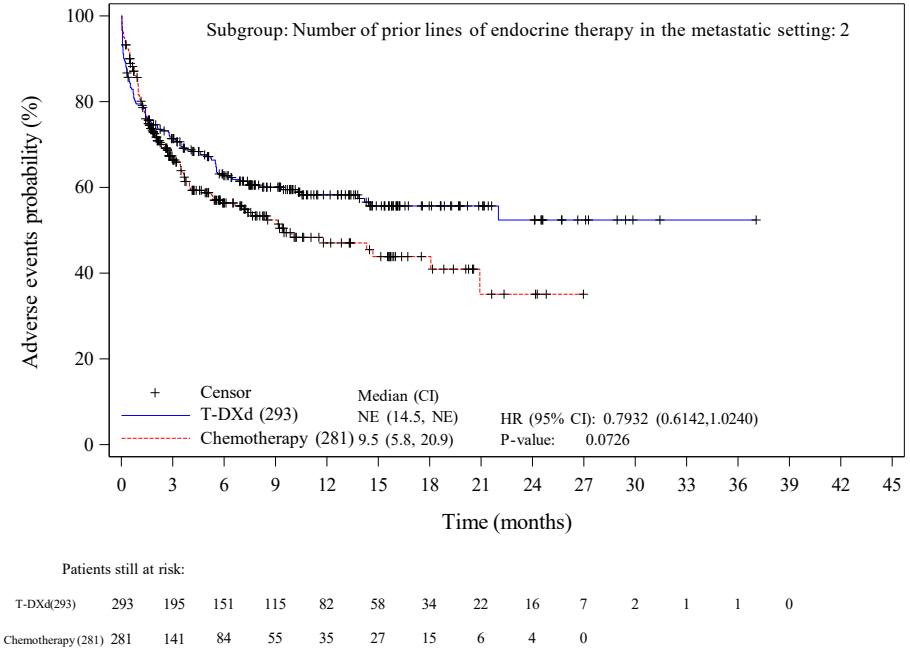

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)

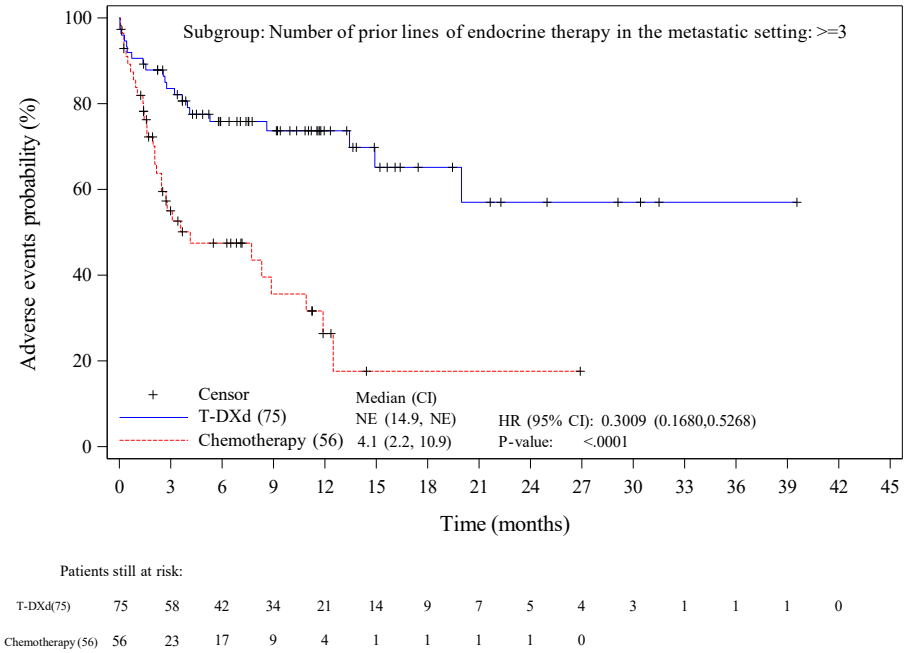

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)

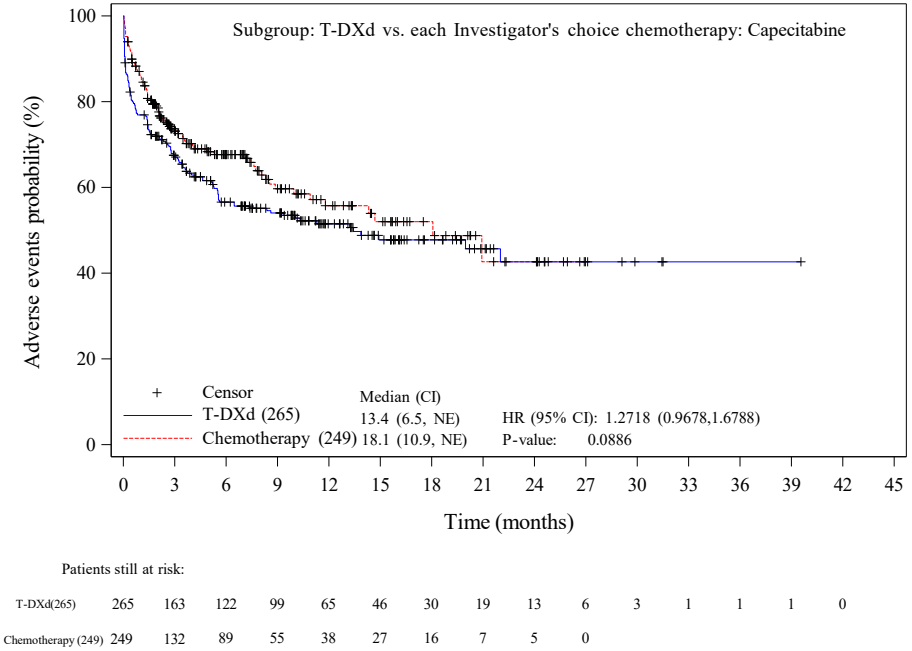

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)

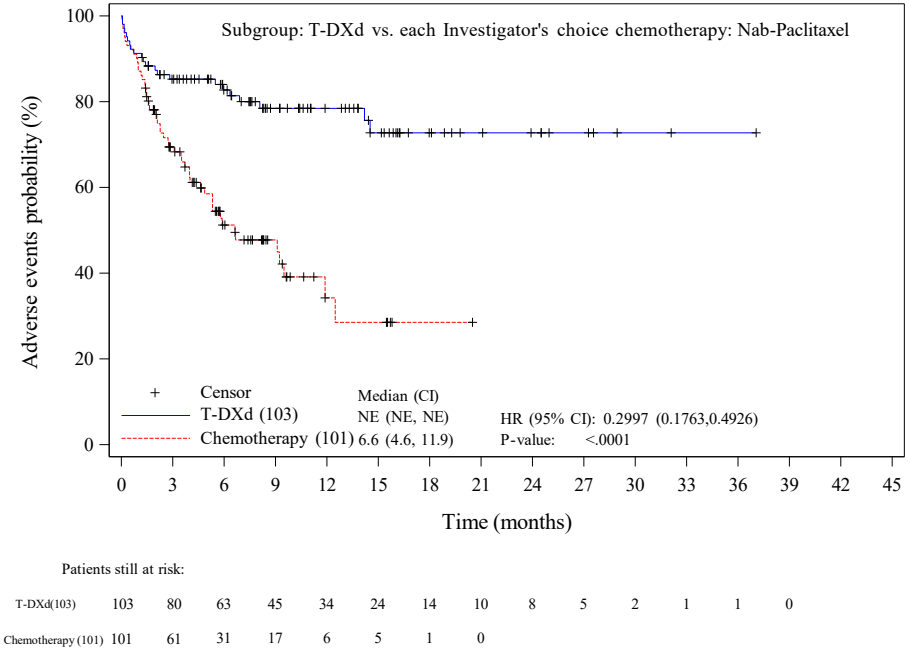

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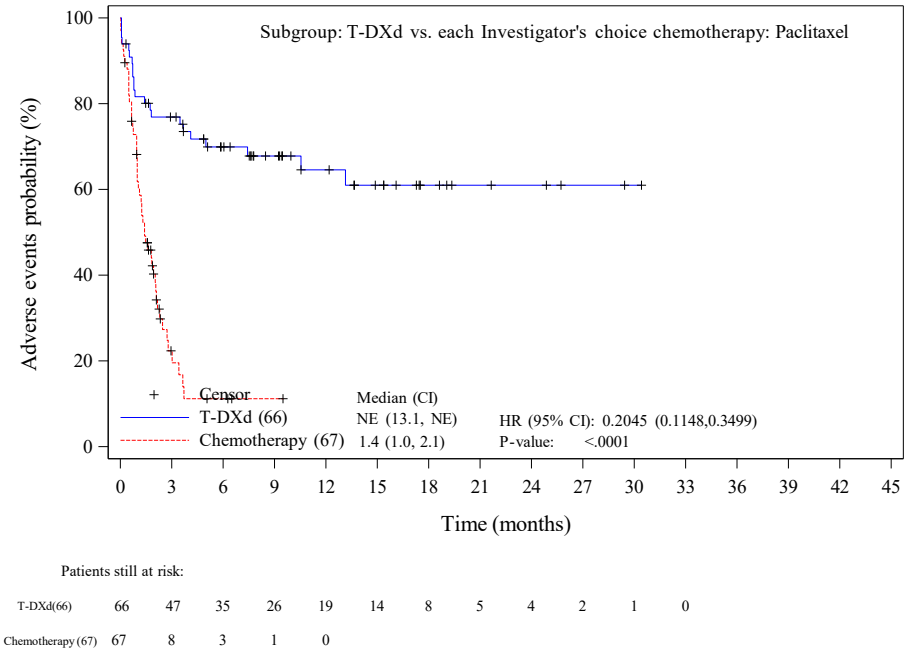
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)



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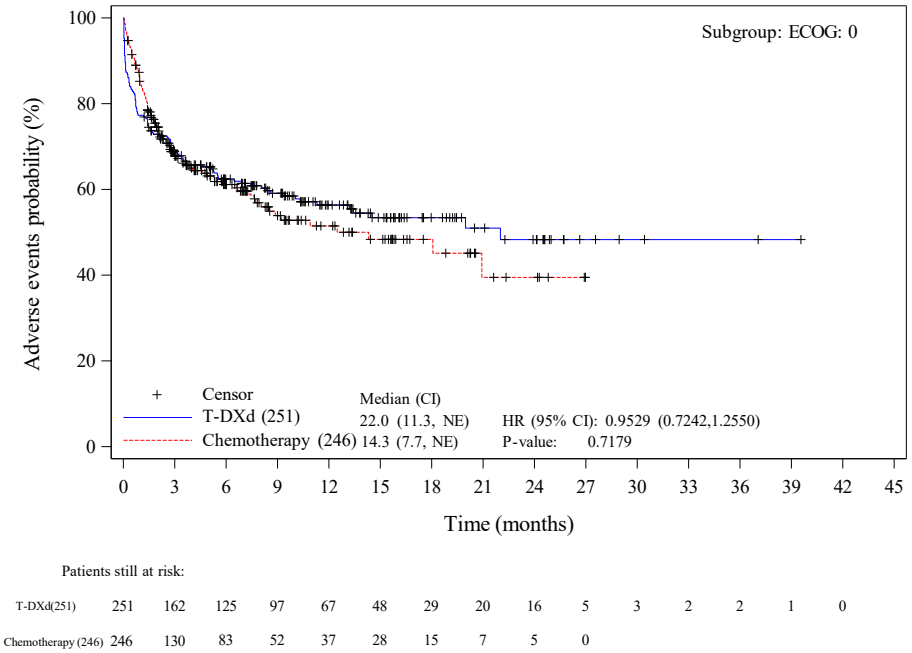

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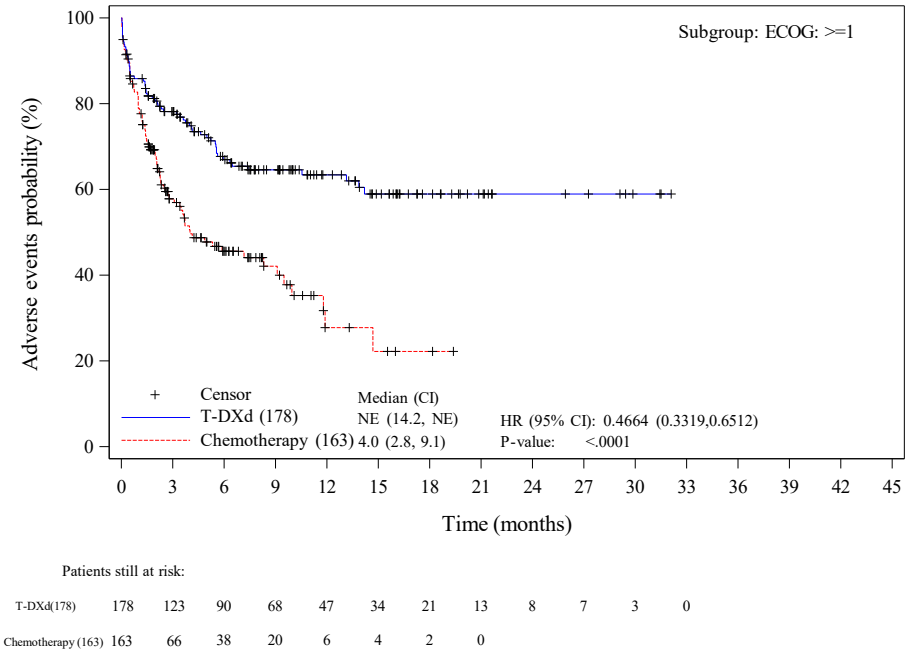

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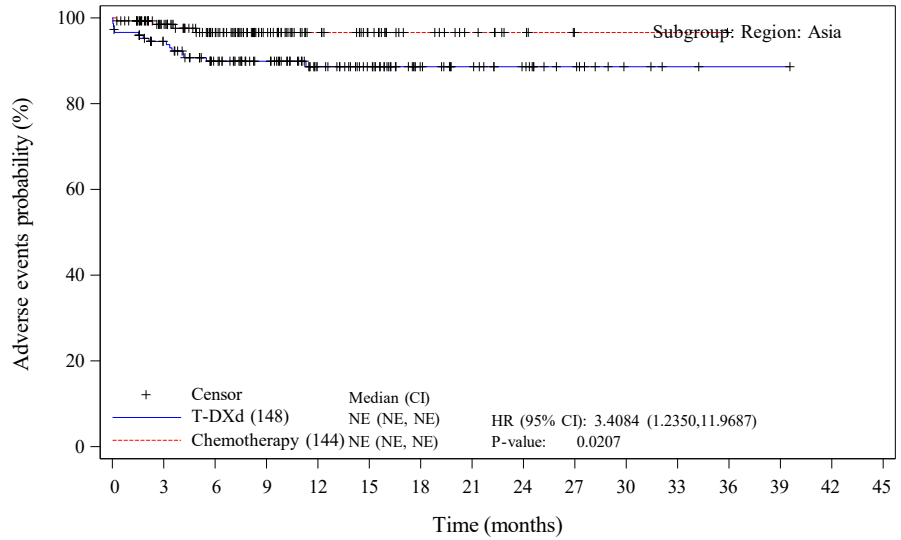
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Dysgeusia



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SOC: Nervous system disorders; PT: Dysgeusia

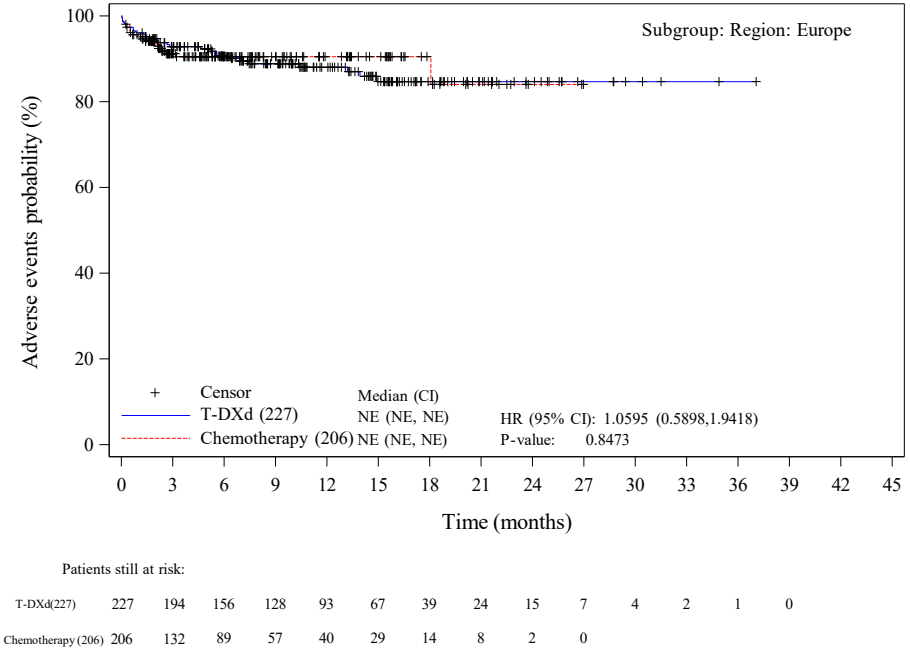

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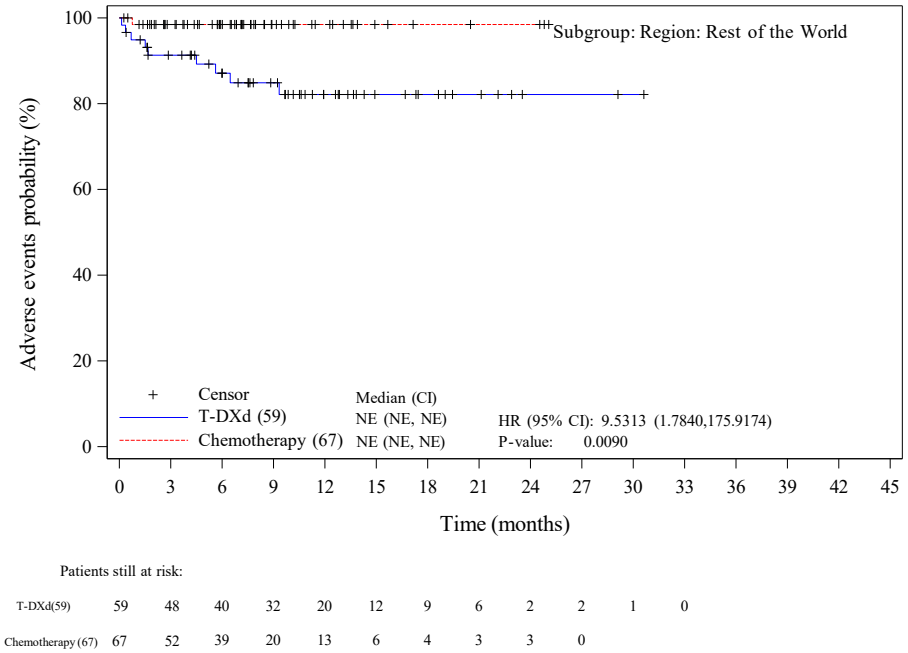
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Dysgeusia



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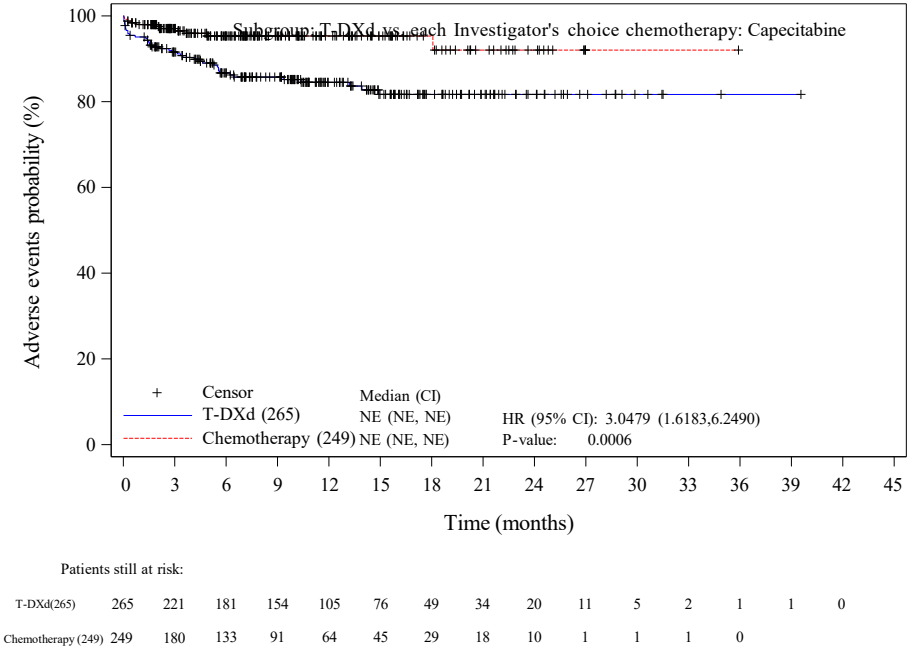
SOC: Nervous system disorders; PT: Dysgeusia



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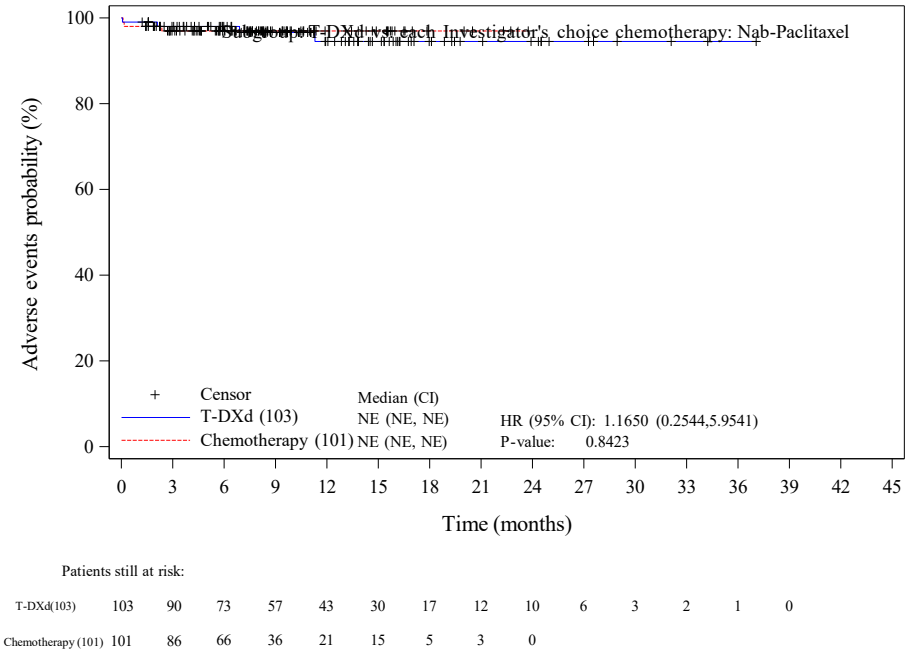
SOC: Nervous system disorders; PT: Dysgeusia



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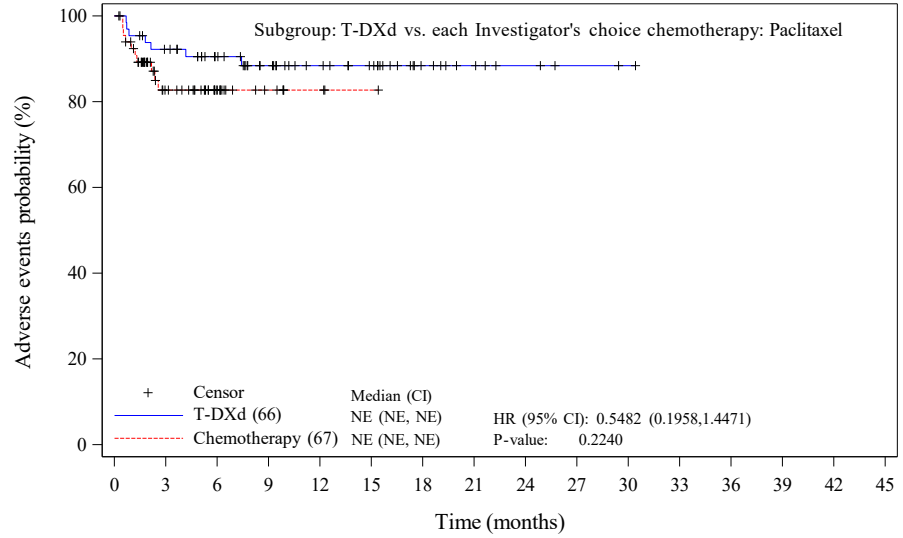
SOC: Nervous system disorders; PT: Dysgeusia



Patients still at risk:

T-DXd(66)	66	57	46	35	27	22	11	7	4	2	1	0
Chemotherapy (67)	67	34	17	7	3	1	0					

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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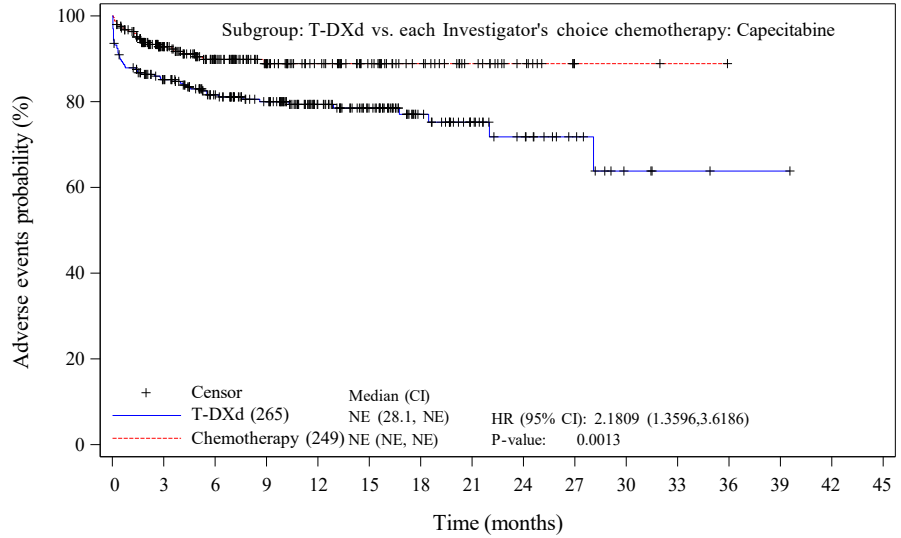
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Headache



Patients still at risk:

T-DXd(265)	265	208	169	142	100	75	43	28	19	11	4	2	1	1	0
Chemotherapy (249)	249	173	125	88	65	47	31	20	11	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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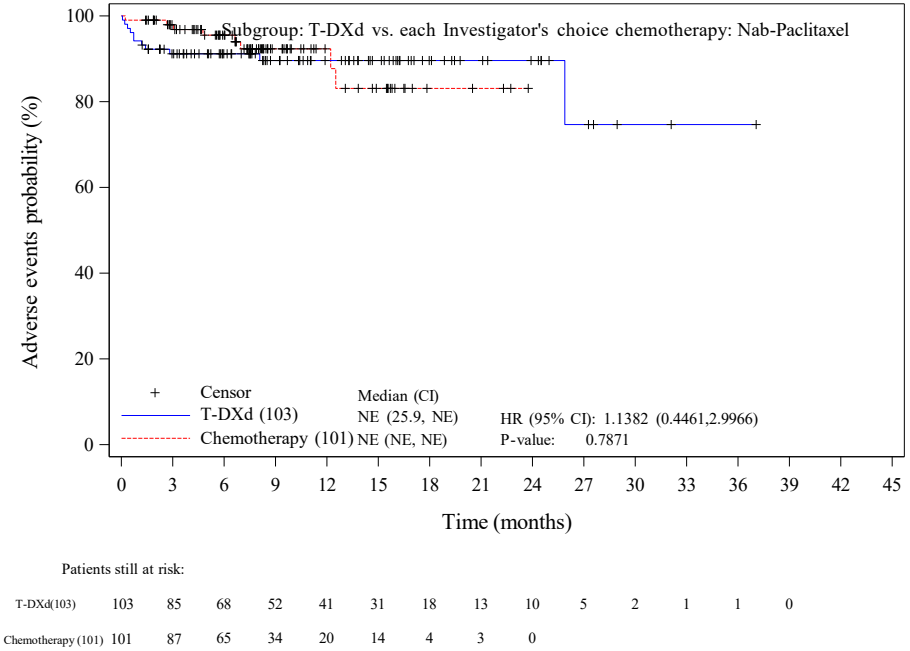

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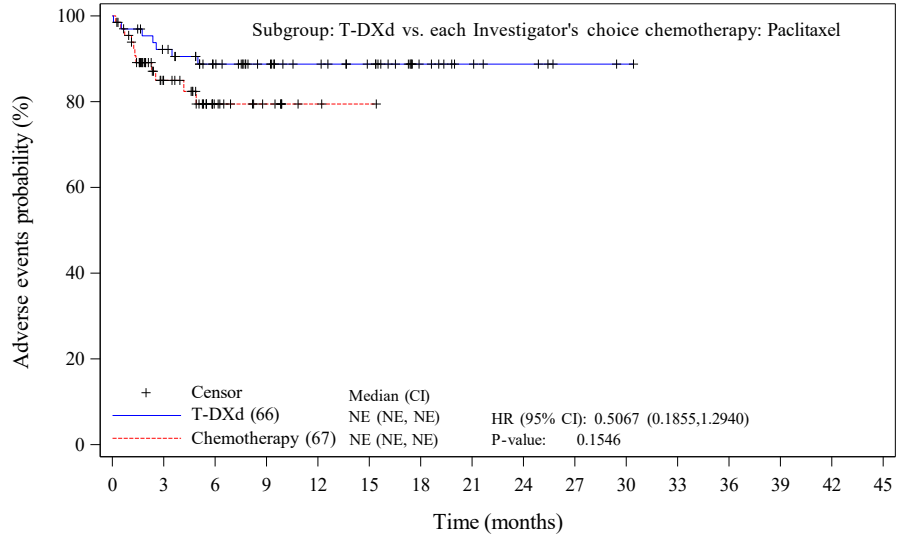
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Headache



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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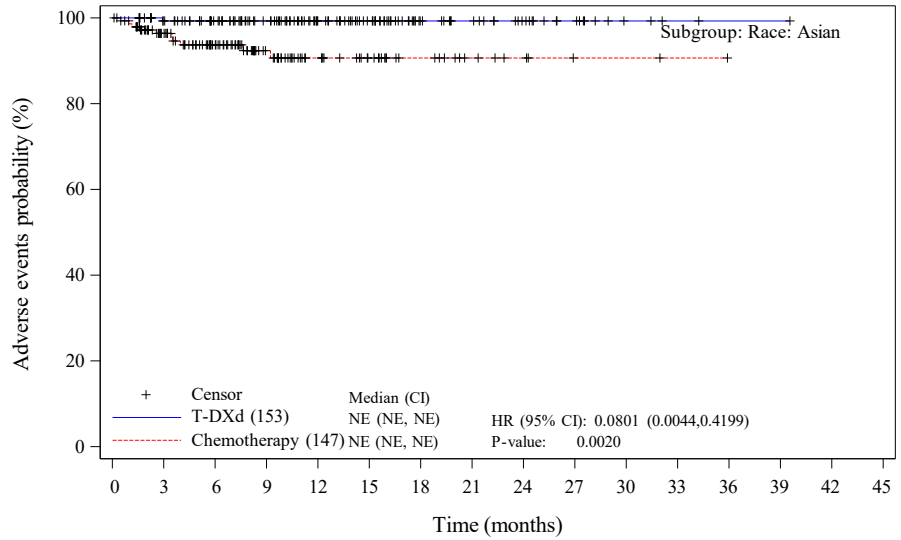
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia

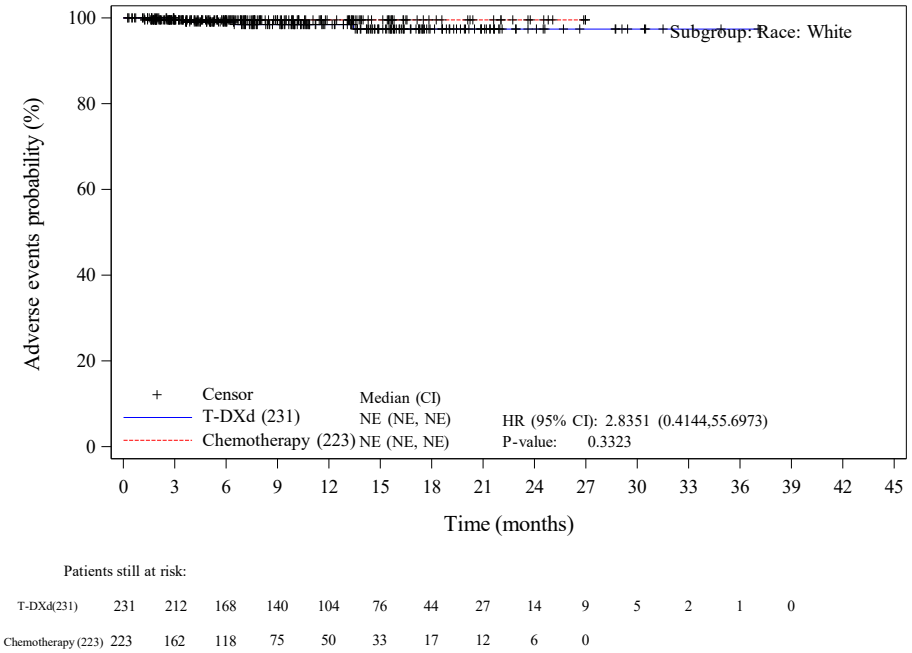

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia

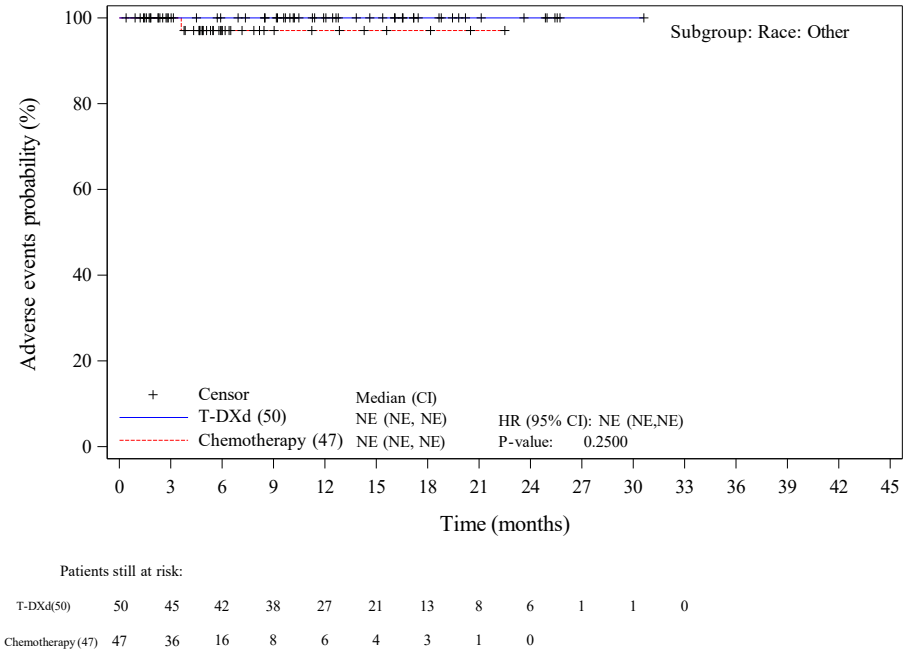

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia

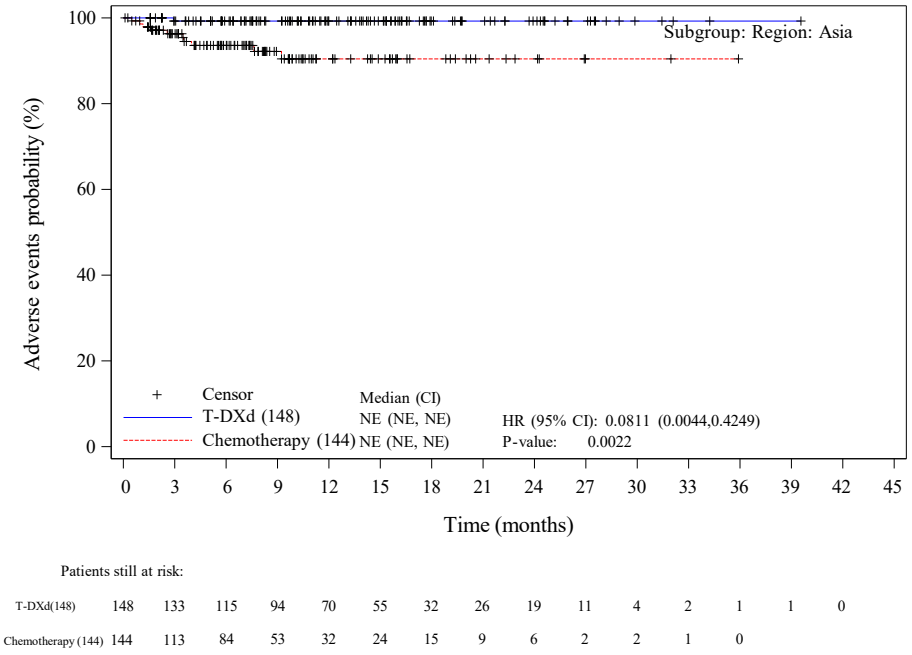

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia

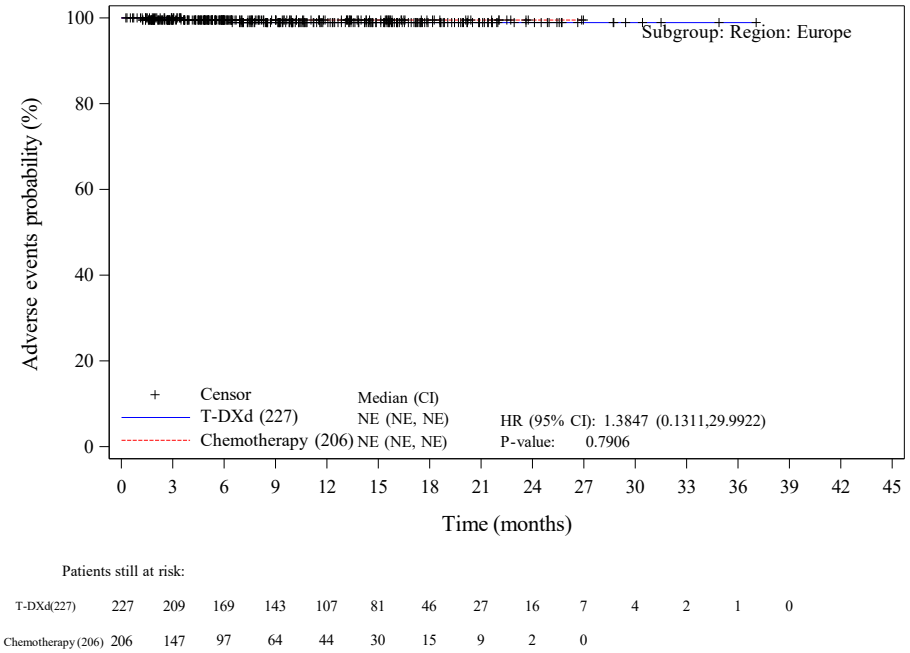

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia

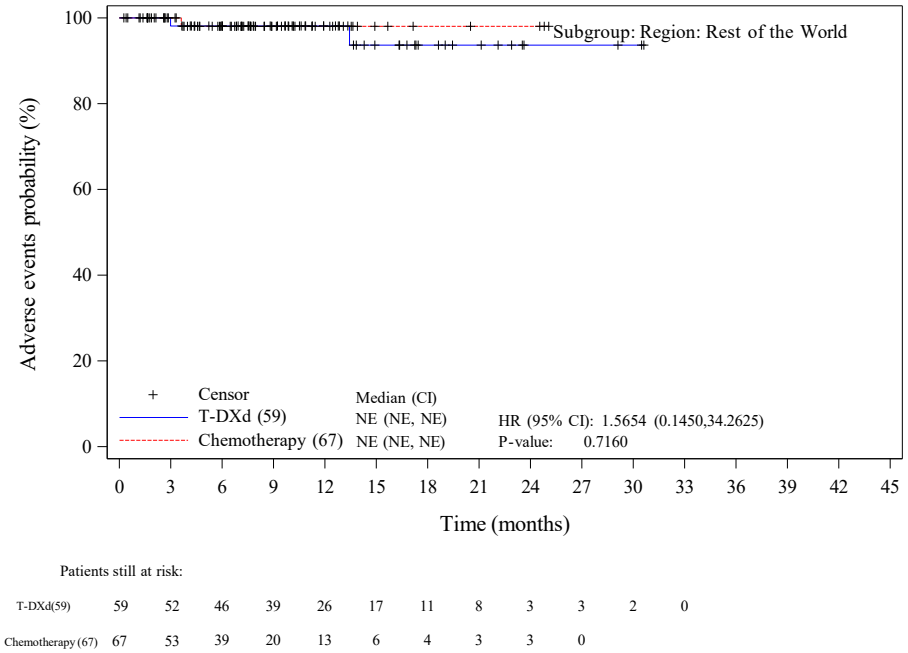

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia

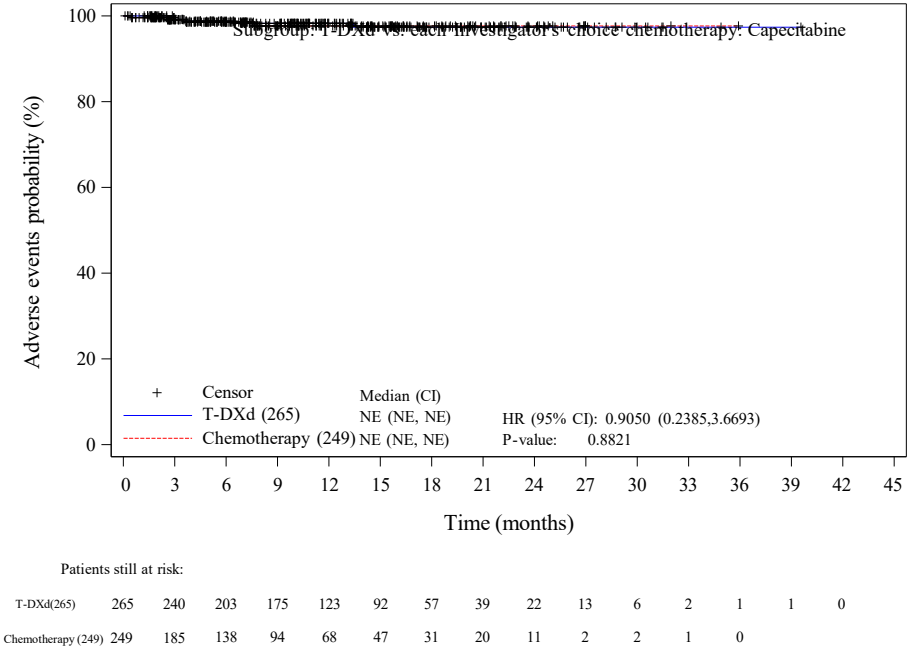

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia

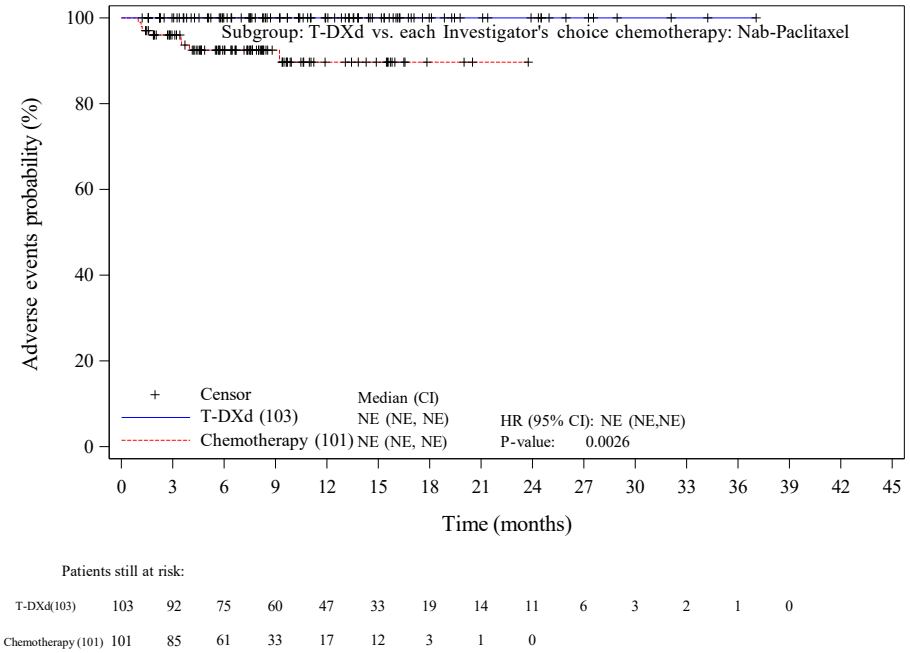

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia

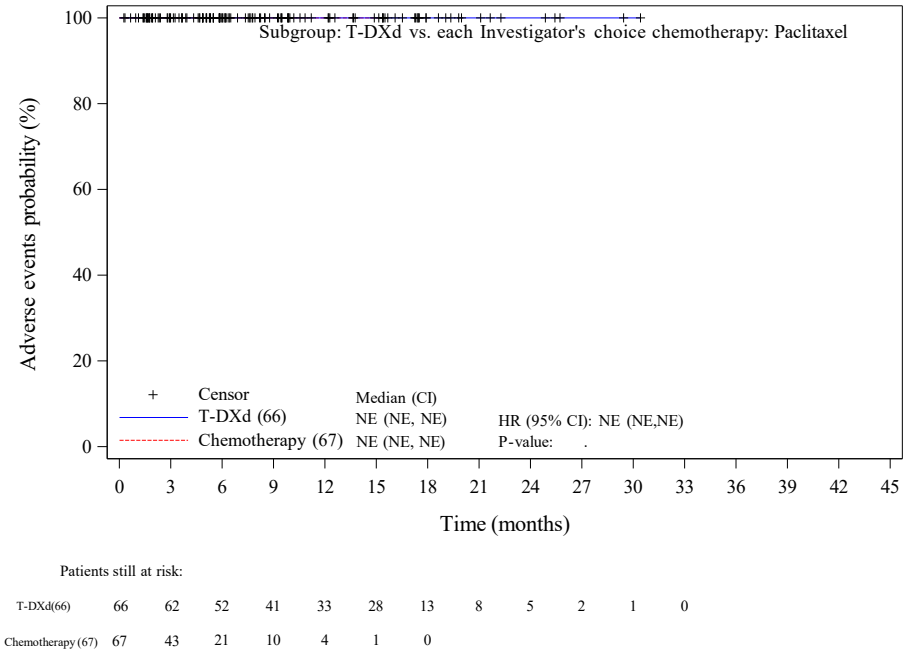

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia

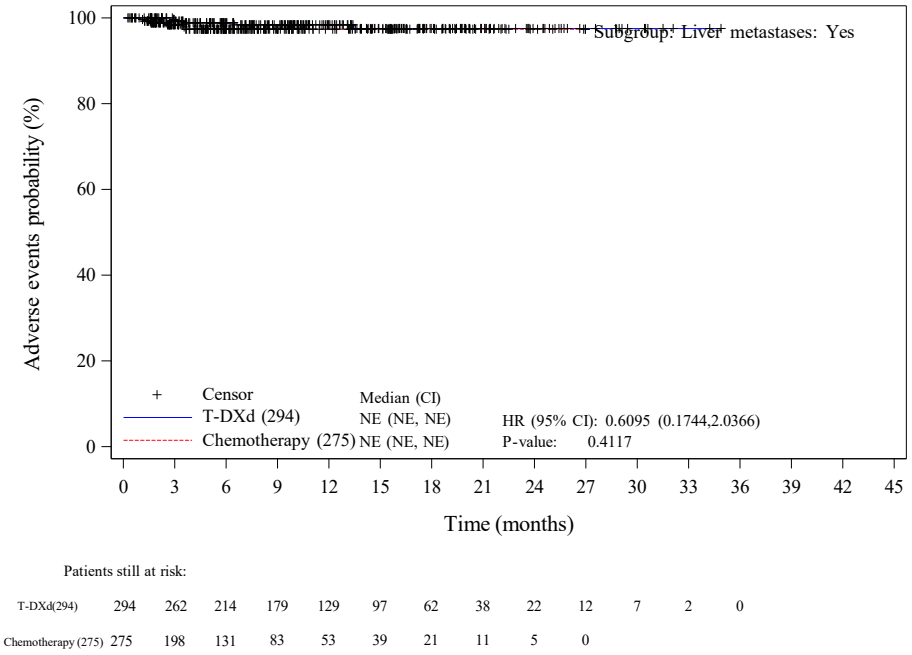

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Hypoaesthesia

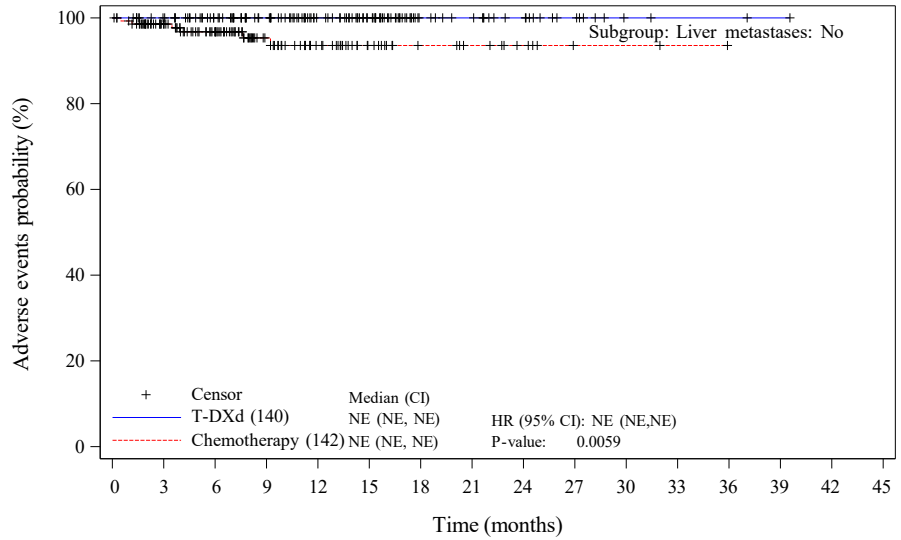

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Neuropathy peripheral

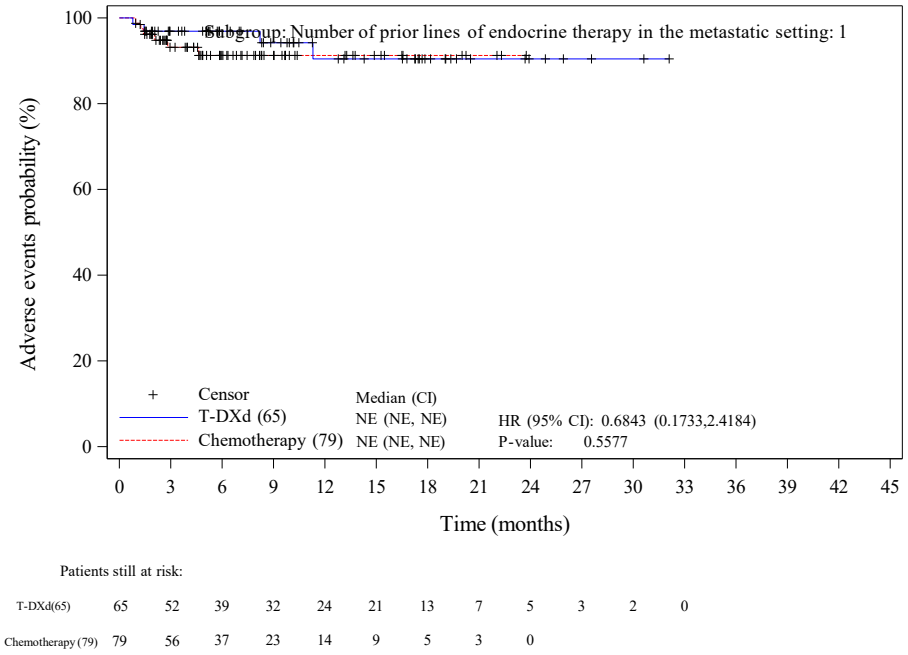

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Neuropathy peripheral

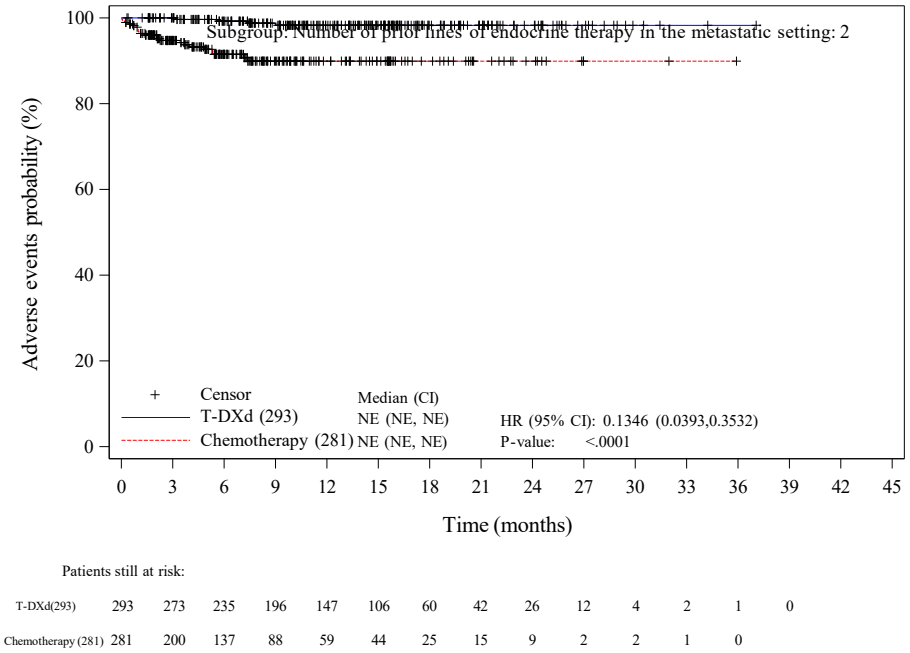

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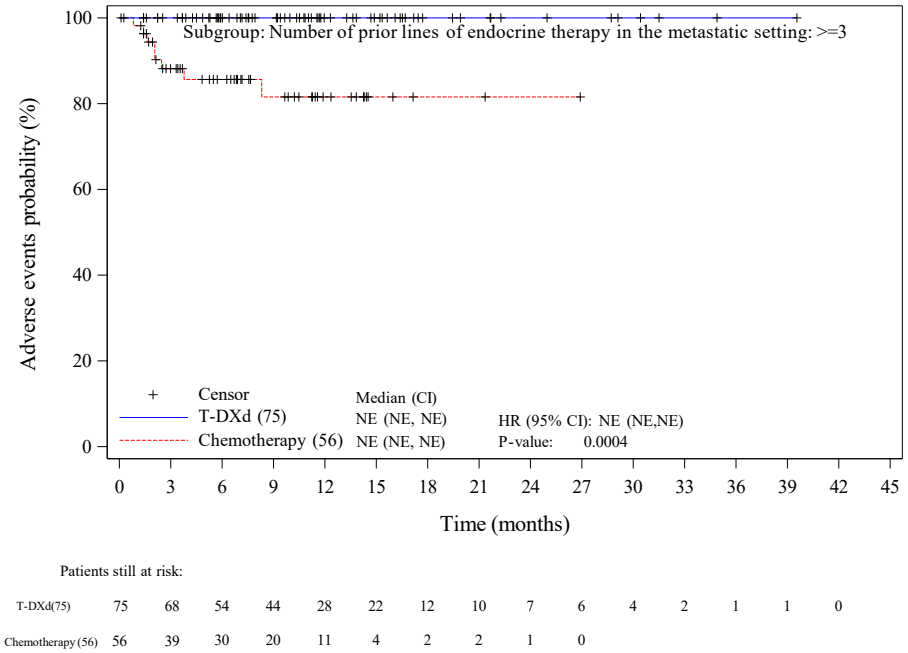
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Neuropathy peripheral



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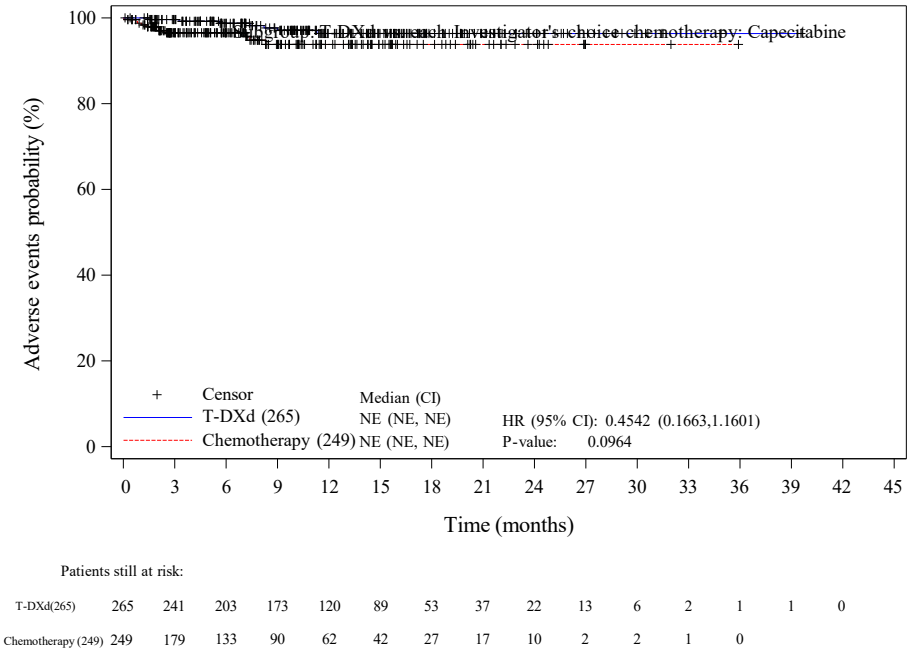
SOC: Nervous system disorders; PT: Neuropathy peripheral



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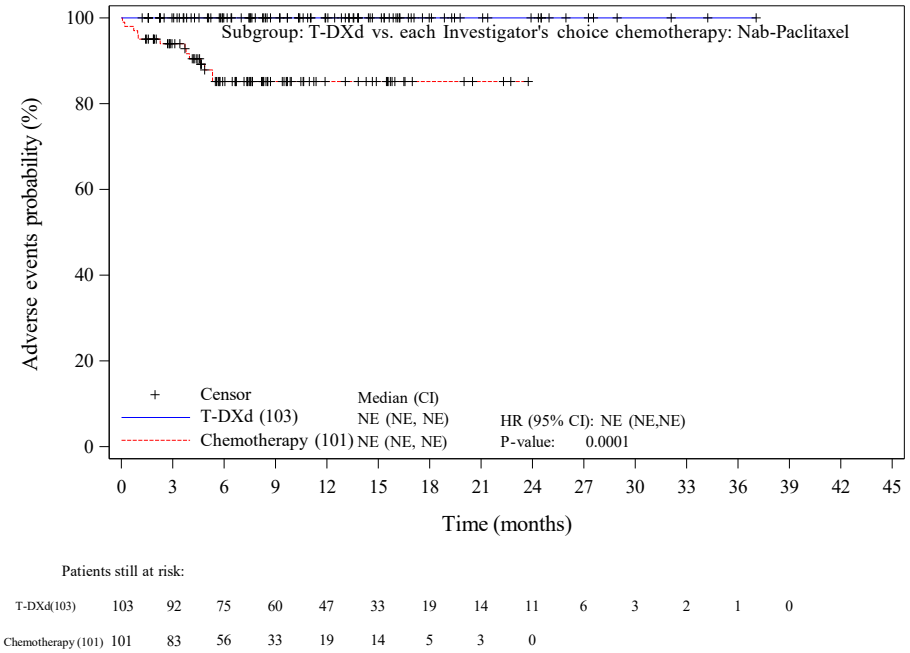
Run date: 11DEC2024 16:20; Program name: F.2.29.2_10TEAE_SAF_SUB.sas; Output name: F.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Neuropathy peripheral



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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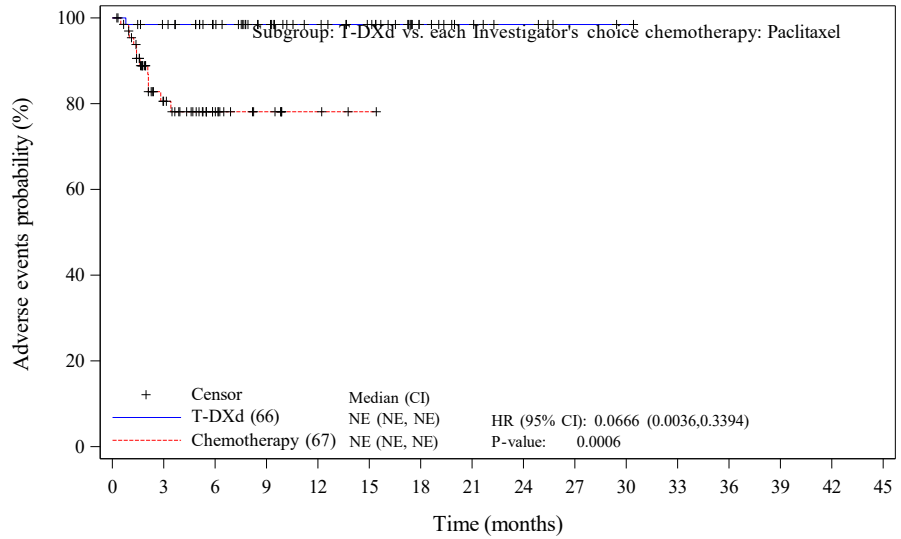
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Neuropathy peripheral



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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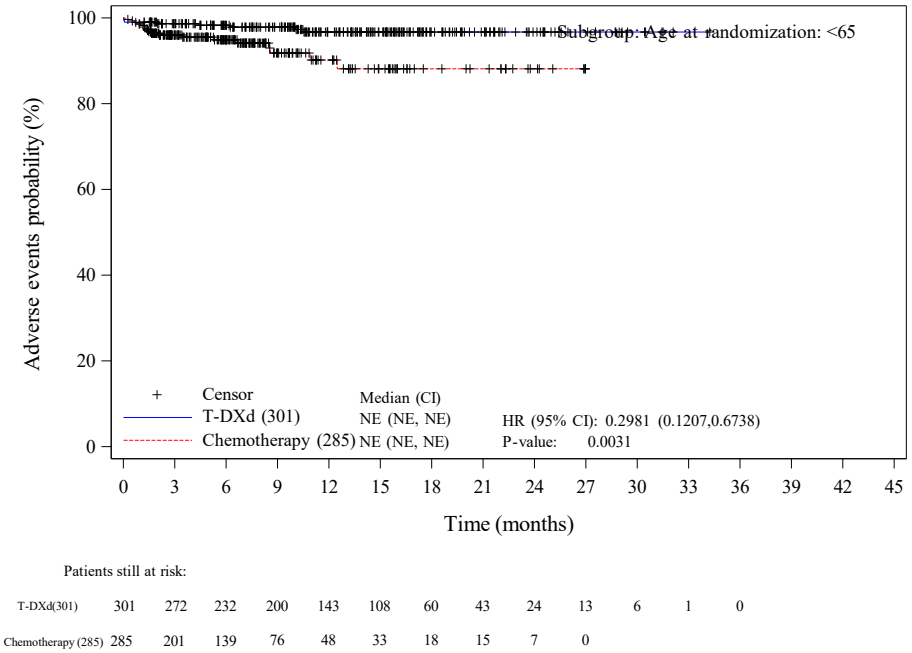
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Paraesthesia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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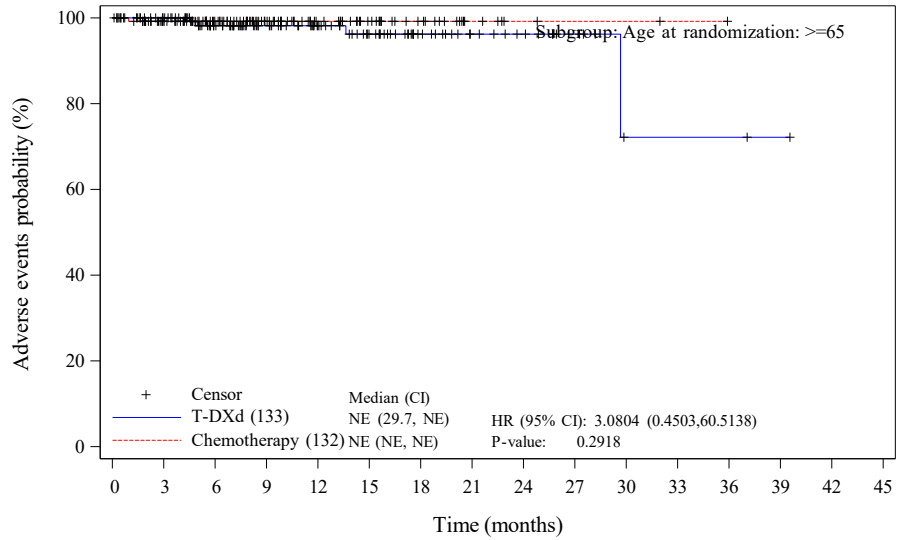
Run date: 11DEC2024 16:20; Program name: F.2.29.2_10TEAE_SAF_SUB.sas; Output name: F.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Paraesthesia



Patients still at risk:

T-DXd(133)	133	121	96	73	56	42	26	17	13	7	2	2	2	1	0
Chemotherapy (132)	132	109	81	56	38	27	17	7	3	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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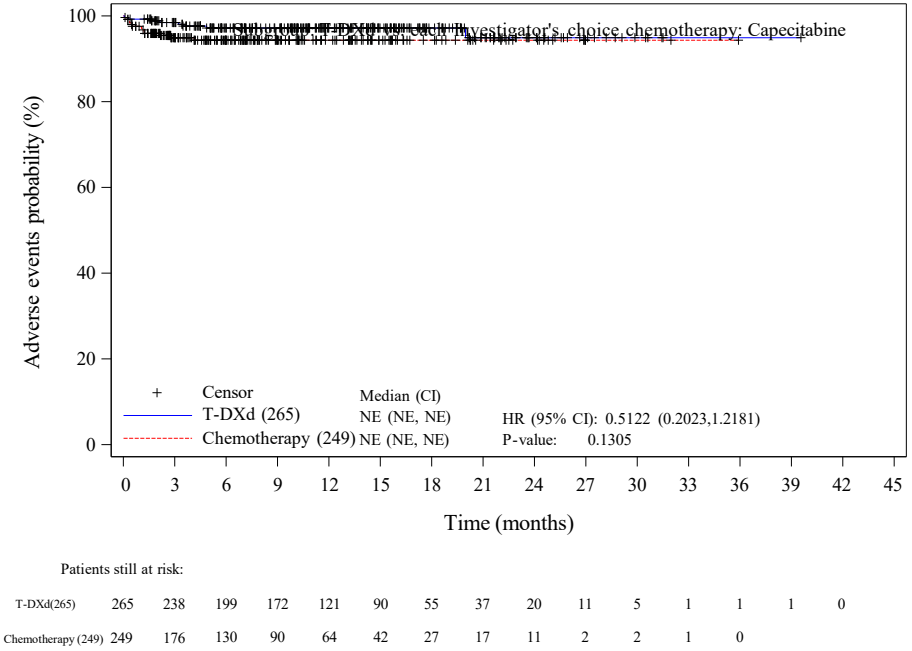
Run date: 11DEC2024 16:20; Program name: F.2.29.2_10TEAE_SAF_SUB.sas; Output name: F.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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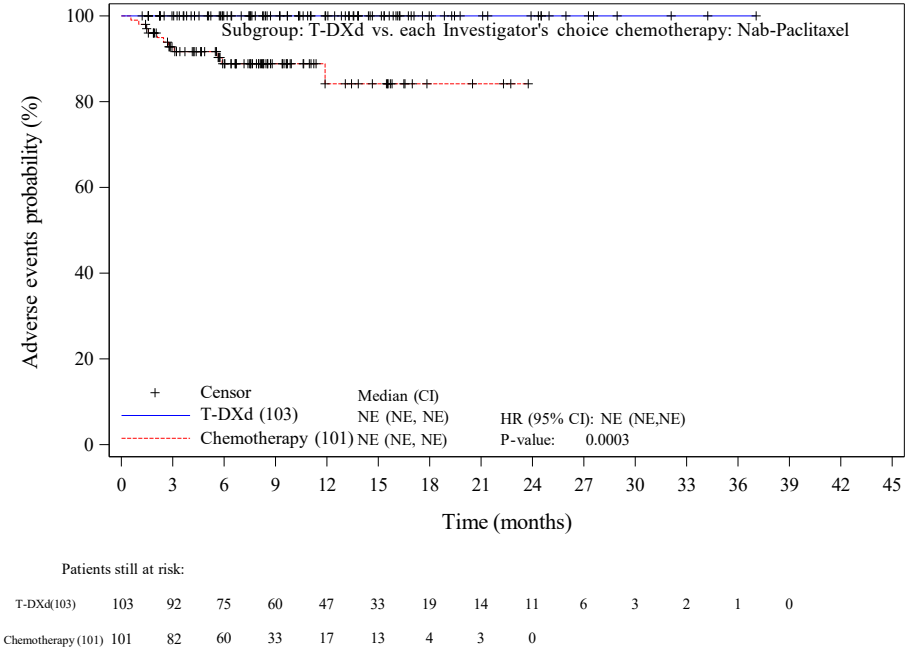
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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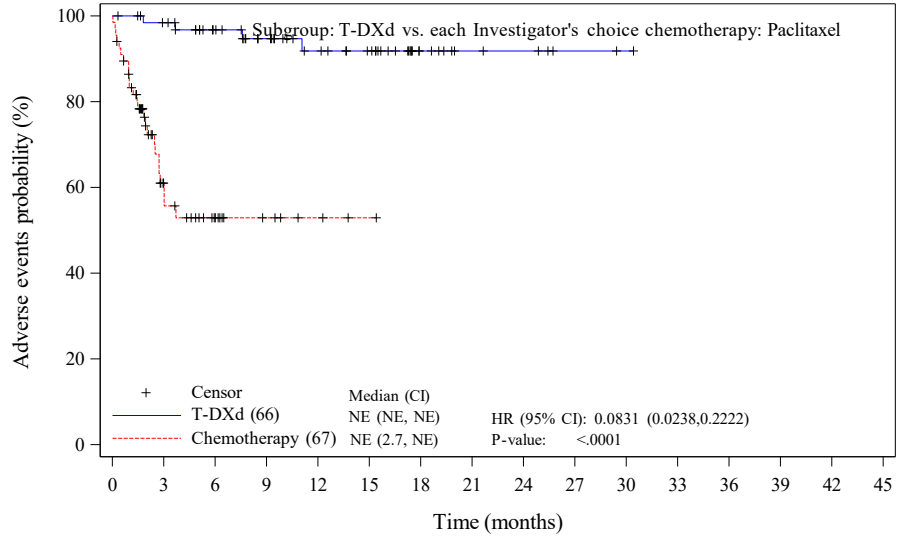
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy



Patients still at risk:

T-DXd(66)	66	61	50	40	31	26	11	6	5	2	1	0
Chemotherapy (67)	67	23	12	6	3	1	0					

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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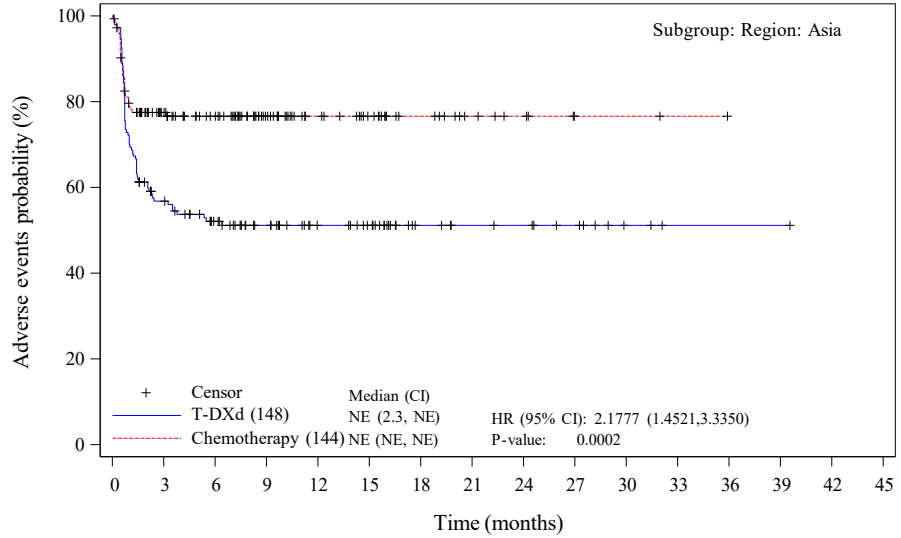
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Patients still at risk:

T-DXd(148)	148	75	59	45	34	29	15	12	11	8	3	1	1	1	0
Chemotherapy (144)	144	90	73	48	32	24	15	9	6	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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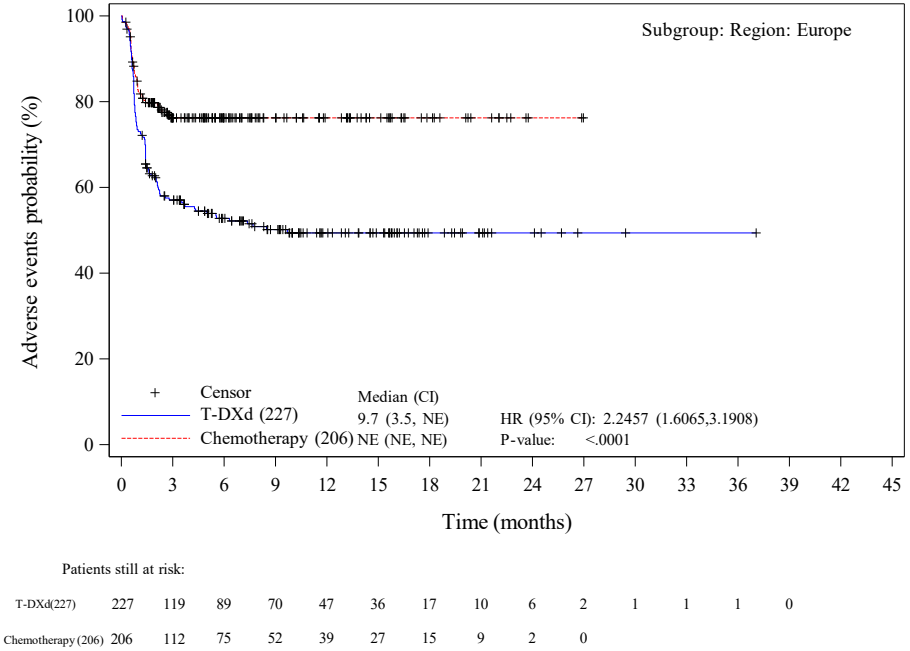
Run date: 11DEC2024 16:20; Program name: F.2.29.2_10TEAE_SAF_SUB.sas; Output name: F.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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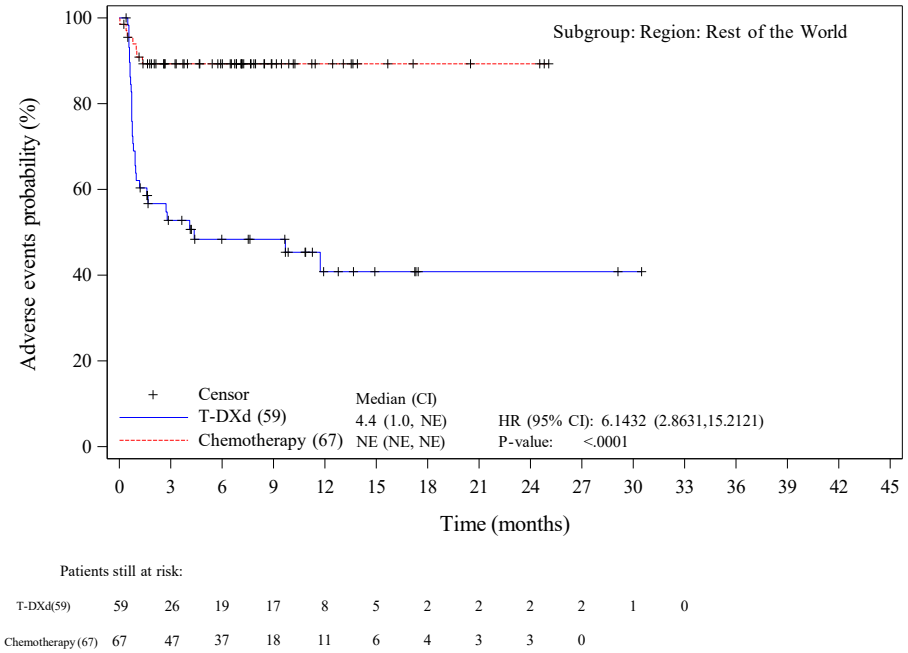
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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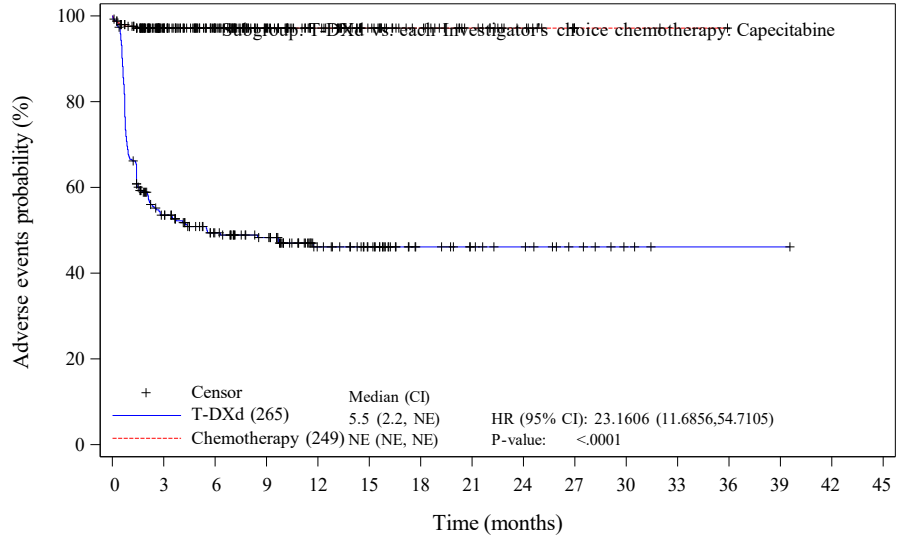
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Patients still at risk:

T-DXd(265)	265	128	97	81	50	38	20	15	12	7	3	1	1	1	0
Chemotherapy (249)	249	183	138	95	68	47	31	20	11	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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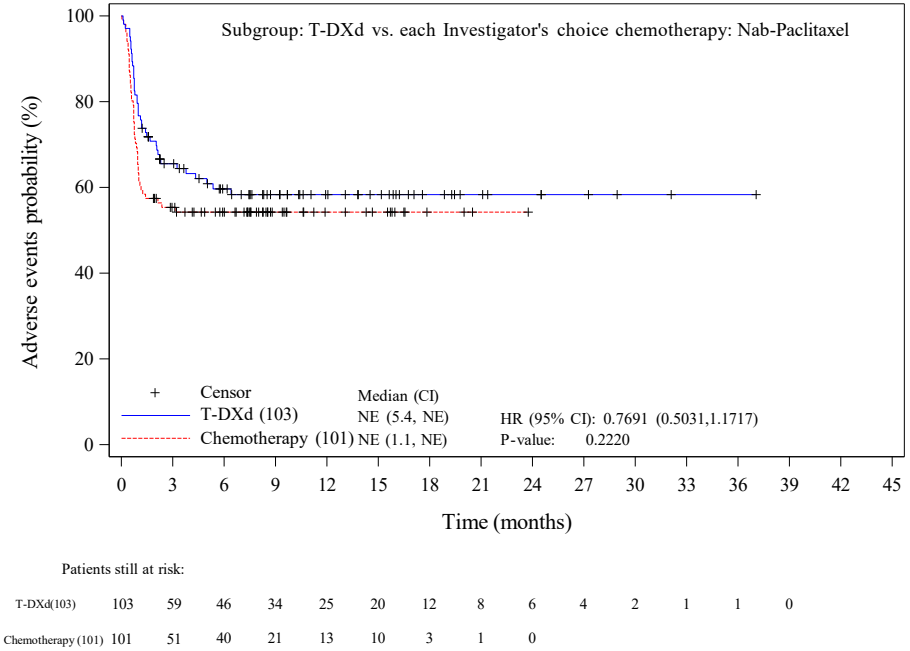
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia

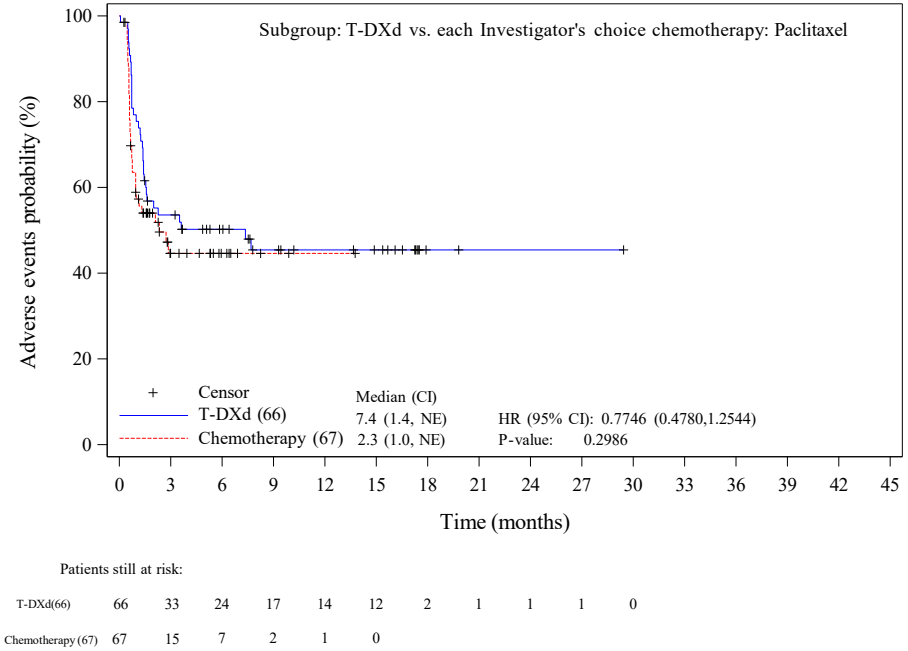

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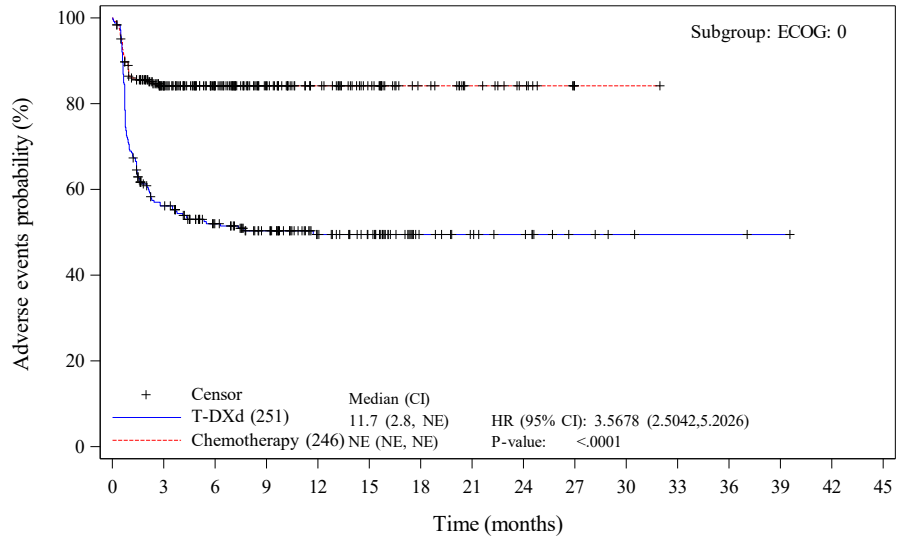
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Patients still at risk:

T-DXd(251)	251	131	100	80	55	43	19	14	11	5	3	2	2	1	0
Chemotherapy (246)	246	165	119	80	56	39	23	15	9	1	1	0			

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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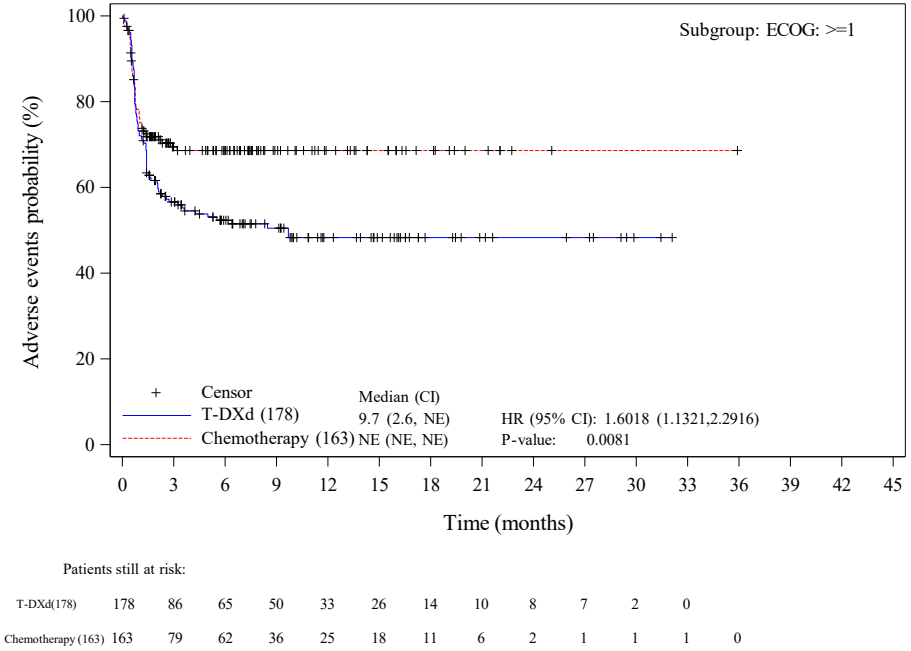
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Alopecia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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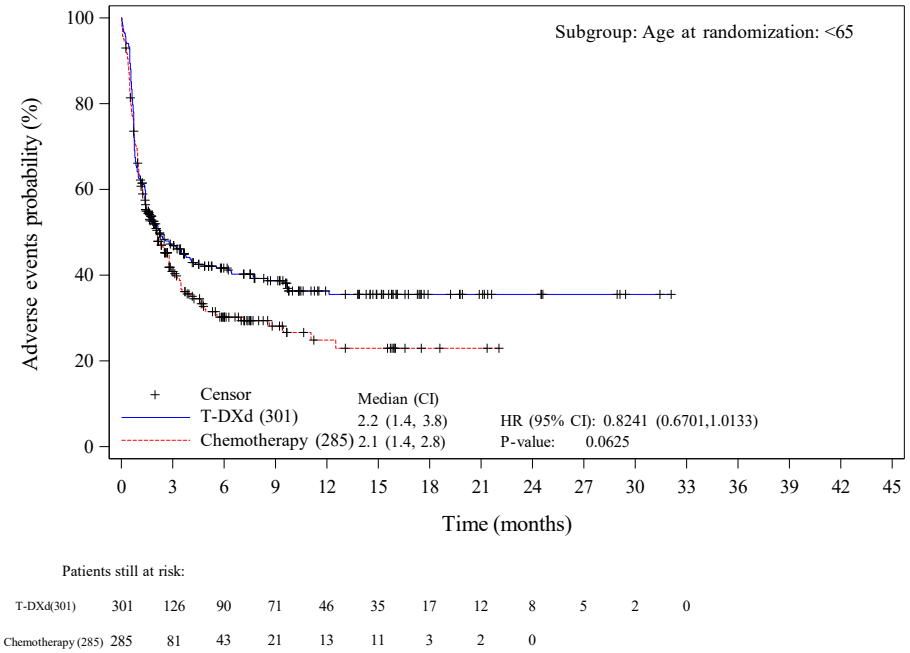
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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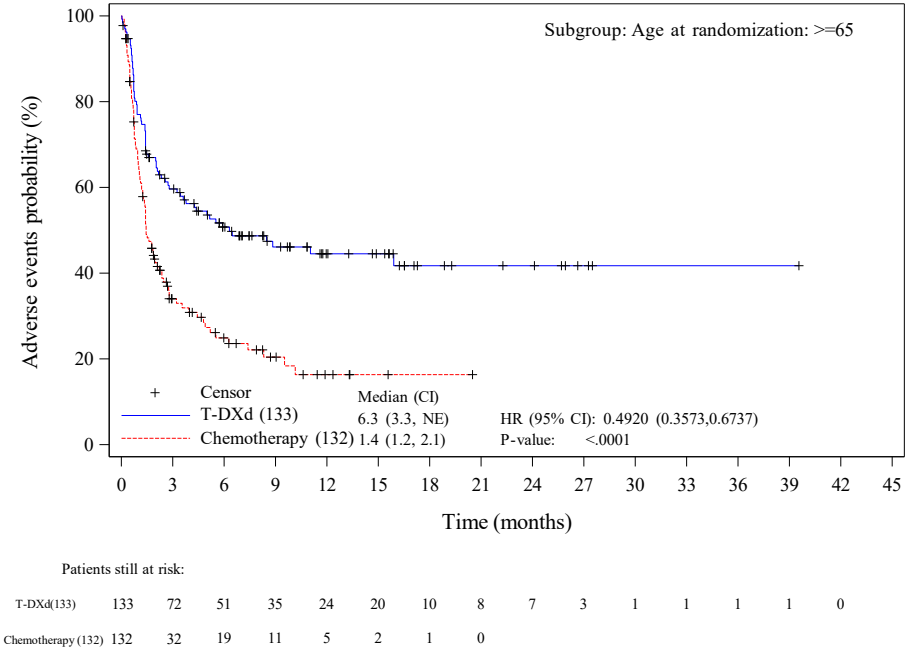
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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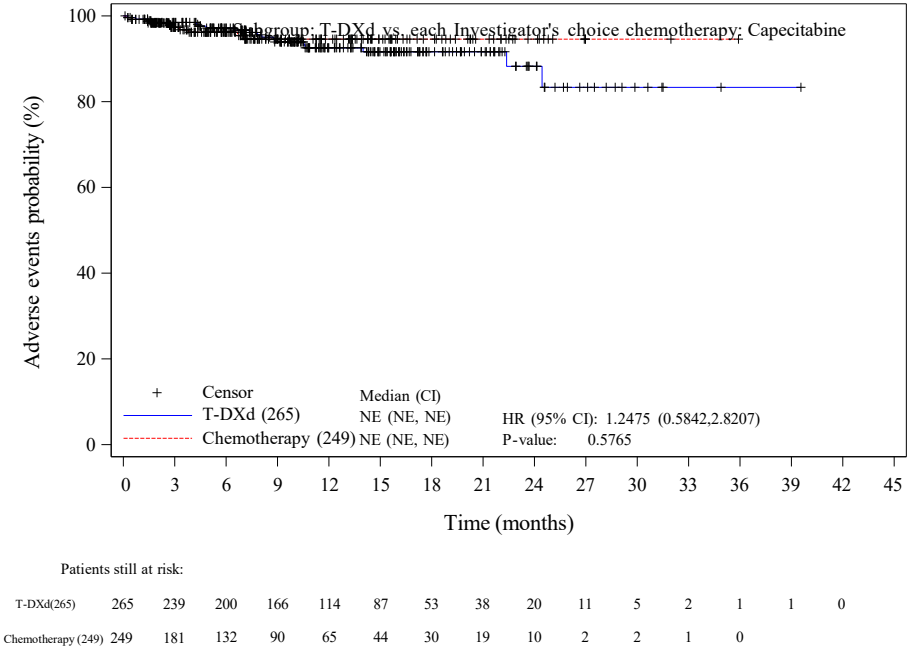
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Rash



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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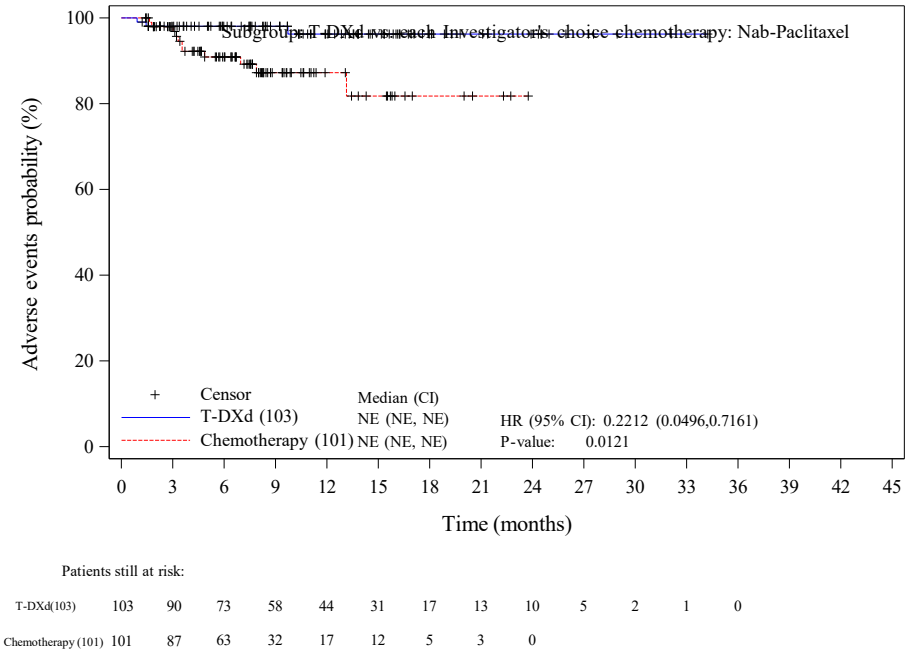
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Rash



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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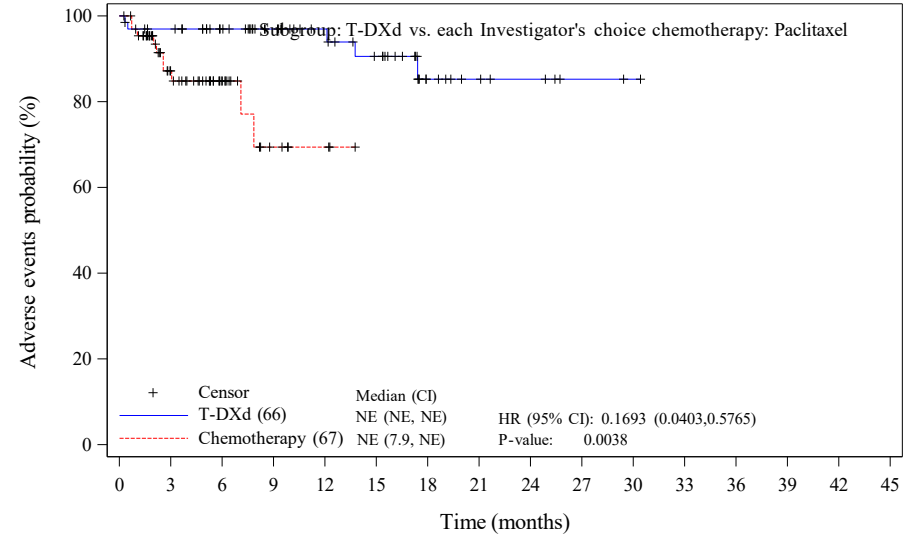
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Rash



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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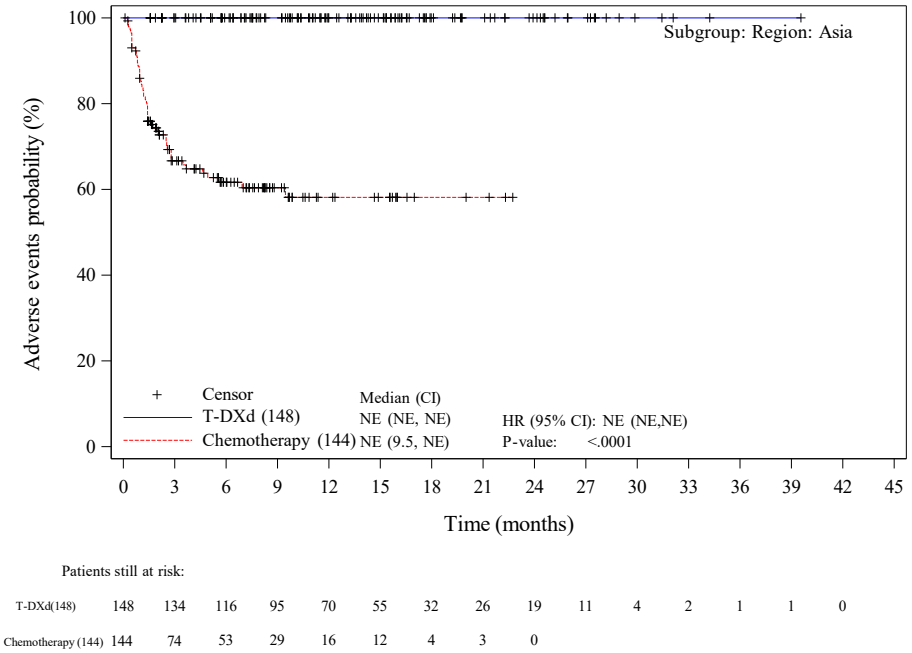
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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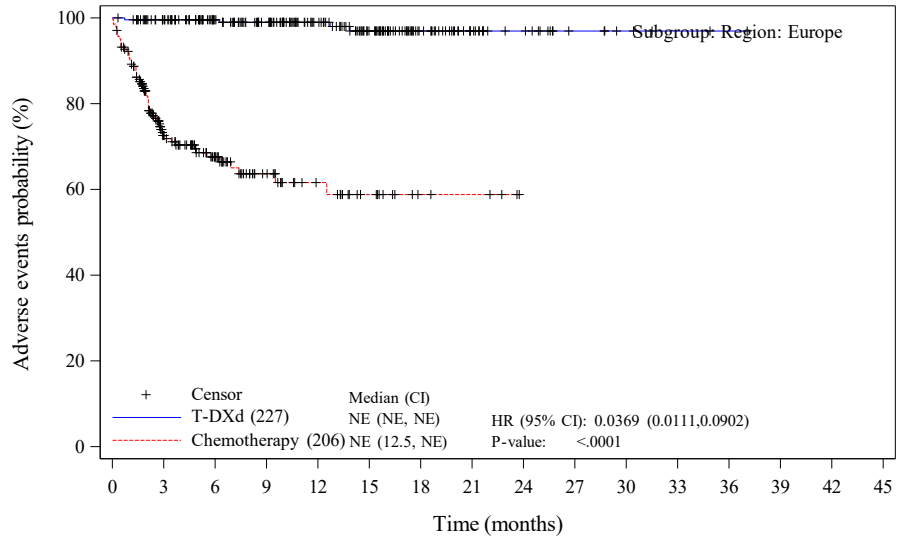
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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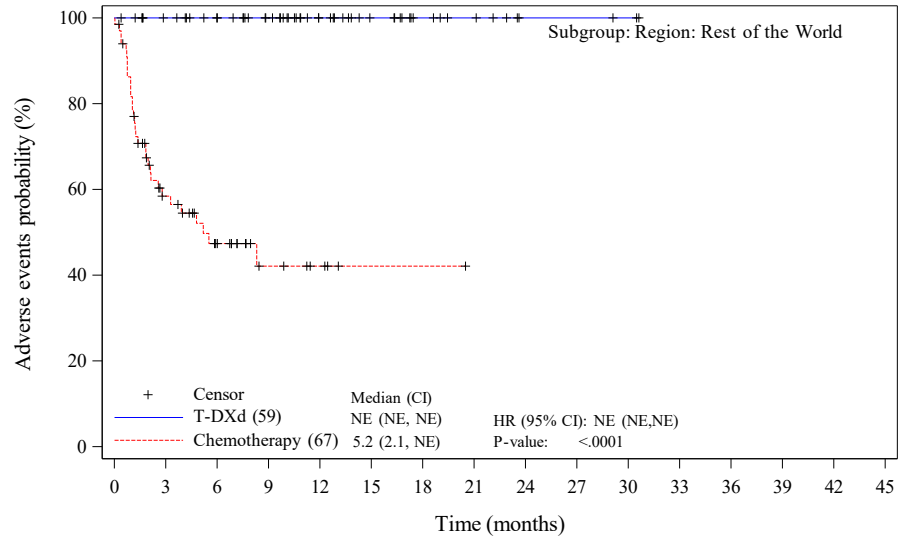
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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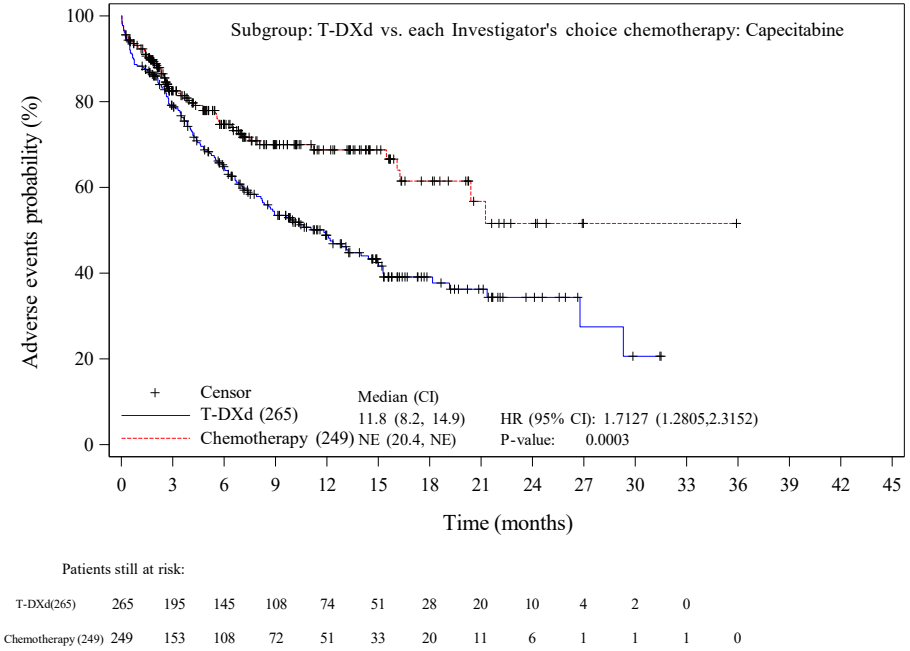
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)

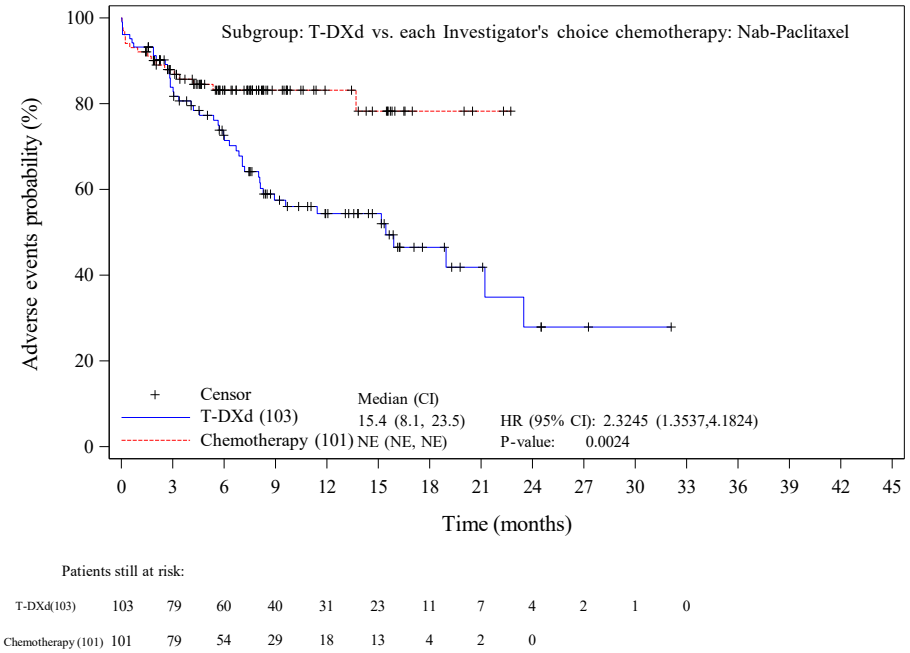

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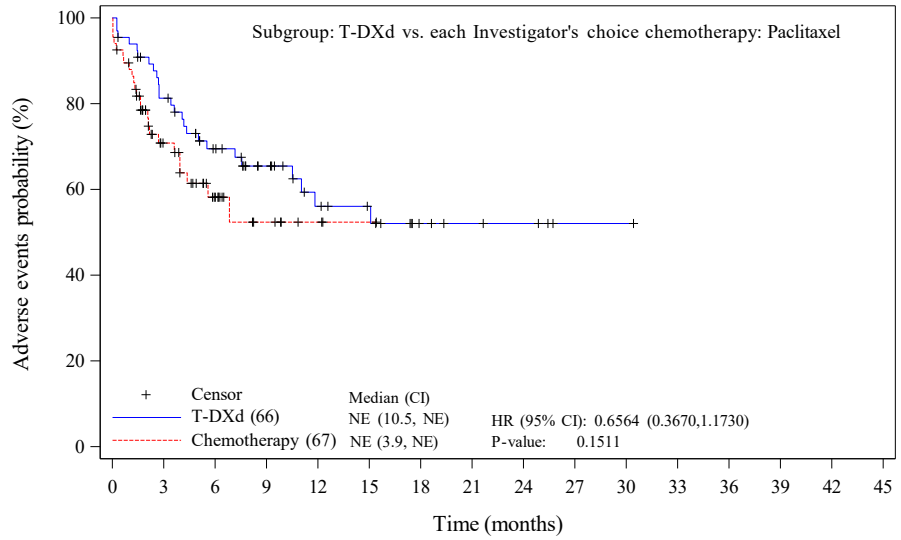
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)



Patients still at risk:

T-DXd(66)	66	51	37	26	17	14	7	5	4	1	1	0
Chemotherapy (67)	67	32	16	7	3	1	0					

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

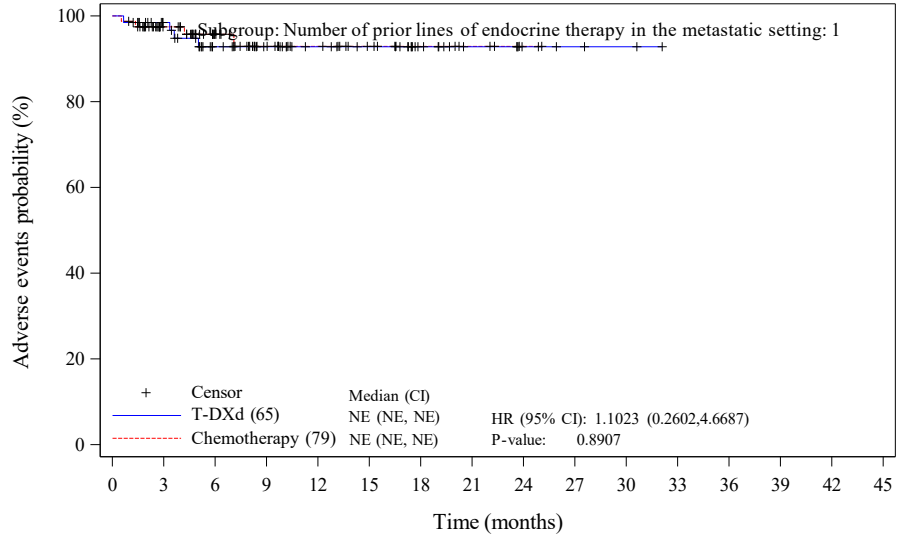

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis

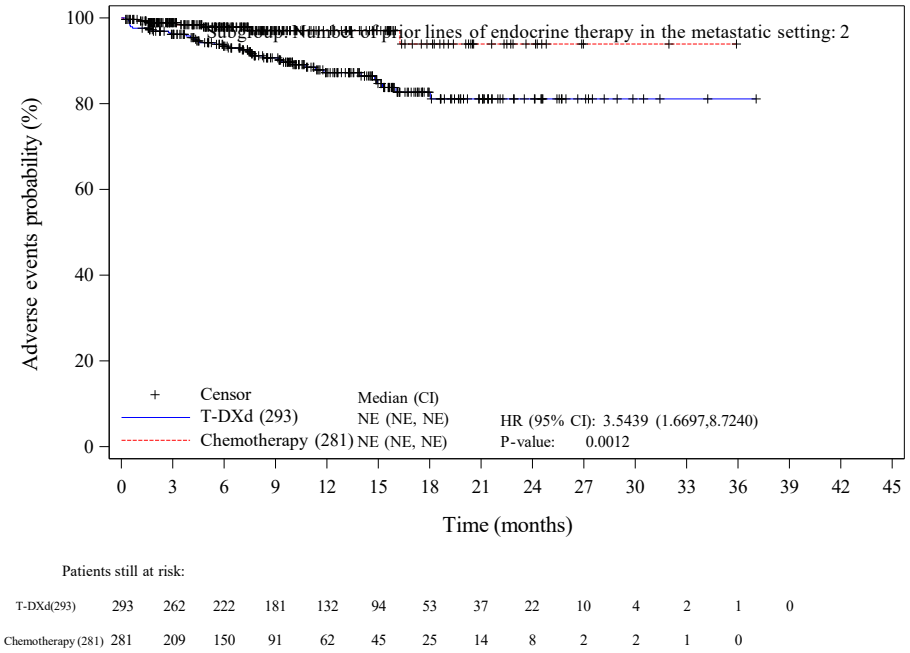

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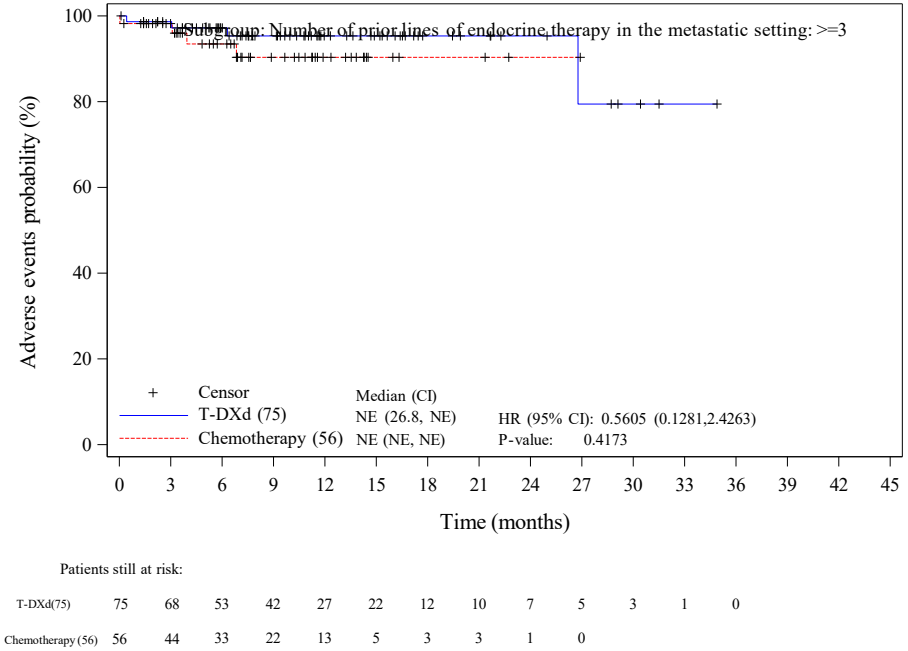
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis



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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

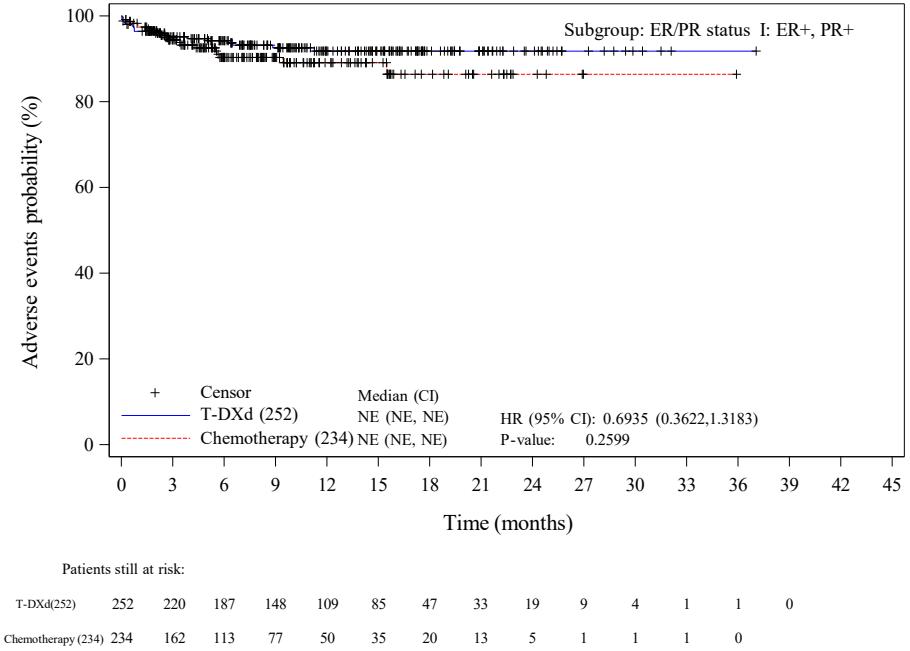

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Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dyspnoea

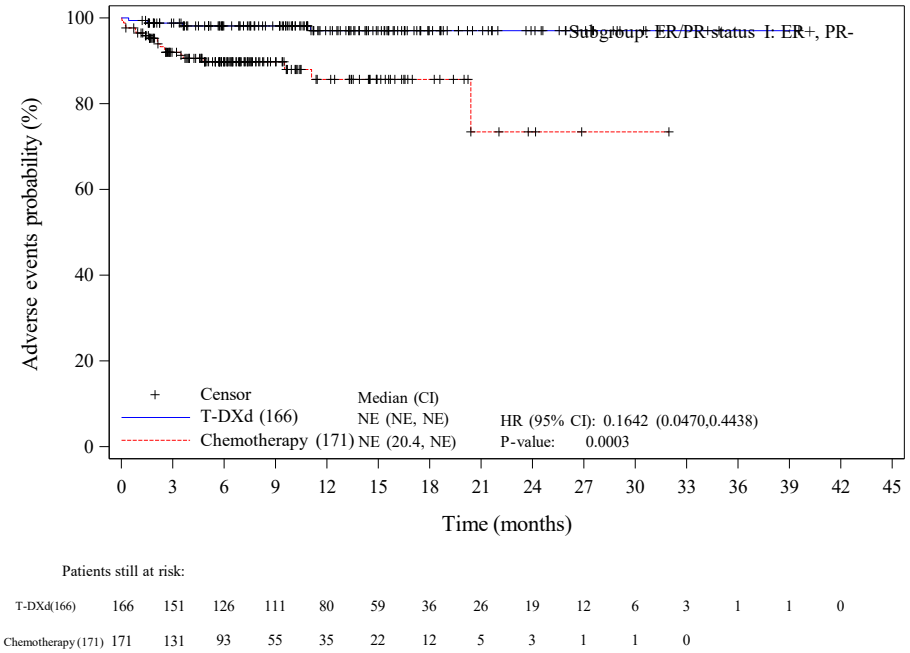

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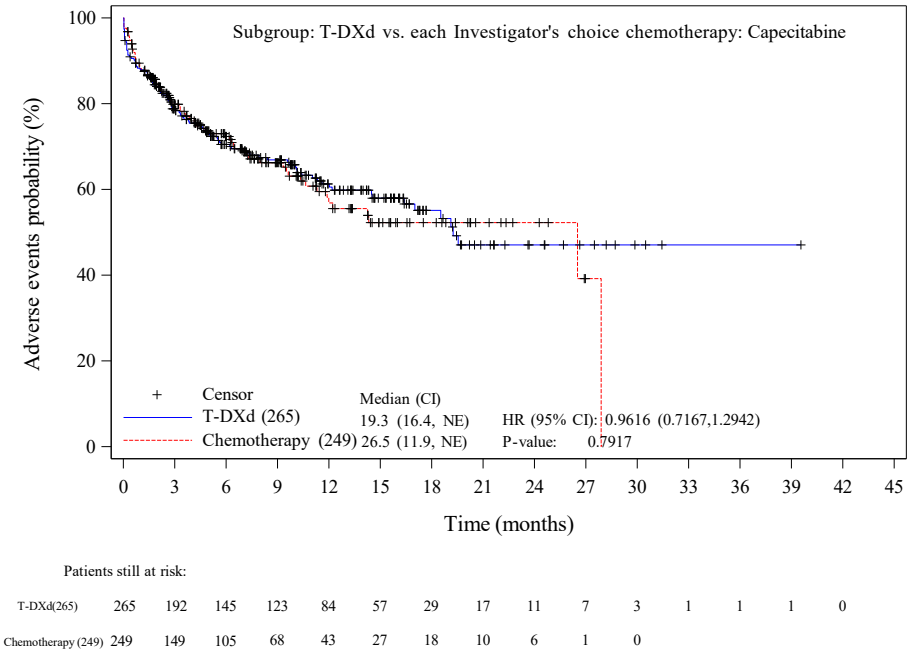
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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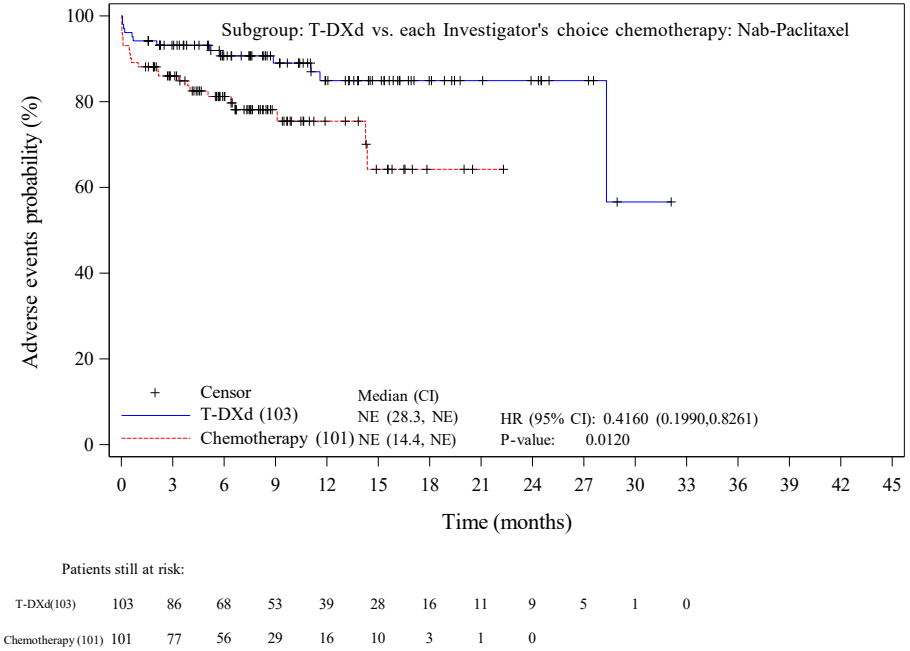
Run date: 11DEC2024 16:21; Program name: F.2.29.2_10TEAE_SAF_SUB.sas; Output name: F.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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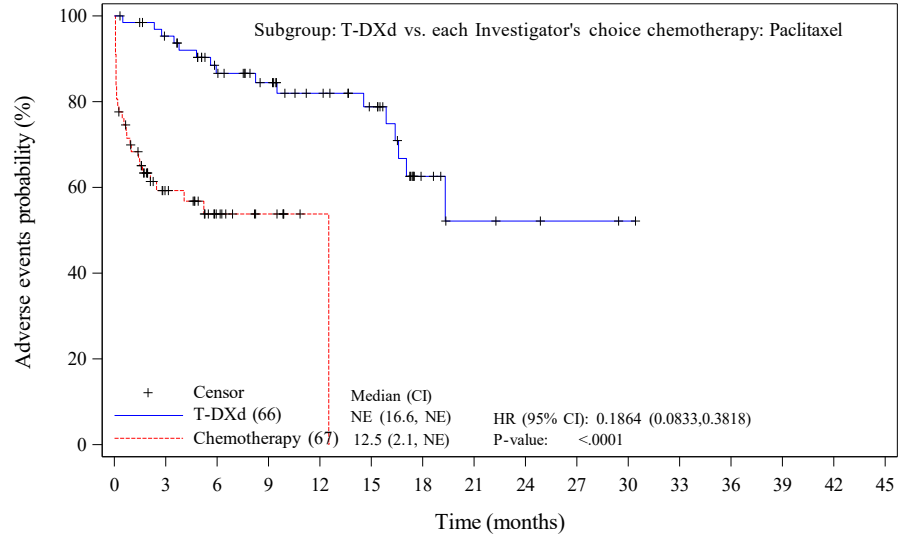
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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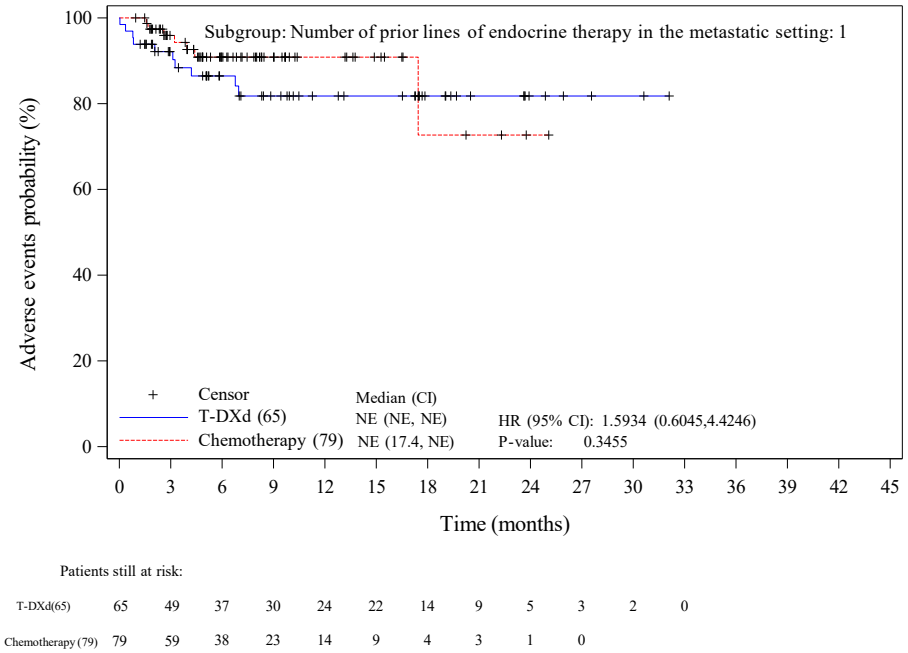
Run date: 11DEC2024 16:21; Program name: F.2.29.2_10TEAE_SAF_SUB.sas; Output name: F.2.29.2_10TEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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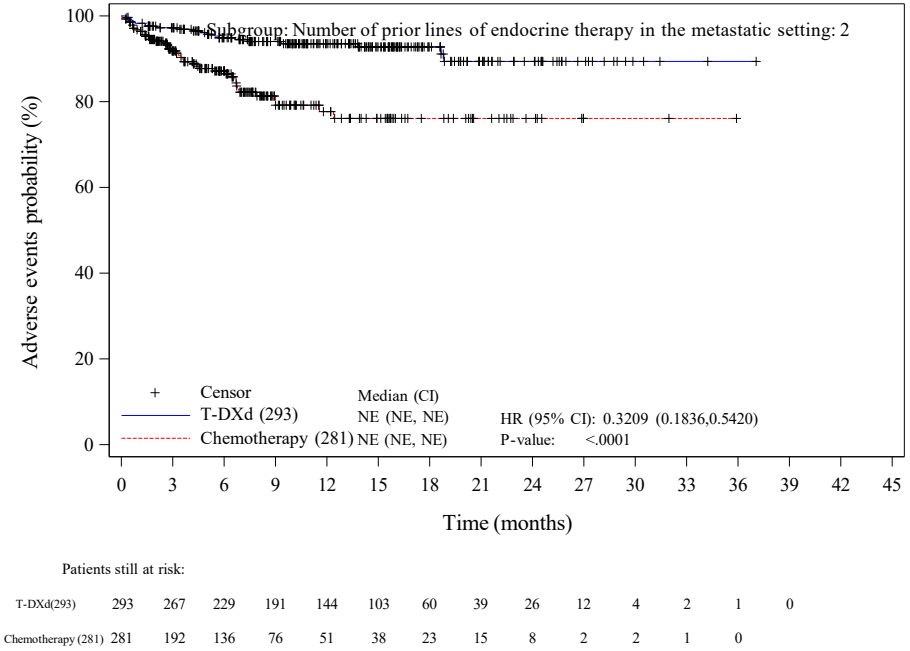
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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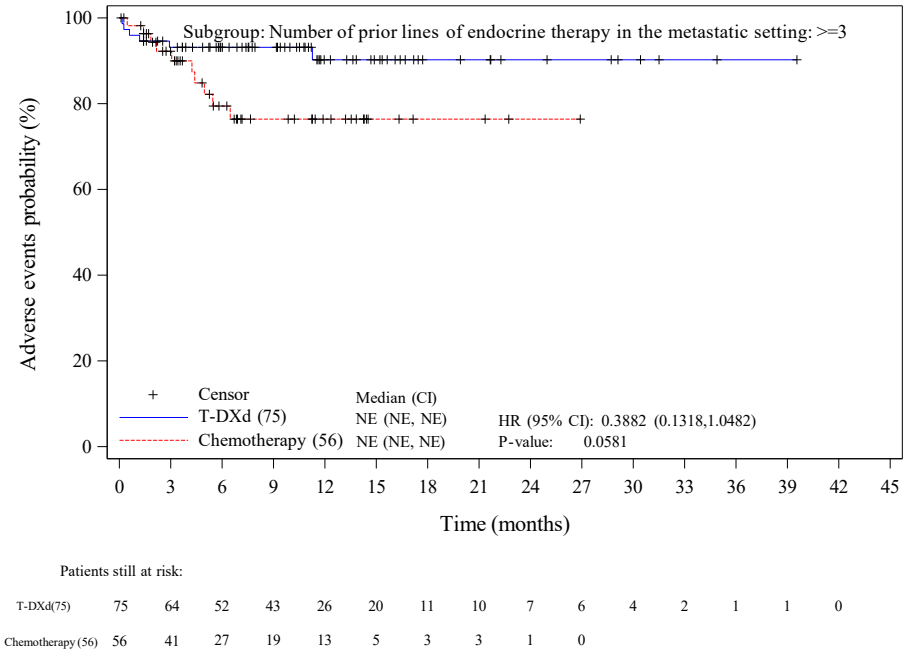
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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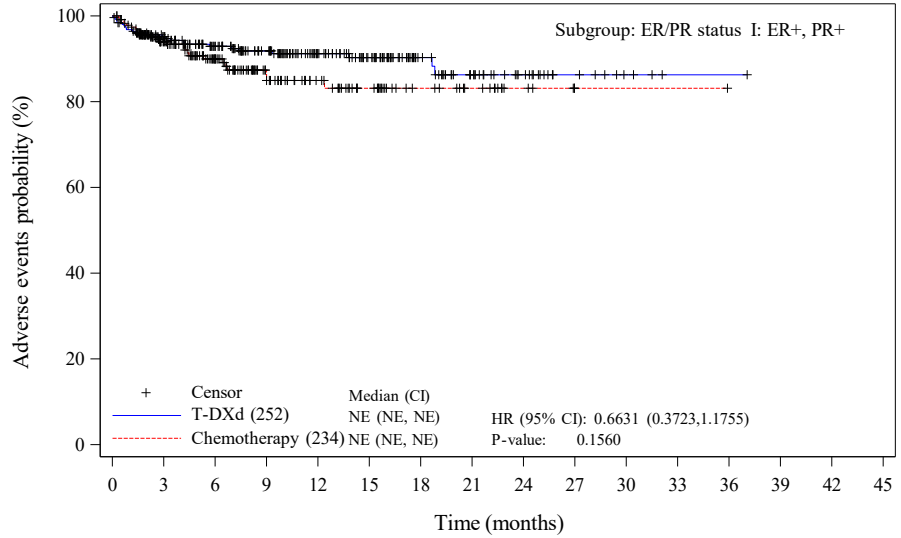
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Patients still at risk:

T-DXd(252)	252	221	186	151	112	85	47	31	19	9	4	1	1	0
Chemotherapy (234)	234	159	112	72	49	34	20	14	6	1	1	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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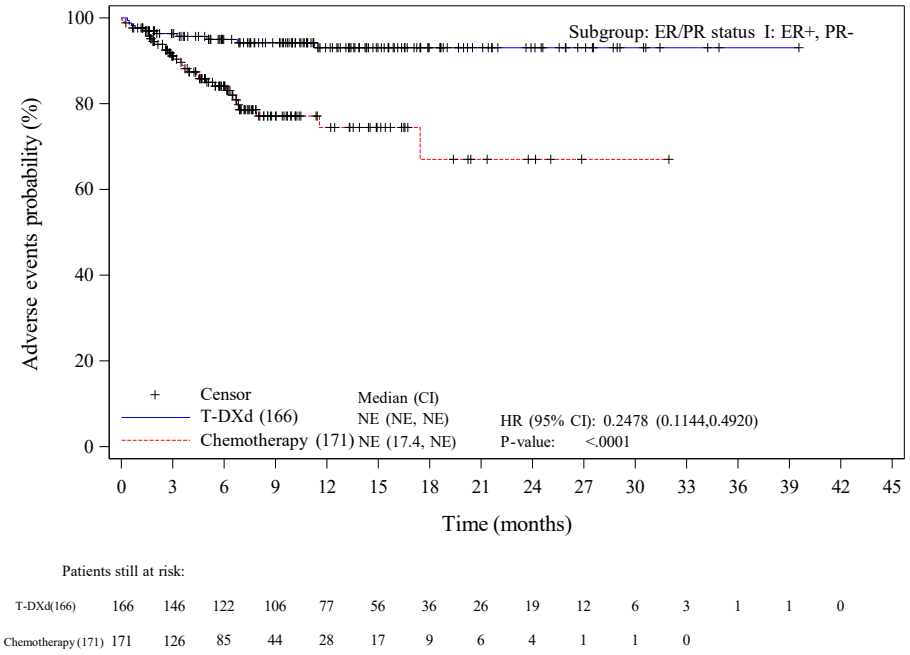
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Oedema peripheral



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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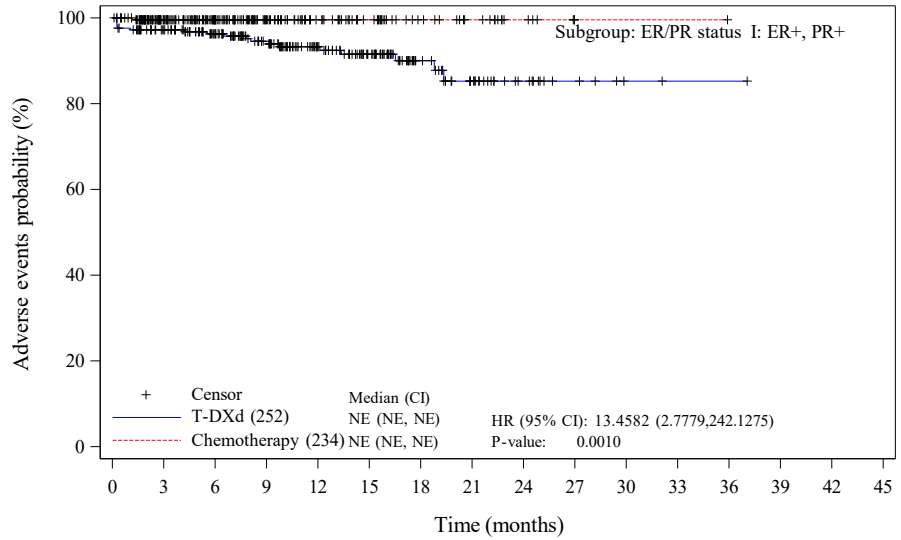
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia



Patients still at risk:

T-DXd(252)	252	225	191	152	112	83	42	26	13	6	2	1	1	0
Chemotherapy (234)	234	171	122	82	54	38	22	15	7	1	1	1	0	

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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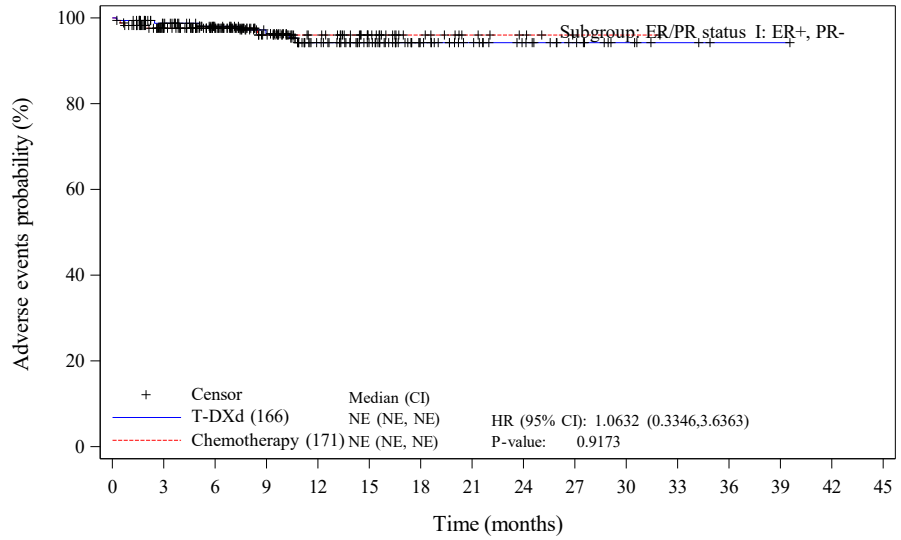
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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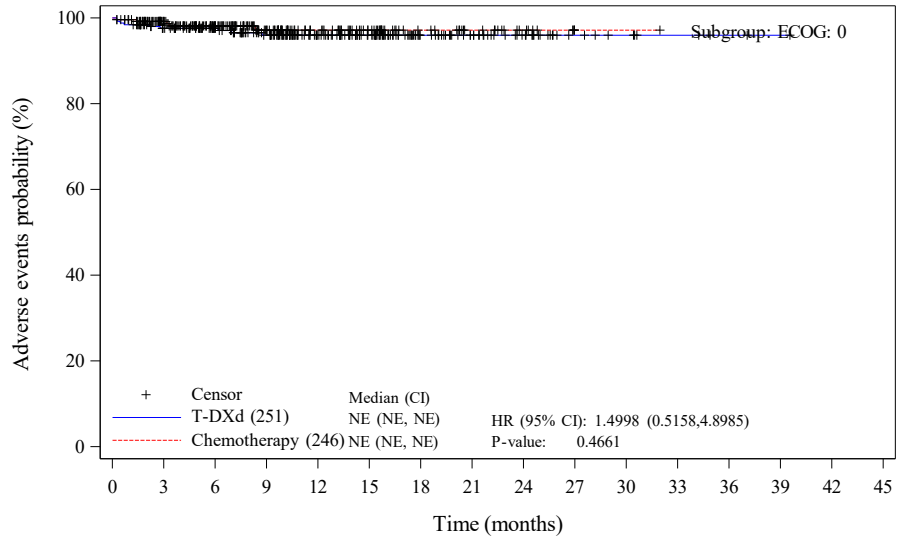
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Lymphopenia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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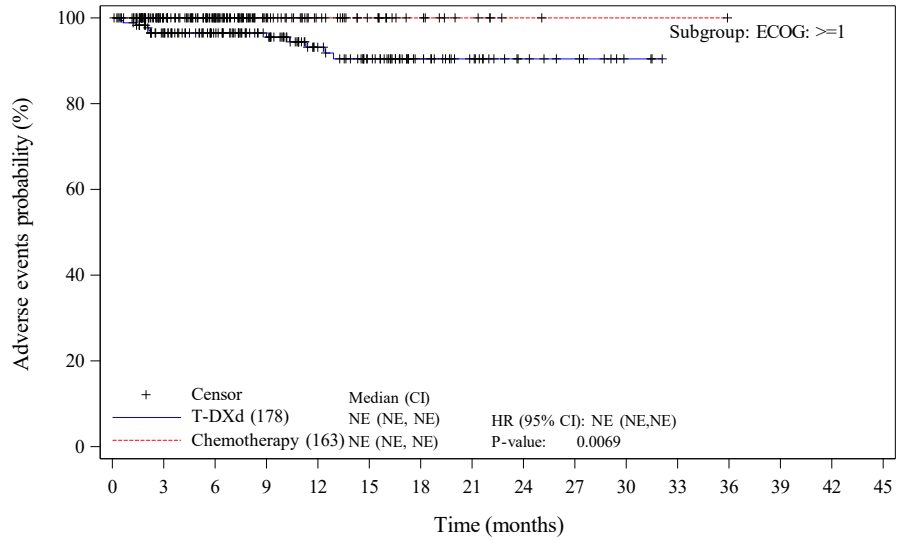
Figure 2.29.2 Adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Lymphopenia



Patients still at risk:

T-DXd(178)	178	151	125	100	70	54	32	22	12	9	3	0
Chemotherapy (163)	163	119	85	47	29	19	11	6	2	1	1	1	0

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Tabelle 2.30.1 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT mit Inzidenz ≥5 % in mindestens einem Arm – SAF

Table 2.30.1 Serious adverse events by SOC and PT with incidence ≥ 5% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Infections and infestations						
All (any PT)	28 (6.5)	NE [NE; NE]	20 (4.8)	NE [23.3; NE]	0.9080 [0.5091; 1.6478] 0.7457	0.7456

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable

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Tabelle 2.30.2 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT mit Inzidenz ≥5 % in mindestens einem Arm – Subgruppenanalyse – SAF

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D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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Table 2.30.2 Serious adverse events by SOC and PT with incidence >= 5% in at least one arm - Subgroup Analysis - Safety Analysis Set

No output displayed as treatment difference p-value >= 0.05 on population level analyses.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Tabelle 2.30.3 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT mit Inzidenz ≥5 % in mindestens einem Arm – Subgruppenanalyse – Interaktions-p-Wert <0,05 – SAF

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Data Intelligence - Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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Table 2.30.3 Serious adverse events by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

No output displayed as treatment difference p-value >= 0.05 on population level analyses.

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Abbildung 2.30.1 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT mit Inzidenz ≥5 % in mindestens einem Arm – Kaplan-Meier-Plot – SAF

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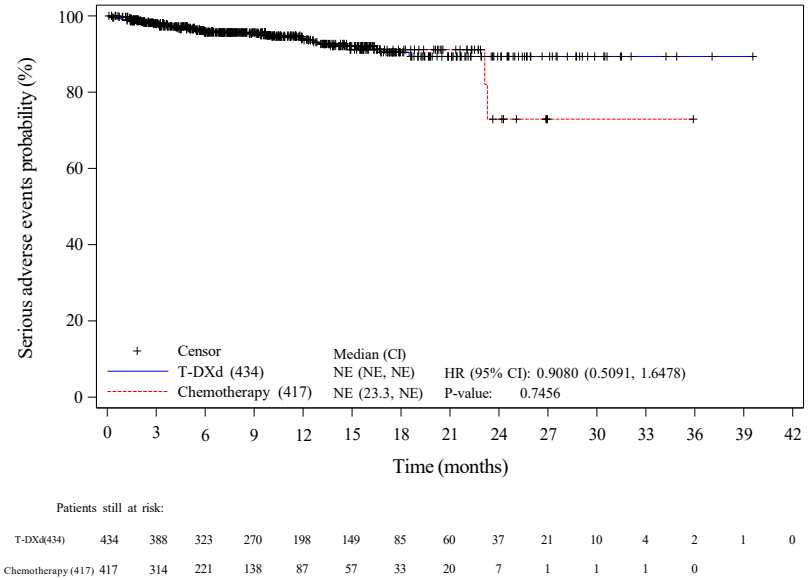
Figure 2.30.1 Serious adverse events by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Run date: 17DEC2024 4:19; Program name: F.2.30.1_5PCTSRTEAE_SAF.sas; Output name: F.2.30.1_5PCTSRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.30.2 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT mit Inzidenz ≥5 % in mindestens einem Arm – Kaplan-Meier-Plot – Analyse nach Subgruppe – SAF

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Figure 2.30.2 Serious adverse events by SOC and PT with incidence ≥ 5% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set

No output displayed as treatment difference p-value >= 0.05 on population level analyses.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 09DEC2024 11:04; Program name: F.2.30.2_5PCTSRTEAE_SAF_SUB.sas; Output name: F.2.30.2_5PCTSRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.31.1 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – SAF

Table 2.31.1 Serious adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Infections and infestations						
All (any PT)	28 (6.5)	NE [NE; NE]	20 (4.8)	NE [23.3; NE]	0.9080 [0.5091; 1.6478] 0.7457	0.7456
SOC: Respiratory, thoracic and mediastinal disorders						
All (any PT)	21 (4.8)	NE [NE; NE]	9 (2.2)	NE [NE; NE]	1.5992 [0.7489; 3.7012] 0.2432	0.2392
SOC: Gastrointestinal disorders						
All (any PT)	13 (3.0)	NE [NE; NE]	11 (2.6)	NE [NE; NE]	0.9800 [0.4365; 2.2397] 0.9608	0.9610
SOC: Metabolism and nutrition disorders						
All (any PT)	9 (2.1)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	1.3580 [0.4641; 4.4556] 0.5867	0.5853

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable

Table 2.31.1 Serious adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Blood and lymphatic system disorders						
All (any PT)	8 (1.8)	NE [NE; NE]	3 (0.7)	NE [NE; NE]	2.2780 [0.6578; 10.4116] 0.2245	0.2117
SOC: Nervous system disorders						
All (any PT)	6 (1.4)	NE [NE; NE]	8 (1.9)	NE [NE; NE]	0.5212 [0.1696; 1.5170] 0.2333	0.2256

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable

Tabelle 2.31.2 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Subgruppenanalyse – SAF

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Table 2.31.2 Serious adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

No output displayed as treatment difference p-value >= 0.05 on population level analyses.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 09DEC2024 10:30; Program name: T.2.31.2_10SRTEAE_SAF_SUB.sas; Output name: T.2.31.2_10SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.31.3 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Subgruppenanalyse – Interaktions-p-Wert <0,05 – SAF

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Table 2.31.3 Serious adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

No output displayed as treatment difference p-value >= 0.05 on population level analyses.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 09DEC2024 10:35; Program name: T.2.31.3_10SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.31.3_10SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.31.1 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Kaplan-Meier-Plot – SAF

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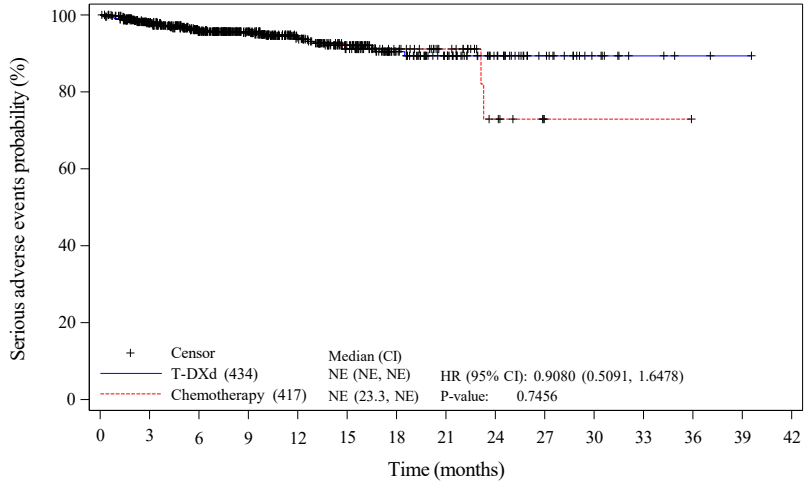
Figure 2.31.1 Serious adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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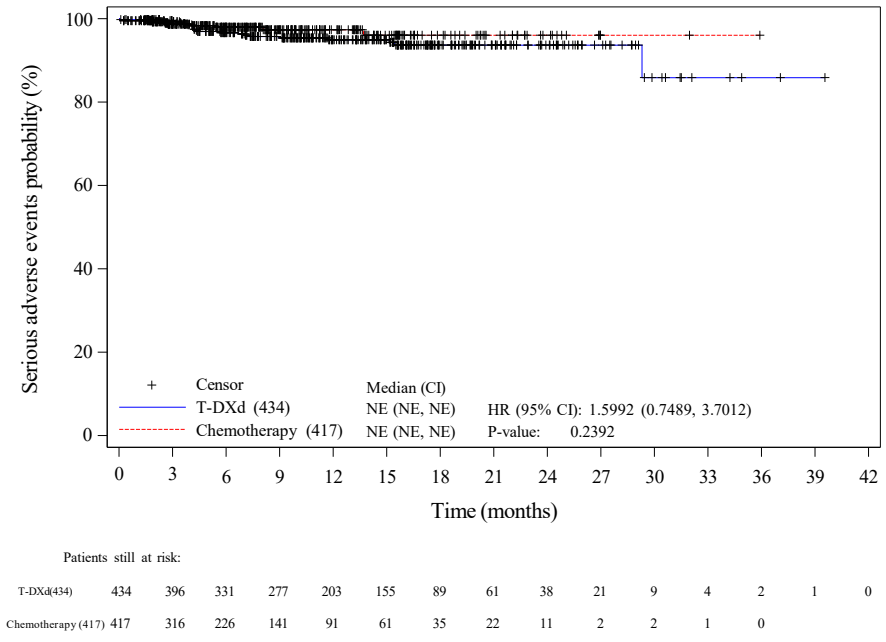
Run date: 11DEC2024 6:10; Program name: F.2.31.1_10SRTEAE_SAF.sas; Output name: F.2.31.1_10SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

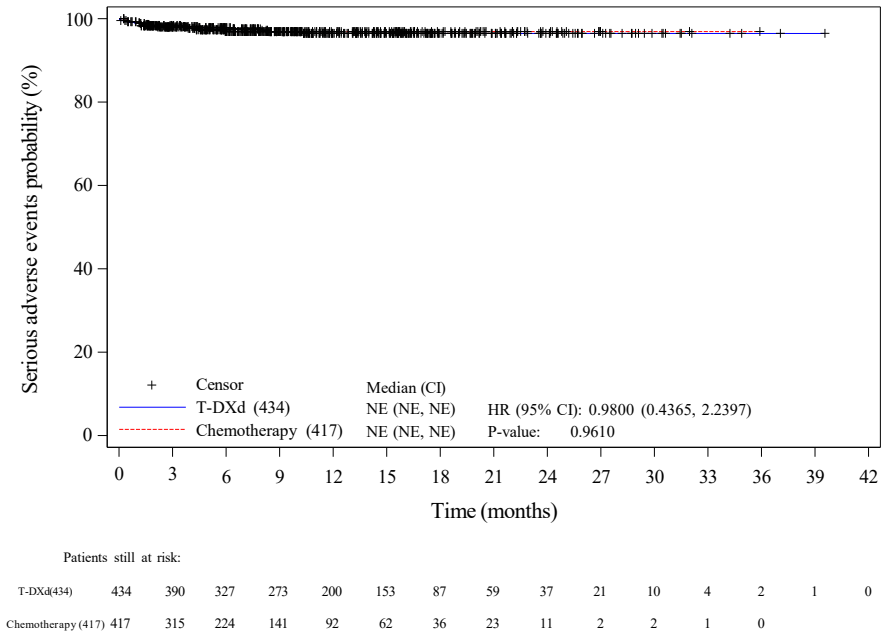
Figure 2.31.1 Serious adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 11DEC2024 6:10; Program name: F.2.31.1_10SRTEAE_SAF.sas; Output name: F.2.31.1_10SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.31.1 Serious adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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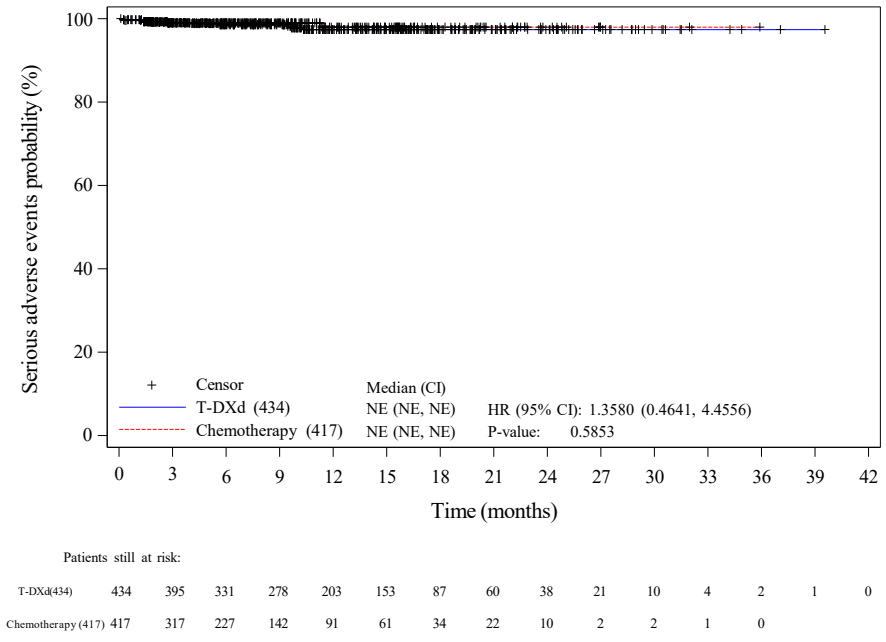
Run date: 11DEC2024 6:10; Program name: F.2.31.1_10SRTEAE_SAF.sas; Output name: F.2.31.1_10SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

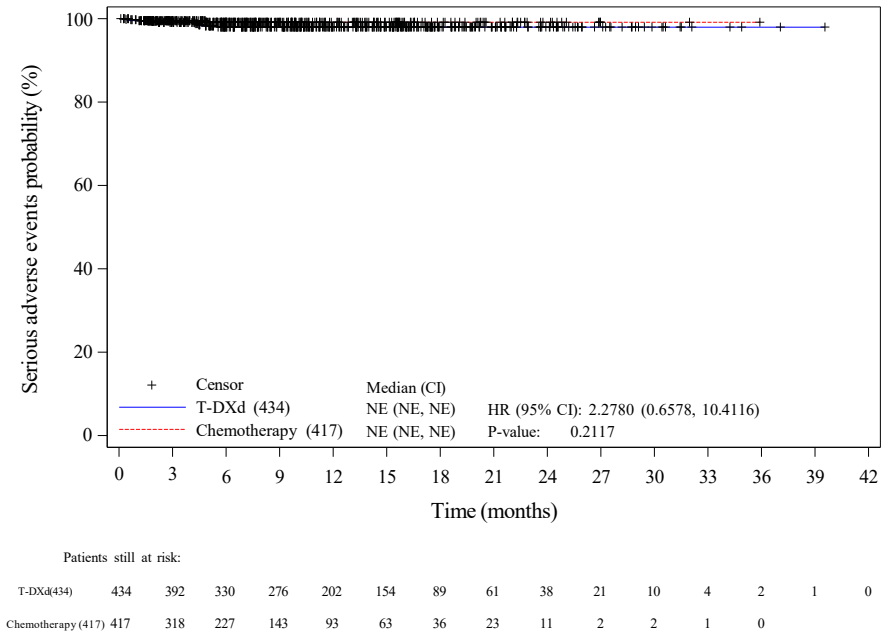
Figure 2.31.1 Serious adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 11DEC2024 6:10; Program name: F.2.31.1_10SRTEAE_SAF.sas; Output name: F.2.31.1_10SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

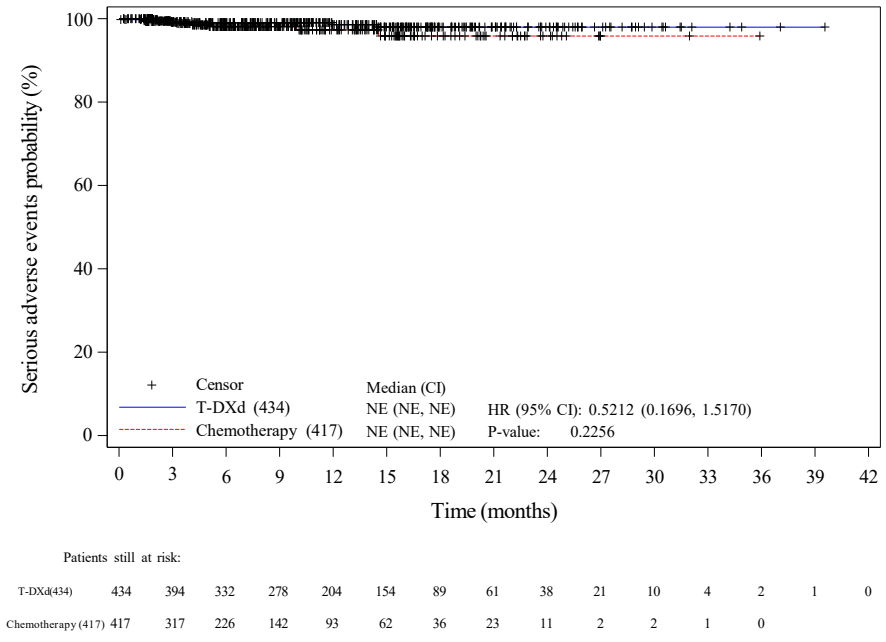
Figure 2.31.1 Serious adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 11DEC2024 6:10; Program name: F.2.31.1_10SRTEAE_SAF.sas; Output name: F.2.31.1_10SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.31.1 Serious adverse events by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 11DEC2024 6:10; Program name: F.2.31.1_10SRTEAE_SAF.sas; Output name: F.2.31.1_10SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.31.2 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Kaplan-Meier-Plot – Analyse nach Subgruppe – SAF

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Figure 2.31.2 Serious adverse events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set

No output displayed as treatment difference p-value >= 0.05 on population level analyses.

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Tabelle 2.32.1 Unerwünschte Ereignisse mit CTCAE-Grad 3 oder höher nach SOC und PT mit Inzidenz ≥5 % in mindestens einem Arm – SAF

Table 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence ≥ 5% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations						
All (any PT)	101 (23.3)	NE [NE; NE]	46 (11.0)	NE [NE; NE]	1.8843 [1.3354; 2.6994] 0.0004	0.0003
PT: Neutrophil count decreased	60 (13.8)	NE [NE; NE]	36 (8.6)	NE [NE; NE]	1.3917 [0.9216; 2.1301] 0.1207	0.1210
PT: White blood cell count decreased	25 (5.8)	NE [NE; NE]	20 (4.8)	NE [NE; NE]	1.0409 [0.5773; 1.9008] 0.8943	0.8943
SOC: Blood and lymphatic system disorders						
All (any PT)	72 (16.6)	NE [NE; NE]	53 (12.7)	NE [NE; NE]	1.1399 [0.7999; 1.6345] 0.4715	0.4719
PT: Anaemia	38 (8.8)	NE [NE; NE]	18 (4.3)	NE [NE; NE]	1.7305 [0.9992; 3.1109] 0.0567	0.0537
PT: Neutropenia	37 (8.5)	NE [NE; NE]	35 (8.4)	NE [NE; NE]	0.8942 [0.5620; 1.4268] 0.6366	0.6396

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 09DEC2024 10:09; Program name: T_2_32_1_GR35PCTSRTEAE_SAF.sas; Output name: T_2_32_1_GR35PCTSRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Table 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence ≥ 5% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders						
All (any PT)	33 (7.6)	NE [NE; NE]	13 (3.1)	NE [NE; NE]	1.9505 [1.0451; 3.8638] 0.0433	0.0396
SOC: Gastrointestinal disorders						
All (any PT)	31 (7.1)	NE [NE; NE]	23 (5.5)	NE [NE; NE]	1.1409 [0.6655; 1.9835] 0.6341	0.6339
SOC: Infections and infestations						
All (any PT)	27 (6.2)	NE [NE; NE]	25 (6.0)	NE [23.3; NE]	0.6700 [0.3847; 1.1707] 0.1560	0.1536
SOC: General disorders and administration site conditions						
All (any PT)	24 (5.5)	NE [NE; NE]	14 (3.4)	NE [NE; NE]	1.4130 [0.7369; 2.8134] 0.3074	0.3054

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable

Table 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence ≥ 5% in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders						
All (any PT)	0 (0.0)	NE [NE; NE]	36 (8.6)	NE [NE; NE]	NE [NE; NE]	<.0001
PT: Palmar-plantar erythrodysaesthesia syndrome	0 (0.0)	NE [NE; NE]	31 (7.4)	NE [NE; NE]	NE [NE; NE]	<.0001

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable

Tabelle 2.32.2 Unerwünschte Ereignisse mit CTCAE-Grad 3 oder höher nach SOC und PT mit Inzidenz ≥5 % in mindestens einem Arm – Subgruppenanalyse – SAF

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: All (any PT)						
Age at randomization						0.5705
<65 years of age	72 / 301 (23.9)	NE [NE; NE]	34 / 285 (11.9)	NE [23.5; NE]	1.8032 [1.2058; 2.7503] 0.0044	
>=65 years of age	29 / 133 (21.8)	28.1 [28.1; NE]	12 / 132 (9.1)	NE [NE; NE]	2.1207 [1.1033; 4.3374] 0.0258	
Race						0.1230
Asian	62 / 153 (40.5)	28.1 [11.9; NE]	31 / 147 (21.1)	NE [23.5; NE]	1.8532 [1.2111; 2.8940] 0.0047	
White	33 / 231 (14.3)	NE [NE; NE]	15 / 223 (6.7)	NE [NE; NE]	1.7612 [0.9705; 3.3481] 0.0671	
Other	6 / 50 (12.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:49; Program name: T.2.32.2_GR35PCTSRTEAE_SAF_SUB.sas; Output name: T.2.32.2_GR35PCTSRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7452
Asia	59 / 148 (39.9)	28.1 [11.9; NE]	31 / 144 (21.5)	NE [23.5; NE]	1.7850 [1.1617; 2.7960] 0.0085	
Europe	34 / 227 (15.0)	NE [NE; NE]	11 / 206 (5.3)	NE [NE; NE]	2.3419 [1.2195; 4.8633] 0.0121	
Rest of the World	8 / 59 (13.6)	NE [NE; NE]	4 / 67 (6.0)	NE [NE; NE]	1.9303 [0.6017; 7.2852] 0.2809	
HER2 IHC expression						0.4660
IHC 1+	54 / 239 (22.6)	NE [28.1; NE]	28 / 226 (12.4)	NE [NE; NE]	1.6202 [1.0318; 2.5993] 0.0375	
IHC 2+/ISH-	29 / 116 (25.0)	NE [NE; NE]	9 / 115 (7.8)	NE [NE; NE]	2.8171 [1.3795; 6.3429] 0.0050	
IHC >0 <1+	17 / 76 (22.4)	NE [21.2; NE]	9 / 74 (12.2)	NE [23.5; NE]	1.8281 [0.8326; 4.2959] 0.1381	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5264
Yes	88 / 393 (22.4)	NE [NE; NE]	41 / 377 (10.9)	NE [NE; NE]	1.8073 [1.2529; 2.6505] 0.0016	
No	13 / 41 (31.7)	NE [11.8; NE]	5 / 40 (12.5)	NE [NE; NE]	2.6620 [1.0034; 8.2998] 0.0532	
Prior Taxane Use In The Non-Metastatic Setting						0.6865
Yes	46 / 177 (26.0)	NE [NE; NE]	20 / 172 (11.6)	NE [NE; NE]	2.1214 [1.2708; 3.6734] 0.0043	
No	55 / 257 (21.4)	NE [28.1; NE]	26 / 245 (10.6)	NE [23.5; NE]	1.7234 [1.0879; 2.8005] 0.0217	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4477
1	14 / 65 (21.5)	NE [NE; NE]	5 / 79 (6.3)	NE [16.3; NE]	3.1501 [1.1843; 9.8464] 0.0225	
2	64 / 293 (21.8)	NE [NE; NE]	32 / 281 (11.4)	NE [NE; NE]	1.6878 [1.1108; 2.6162] 0.0150	
>=3	22 / 75 (29.3)	NE [28.1; NE]	9 / 56 (16.1)	23.5 [NE; NE]	1.5951 [0.7506; 3.6779] 0.2447	
ER/PR status I						0.4933
ER+, PR+	52 / 252 (20.6)	NE [NE; NE]	25 / 234 (10.7)	NE [23.5; NE]	1.6940 [1.0608; 2.7781] 0.0288	
ER+, PR-	46 / 166 (27.7)	NE [28.1; NE]	20 / 171 (11.7)	NE [NE; NE]	2.1594 [1.2879; 3.7508] 0.0037	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5322
ER <=10%	6 / 21 (28.6)	NE [4.9; NE]	1 / 14 (7.1)	NE [NE; NE]	4.1454 [0.7056; 78.4118] 0.1577	
ER >10%	82 / 362 (22.7)	NE [NE; NE]	35 / 343 (10.2)	NE [NE; NE]	2.0161 [1.3661; 3.0389] 0.0004	
Positive	13 / 51 (25.5)	21.2 [16.9; NE]	10 / 60 (16.7)	NE [NE; NE]	1.2833 [0.5631; 3.0130] 0.5452	
Endocrine Resistance						0.7093
Primary	28 / 127 (22.0)	NE [NE; NE]	16 / 137 (11.7)	NE [NE; NE]	1.7034 [0.9282; 3.2327] 0.0885	
Secondary	73 / 307 (23.8)	NE [28.1; NE]	30 / 279 (10.8)	NE [23.5; NE]	1.9678 [1.2972; 3.0620] 0.0016	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:49; Program name: T.2.32.2_GR35PCTSRTEAE_SAF_SUB.sas; Output name: T.2.32.2_GR35PCTSRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0477
Capecitabine	56 / 265 (21.1)	NE [28.1; NE]	16 / 249 (6.4)	NE [NE; NE]	2.9507 [1.7301; 5.3267] 0.0001	
Nab-Paclitaxel	30 / 103 (29.1)	NE [NE; NE]	19 / 101 (18.8)	NE [NE; NE]	1.5114 [0.8561; 2.7345] 0.1581	
Paclitaxel	15 / 66 (22.7)	NE [NE; NE]	11 / 67 (16.4)	NE [NE; NE]	1.0490 [0.4718; 2.3875] 0.9075	
Prior anthracycline use						0.3441
Yes	45 / 197 (22.8)	NE [NE; NE]	25 / 198 (12.6)	NE [NE; NE]	1.6324 [1.0072; 2.7059] 0.0486	
No	56 / 237 (23.6)	NE [28.1; NE]	21 / 219 (9.6)	NE [23.5; NE]	2.1856 [1.3403; 3.7004] 0.0019	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.3421
Yes	69 / 294 (23.5)	NE [NE; NE]	27 / 275 (9.8)	NE [NE; NE]	2.2208 [1.4386; 3.5282] 0.0003	
No	32 / 140 (22.9)	28.1 [28.1; NE]	19 / 142 (13.4)	NE [23.5; NE]	1.4175 [0.8050; 2.5613] 0.2327	
ECOG						0.3799
0	53 / 251 (21.1)	NE [28.1; NE]	21 / 246 (8.5)	NE [NE; NE]	2.1972 [1.3405; 3.7335] 0.0019	
>=1	48 / 178 (27.0)	NE [21.2; NE]	24 / 163 (14.7)	NE [NE; NE]	1.6455 [1.0166; 2.7351] 0.0450	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: All (any PT)						
Age at randomization						0.5863
<65 years of age	17 / 301 (5.6)	NE [NE; NE]	5 / 285 (1.8)	NE [NE; NE]	2.3474 [0.9156; 7.2062] 0.0882	
>=65 years of age	16 / 133 (12.0)	NE [NE; NE]	8 / 132 (6.1)	NE [NE; NE]	1.7780 [0.7790; 4.3987] 0.1794	
Race						0.2707
Asian	19 / 153 (12.4)	NE [NE; NE]	7 / 147 (4.8)	NE [NE; NE]	2.1761 [0.9495; 5.5974] 0.0736	
White	13 / 231 (5.6)	NE [NE; NE]	4 / 223 (1.8)	NE [NE; NE]	2.5856 [0.9055; 9.2384] 0.0875	
Other	1 / 50 (2.0)	NE [NE; NE]	2 / 47 (4.3)	NE [NE; NE]	0.2343 [0.0095; 2.9270] 0.2556	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2286
Asia	19 / 148 (12.8)	NE [NE; NE]	7 / 144 (4.9)	NE [NE; NE]	2.2133 [0.9667; 5.6895] 0.0670	
Europe	11 / 227 (4.8)	NE [NE; NE]	6 / 206 (2.9)	NE [NE; NE]	1.3981 [0.5252; 4.0946] 0.5114	
Rest of the World	3 / 59 (5.1)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
HER2 IHC expression						0.8156
IHC 1+	18 / 239 (7.5)	NE [NE; NE]	7 / 226 (3.1)	NE [NE; NE]	1.9344 [0.8342; 5.0143] 0.1355	
IHC 2+/ISH-	8 / 116 (6.9)	NE [NE; NE]	4 / 115 (3.5)	NE [NE; NE]	1.4480 [0.4432; 5.5286] 0.5517	
IHC >0 <1+	7 / 76 (9.2)	NE [NE; NE]	2 / 74 (2.7)	NE [NE; NE]	3.0119 [0.7238; 20.2700] 0.1497	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6231
Yes	29 / 393 (7.4)	NE [NE; NE]	12 / 377 (3.2)	NE [NE; NE]	1.8642 [0.9687; 3.8181] 0.0678	
No	4 / 41 (9.8)	NE [25.8; NE]	1 / 40 (2.5)	NE [NE; NE]	2.5939 [0.3289; 52.6461] 0.3935	
Prior Taxane Use In The Non-Metastatic Setting						0.0727
Yes	11 / 177 (6.2)	NE [NE; NE]	8 / 172 (4.7)	NE [NE; NE]	1.1178 [0.4478; 2.9100] 0.8112	
No	22 / 257 (8.6)	NE [NE; NE]	5 / 245 (2.0)	NE [NE; NE]	3.3244 [1.3529; 9.9738] 0.0107	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1481
1	3 / 65 (4.6)	NE [NE; NE]	2 / 79 (2.5)	NE [NE; NE]	1.5314 [0.2482; 11.7891] 0.6421	
2	24 / 293 (8.2)	NE [NE; NE]	11 / 281 (3.9)	NE [NE; NE]	1.6434 [0.8178; 3.5143] 0.1726	
>=3	6 / 75 (8.0)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER/PR status I						0.0534
ER+, PR+	23 / 252 (9.1)	NE [NE; NE]	5 / 234 (2.1)	NE [NE; NE]	3.5004 [1.4343; 10.4627] 0.0072	
ER+, PR-	8 / 166 (4.8)	NE [NE; NE]	7 / 171 (4.1)	NE [NE; NE]	0.8771 [0.3052; 2.5572] 0.8050	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.0558
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER >10%	30 / 362 (8.3)	NE [NE; NE]	8 / 343 (2.3)	NE [NE; NE]	2.8790 [1.3754; 6.7734] 0.0059	
Positive	2 / 51 (3.9)	NE [NE; NE]	5 / 60 (8.3)	NE [NE; NE]	0.3592 [0.0510; 1.6895] 0.2059	
Endocrine Resistance						0.6138
Primary	9 / 127 (7.1)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	1.5014 [0.5120; 4.9335] 0.4675	
Secondary	24 / 307 (7.8)	NE [NE; NE]	8 / 279 (2.9)	NE [NE; NE]	2.2309 [1.0384; 5.3303] 0.0454	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0957
Capecitabine	23 / 265 (8.7)	NE [NE; NE]	10 / 249 (4.0)	NE [NE; NE]	1.7509 [0.8529; 3.8656] 0.1362	
Nab-Paclitaxel	9 / 103 (8.7)	NE [25.8; NE]	1 / 101 (1.0)	NE [NE; NE]	6.7954 [1.2246; 126.6960] 0.0379	
Paclitaxel	1 / 66 (1.5)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	0.4813 [0.0224; 5.0318] 0.5419	
Prior anthracycline use						0.4113
Yes	13 / 197 (6.6)	NE [NE; NE]	7 / 198 (3.5)	NE [NE; NE]	1.4812 [0.5990; 3.9773] 0.4041	
No	20 / 237 (8.4)	NE [NE; NE]	6 / 219 (2.7)	NE [NE; NE]	2.5011 [1.0566; 6.8771] 0.0433	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.4703
Yes	20 / 294 (6.8)	NE [NE; NE]	9 / 275 (3.3)	NE [NE; NE]	1.6537 [0.7678; 3.8483] 0.2104	
No	13 / 140 (9.3)	NE [NE; NE]	4 / 142 (2.8)	NE [NE; NE]	2.6963 [0.9454; 9.6266] 0.0731	
ECOG						0.3295
0	15 / 251 (6.0)	NE [NE; NE]	4 / 246 (1.6)	NE [NE; NE]	2.6215 [0.9410; 9.2609] 0.0782	
>=1	17 / 178 (9.6)	NE [NE; NE]	8 / 163 (4.9)	NE [NE; NE]	1.7069 [0.7558; 4.1983] 0.2090	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)						
Age at randomization						0.9993
<65 years of age	0 / 301 (0.0)	NE [NE; NE]	19 / 285 (6.7)	NE [NE; NE]	NE [NE; NE] NE	
>=65 years of age	0 / 133 (0.0)	NE [NE; NE]	17 / 132 (12.9)	NE [NE; NE]	NE [NE; NE] NE	
Race						1.0000
Asian	0 / 153 (0.0)	NE [NE; NE]	11 / 147 (7.5)	NE [NE; NE]	NE [NE; NE] NE	
White	0 / 231 (0.0)	NE [NE; NE]	21 / 223 (9.4)	NE [NE; NE]	NE [NE; NE] NE	
Other	0 / 50 (0.0)	NE [NE; NE]	4 / 47 (8.5)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						1.0000
Asia	0 / 148 (0.0)	NE [NE; NE]	12 / 144 (8.3)	NE [NE; NE]	NE [NE; NE] NE	
Europe	0 / 227 (0.0)	NE [NE; NE]	15 / 206 (7.3)	NE [NE; NE]	NE [NE; NE] NE	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	9 / 67 (13.4)	NE [14.4; NE]	NE [NE; NE] NE	
HER2 IHC expression						1.0000
IHC 1+	0 / 239 (0.0)	NE [NE; NE]	22 / 226 (9.7)	NE [NE; NE]	NE [NE; NE] NE	
IHC 2+/ISH-	0 / 116 (0.0)	NE [NE; NE]	6 / 115 (5.2)	NE [NE; NE]	NE [NE; NE] NE	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	8 / 74 (10.8)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9998
Yes	0 / 393 (0.0)	NE [NE; NE]	33 / 377 (8.8)	NE [NE; NE]	NE [NE; NE] NE	
No	0 / 41 (0.0)	NE [NE; NE]	3 / 40 (7.5)	NE [NE; NE]	NE [NE; NE] NE	
Prior Taxane Use In The Non-Metastatic Setting						0.9999
Yes	0 / 177 (0.0)	NE [NE; NE]	16 / 172 (9.3)	NE [NE; NE]	NE [NE; NE] NE	
No	0 / 257 (0.0)	NE [NE; NE]	20 / 245 (8.2)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						1.0000
1	0 / 65 (0.0)	NE [NE; NE]	6 / 79 (7.6)	NE [NE; NE]	NE [NE; NE] NE	
2	0 / 293 (0.0)	NE [NE; NE]	26 / 281 (9.3)	NE [NE; NE]	NE [NE; NE] NE	
>=3	0 / 75 (0.0)	NE [NE; NE]	4 / 56 (7.1)	NE [NE; NE]	NE [NE; NE] NE	
ER/PR status I						0.9998
ER+, PR+	0 / 252 (0.0)	NE [NE; NE]	18 / 234 (7.7)	NE [NE; NE]	NE [NE; NE] NE	
ER+, PR-	0 / 166 (0.0)	NE [NE; NE]	17 / 171 (9.9)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						1.0000
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER >10%	0 / 362 (0.0)	NE [NE; NE]	28 / 343 (8.2)	NE [NE; NE]	NE [NE; NE] NE	
Positive	0 / 51 (0.0)	NE [NE; NE]	8 / 60 (13.3)	NE [NE; NE]	NE [NE; NE] NE	
Endocrine Resistance						0.9993
Primary	0 / 127 (0.0)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	NE [NE; NE] NE	
Secondary	0 / 307 (0.0)	NE [NE; NE]	31 / 279 (11.1)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						NE
Capecitabine	0 / 265 (0.0)	NE [NE; NE]	33 / 249 (13.3)	NE [NE; NE]	NE [NE; NE] NE	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	1 / 101 (1.0)	NE [NE; NE]	NE [NE; NE] NE	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	NE [NE; NE] NE	
Prior anthracycline use						0.9998
Yes	0 / 197 (0.0)	NE [NE; NE]	19 / 198 (9.6)	NE [NE; NE]	NE [NE; NE] NE	
No	0 / 237 (0.0)	NE [NE; NE]	17 / 219 (7.8)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9997
Yes	0 / 294 (0.0)	NE [NE; NE]	26 / 275 (9.5)	NE [NE; NE]	NE [NE; NE] NE	
No	0 / 140 (0.0)	NE [NE; NE]	10 / 142 (7.0)	NE [NE; NE]	NE [NE; NE] NE	
ECOG						0.9996
0	0 / 251 (0.0)	NE [NE; NE]	25 / 246 (10.2)	NE [NE; NE]	NE [NE; NE] NE	
>=1	0 / 178 (0.0)	NE [NE; NE]	11 / 163 (6.7)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome						
Age at randomization						NE
<65 years of age	0 / 301 (0.0)	NE [NE; NE]	15 / 285 (5.3)	NE [NE; NE]	NE [NE; NE] NE	
>=65 years of age	0 / 133 (0.0)	NE [NE; NE]	16 / 132 (12.1)	NE [NE; NE]	NE [NE; NE] NE	
Race						1.0000
Asian	0 / 153 (0.0)	NE [NE; NE]	10 / 147 (6.8)	NE [NE; NE]	NE [NE; NE] NE	
White	0 / 231 (0.0)	NE [NE; NE]	18 / 223 (8.1)	NE [NE; NE]	NE [NE; NE] NE	
Other	0 / 50 (0.0)	NE [NE; NE]	3 / 47 (6.4)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:49; Program name: T.2.32.2_GR35PCTSRTEAE_SAF_SUB.sas; Output name: T.2.32.2_GR35PCTSRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						NE
Asia	0 / 148 (0.0)	NE [NE; NE]	11 / 144 (7.6)	NE [NE; NE]	NE [NE; NE] NE	
Europe	0 / 227 (0.0)	NE [NE; NE]	11 / 206 (5.3)	NE [NE; NE]	NE [NE; NE] NE	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	9 / 67 (13.4)	NE [14.4; NE]	NE [NE; NE] NE	
HER2 IHC expression						1.0000
IHC 1+	0 / 239 (0.0)	NE [NE; NE]	19 / 226 (8.4)	NE [NE; NE]	NE [NE; NE] NE	
IHC 2+/ISH-	0 / 116 (0.0)	NE [NE; NE]	5 / 115 (4.3)	NE [NE; NE]	NE [NE; NE] NE	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	7 / 74 (9.5)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9999
Yes	0 / 393 (0.0)	NE [NE; NE]	28 / 377 (7.4)	NE [NE; NE]	NE [NE; NE] NE	
No	0 / 41 (0.0)	NE [NE; NE]	3 / 40 (7.5)	NE [NE; NE]	NE [NE; NE] NE	
Prior Taxane Use In The Non-Metastatic Setting						0.9998
Yes	0 / 177 (0.0)	NE [NE; NE]	14 / 172 (8.1)	NE [NE; NE]	NE [NE; NE] NE	
No	0 / 257 (0.0)	NE [NE; NE]	17 / 245 (6.9)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						1.0000
1	0 / 65 (0.0)	NE [NE; NE]	5 / 79 (6.3)	NE [NE; NE]	NE [NE; NE] NE	
2	0 / 293 (0.0)	NE [NE; NE]	22 / 281 (7.8)	NE [NE; NE]	NE [NE; NE] NE	
>=3	0 / 75 (0.0)	NE [NE; NE]	4 / 56 (7.1)	NE [NE; NE]	NE [NE; NE] NE	
ER/PR status I						1.0000
ER+, PR+	0 / 252 (0.0)	NE [NE; NE]	17 / 234 (7.3)	NE [NE; NE]	NE [NE; NE] NE	
ER+, PR-	0 / 166 (0.0)	NE [NE; NE]	13 / 171 (7.6)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						1.0000
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
ER >10%	0 / 362 (0.0)	NE [NE; NE]	24 / 343 (7.0)	NE [NE; NE]	NE [NE; NE] NE	
Positive	0 / 51 (0.0)	NE [NE; NE]	7 / 60 (11.7)	NE [NE; NE]	NE [NE; NE] NE	
Endocrine Resistance						0.9994
Primary	0 / 127 (0.0)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	NE [NE; NE] NE	
Secondary	0 / 307 (0.0)	NE [NE; NE]	26 / 279 (9.3)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-Dxd Vs. Each Investigator's Choice Chemotherapy						NE
Capecitabine	0 / 265 (0.0)	NE [NE; NE]	31 / 249 (12.4)	NE [NE; NE]	NE [NE; NE] NE	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	0 / 101 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE] NE	
Prior anthracycline use						0.9997
Yes	0 / 197 (0.0)	NE [NE; NE]	17 / 198 (8.6)	NE [NE; NE]	NE [NE; NE] NE	
No	0 / 237 (0.0)	NE [NE; NE]	14 / 219 (6.4)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9998
Yes	0 / 294 (0.0)	NE [NE; NE]	22 / 275 (8.0)	NE [NE; NE]	NE [NE; NE] NE	
No	0 / 140 (0.0)	NE [NE; NE]	9 / 142 (6.3)	NE [NE; NE]	NE [NE; NE] NE	
ECOG						0.9995
0	0 / 251 (0.0)	NE [NE; NE]	23 / 246 (9.3)	NE [NE; NE]	NE [NE; NE] NE	
>=1	0 / 178 (0.0)	NE [NE; NE]	8 / 163 (4.9)	NE [NE; NE]	NE [NE; NE] NE	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Tabelle 2.32.3 Unerwünschte Ereignisse mit CTCAE-Grad 3 oder höher nach SOC und PT mit Inzidenz ≥5 % in mindestens einem Arm – Subgruppenanalyse – Interaktions-p-Wert <0,05 – SAF

Daiichi Sankyo Europe GmbH
Data Intelligence - Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 18-MAR-2024)

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Table 2.32.3 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Subgroup Anlysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: All (any PT)						
T-Dxd Vs. Each Investigator's Choice Chemotherapy						0.0477
Capecitabine	56 / 265 (21.1)	NE [28.1, NE]	16 / 249 (6.4)	NE [NE, NE]	2.9507 [1.7301, 5.3267] 0.0001	
Nab-Paclitaxel	30 / 103 (29.1)	NE [NE, NE]	19 / 101 (18.8)	NE [NE, NE]	1.5114 [0.8561, 2.7345] 0.1581	
Paclitaxel	15 / 66 (22.7)	NE [NE, NE]	11 / 67 (16.4)	NE [NE, NE]	1.0490 [0.4718, 2.3875] 0.9075	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 13DEC2024 11:15; Program name: T.2.32.3_GR35PCTSRTEAE_SAF_SUB_SIG.sas; Output name: T.2.32.3_GR35PCTSRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.32.1 Unerwünschte Ereignisse mit CTCAE-Grad 3 oder höher nach SOC und PT mit Inzidenz ≥5 % in mindestens einem Arm – Kaplan-Meier-Plot – SAF

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Data Intelligence - Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 2024-03-18)

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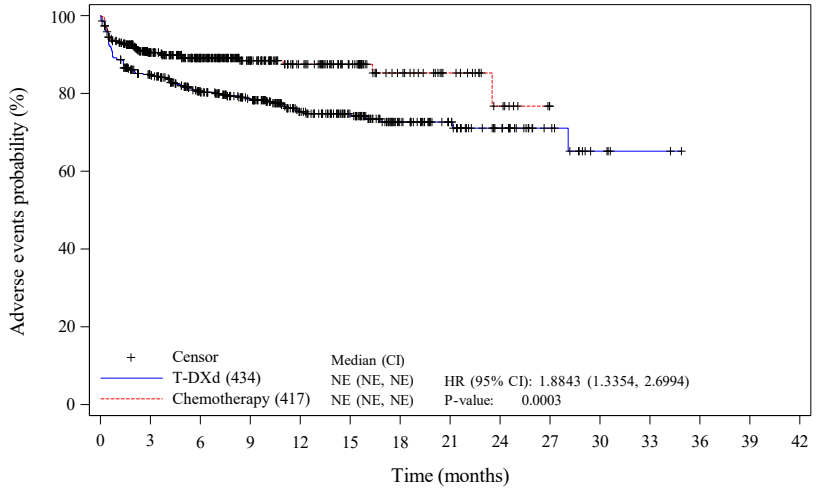
Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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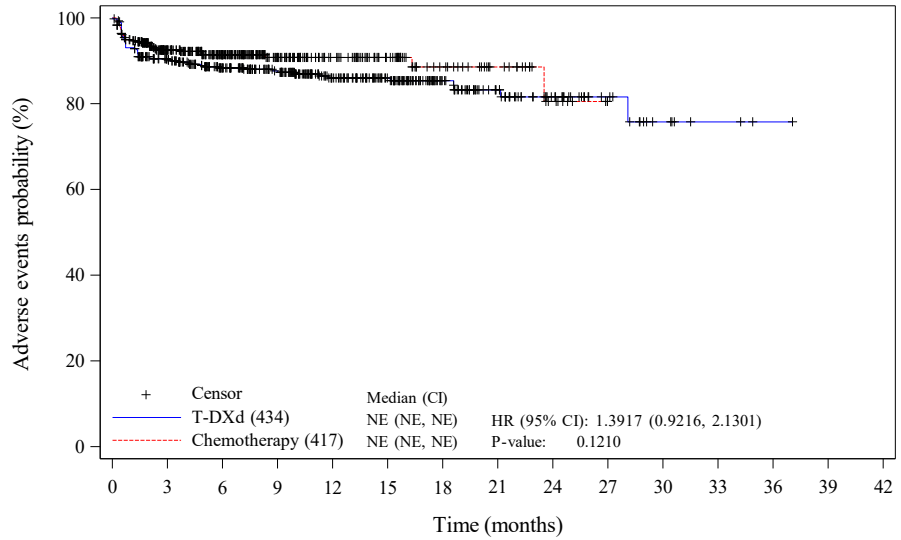
Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Neutrophil count decreased



Patients still at risk:

T-DXd(434)	434	358	295	244	180	139	82	53	31	16	7	3	1	0
Chemotherapy (417)	417	294	208	129	85	57	32	20	8	0				

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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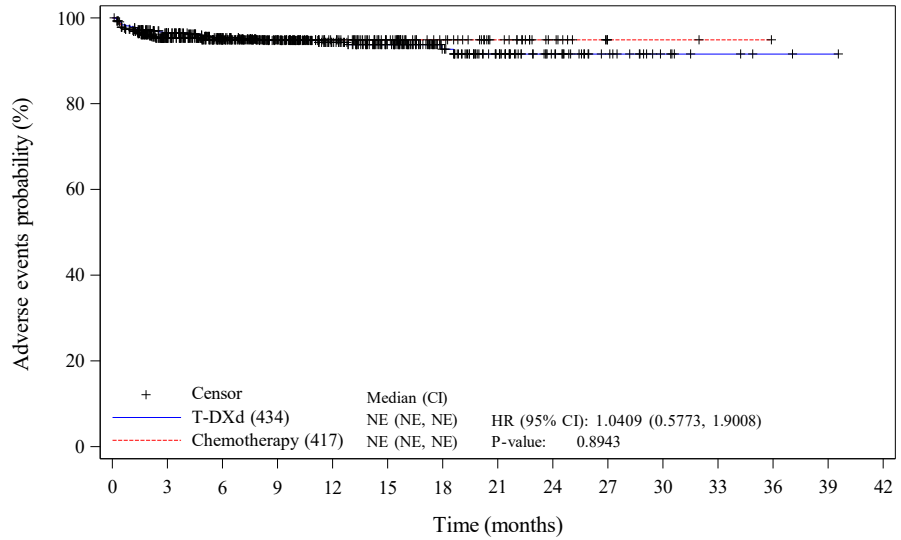
Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: White blood cell count decreased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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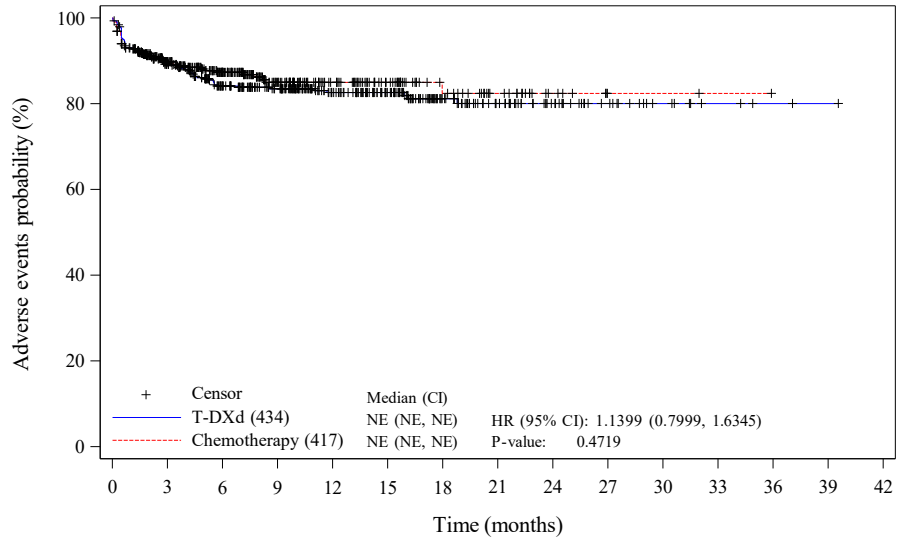
Run date: 17DEC2024 4:21; Program name: F.2.32.1_GR35PCTSRTEAE_SAF.sas; Output name: F.2.32.1_GR35PCTSRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: All (any PT)



Patients still at risk:

T-DXd(434)	434	355	288	242	178	136	77	52	31	18	9	4	2	1	0
Chemotherapy (417)	417	287	200	125	80	54	32	20	8	2	2	1	0		

Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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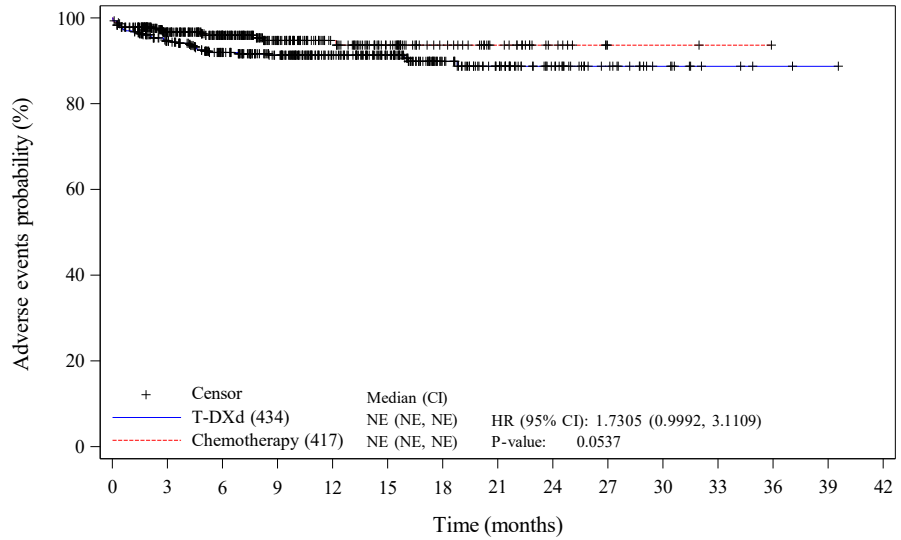
Run date: 17DEC2024 4:21; Program name: F.2.32.1_GR35PCTSRTEAE_SAF.sas; Output name: F.2.32.1_GR35PCTSRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Anaemia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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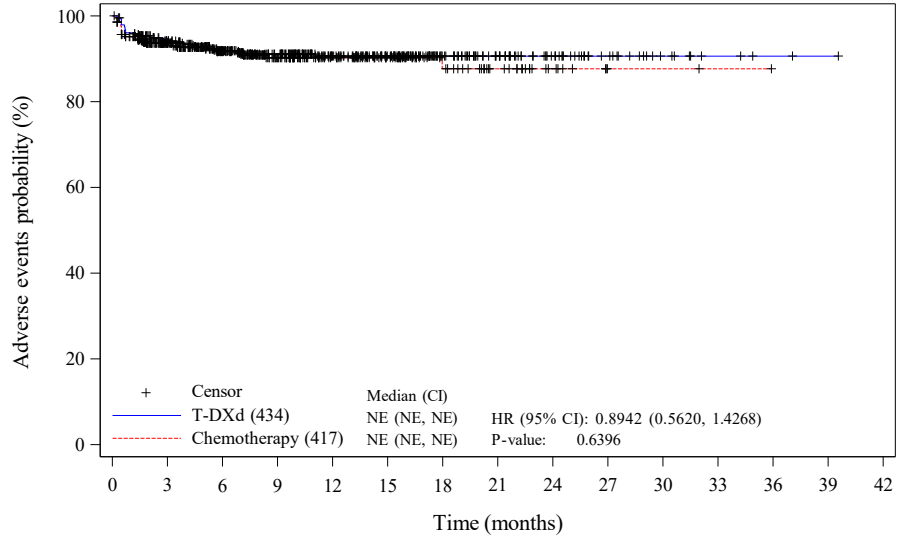
Run date: 17DEC2024 4:21; Program name: F.2.32.1_GR35PCTSRTEAE_SAF.sas; Output name: F.2.32.1_GR35PCTSRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Neutropenia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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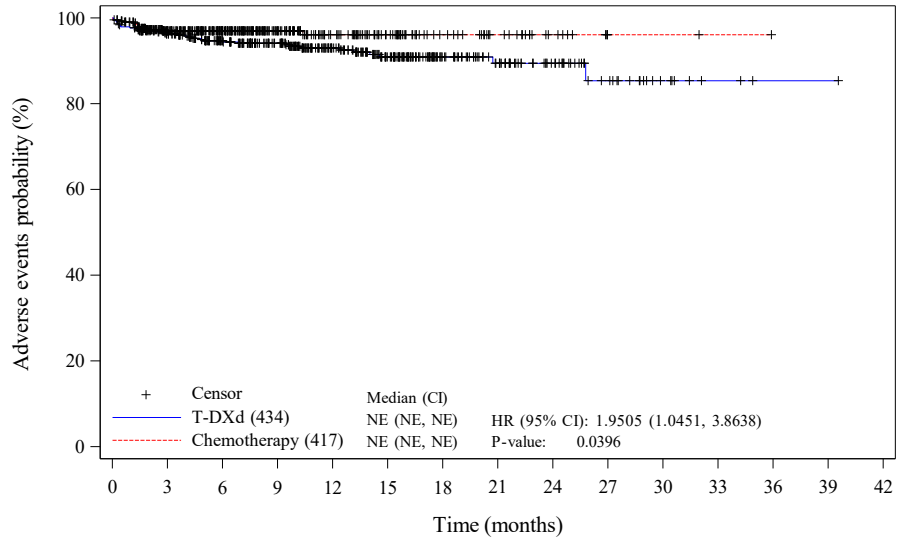
Run date: 17DEC2024 4:21; Program name: F.2.32.1_GR35PCTSRTEAE_SAF.sas; Output name: F.2.32.1_GR35PCTSRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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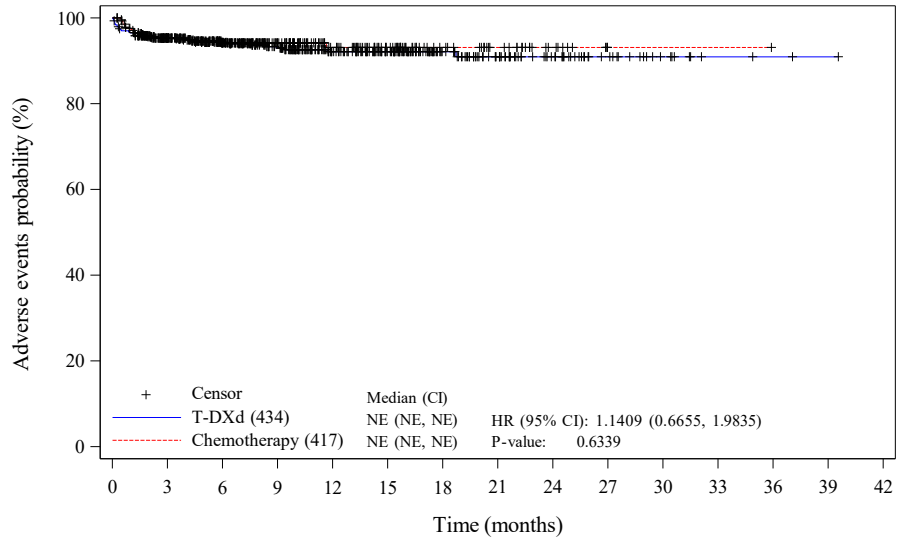
Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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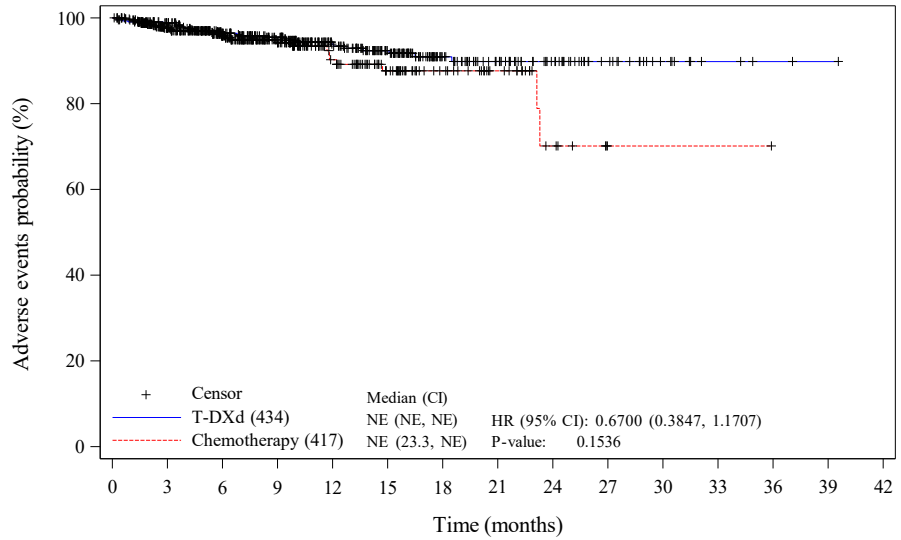
Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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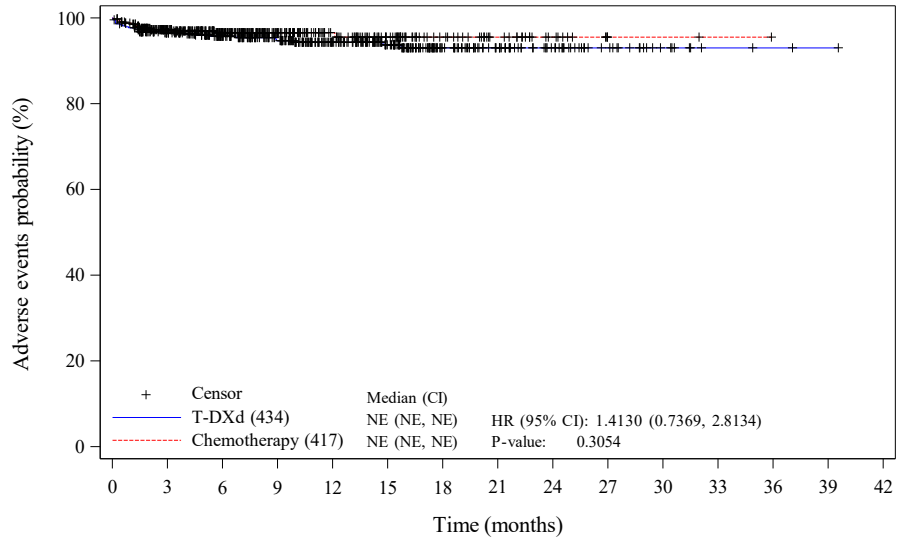
Run date: 17DEC2024 4:22; Program name: F.2.32.1_GR35PCTSRTEAE_SAF.sas; Output name: F.2.32.1_GR35PCTSRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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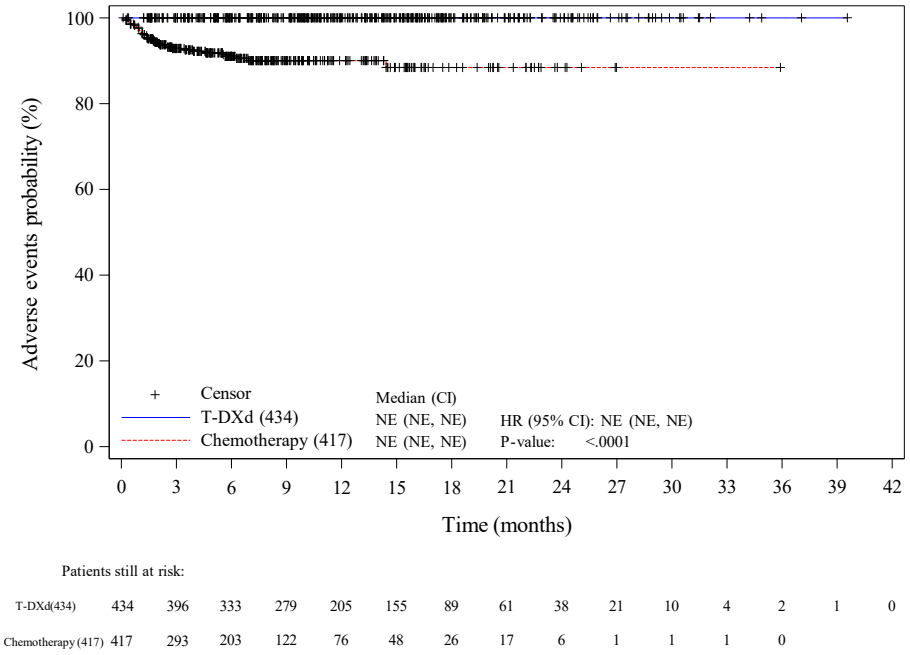
Run date: 17DEC2024 4:22; Program name: F.2.32.1_GR35PCTSRTEAE_SAF.sas; Output name: F.2.32.1_GR35PCTSRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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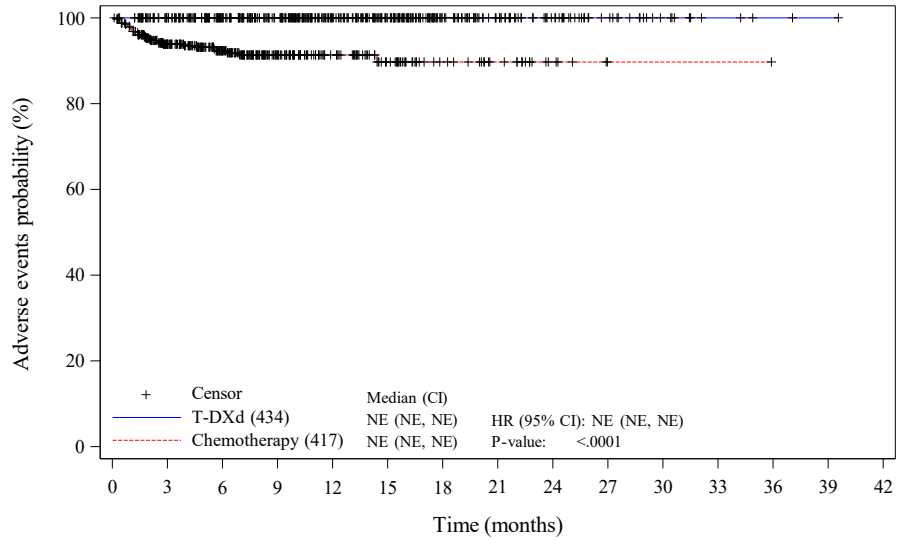
Run date: 17DEC2024 4:22; Program name: F.2.32.1_GR35PCTSRTEAE_SAF.sas; Output name: F.2.32.1_GR35PCTSRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.32.1 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence >= 5% in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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Run date: 17DEC2024 4:22; Program name: F.2.32.1_GR35PCTSRTEAE_SAF.sas; Output name: F.2.32.1_GR35PCTSRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Abbildung 2.32.2 Unerwünschte Ereignisse mit CTCAE-Grad 3 oder höher nach SOC und PT mit Inzidenz ≥5 % in mindestens einem Arm – Kaplan-Meier-Plot – Analyse nach Subgruppe – SAF

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Data Intelligence - Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 2024-03-18)

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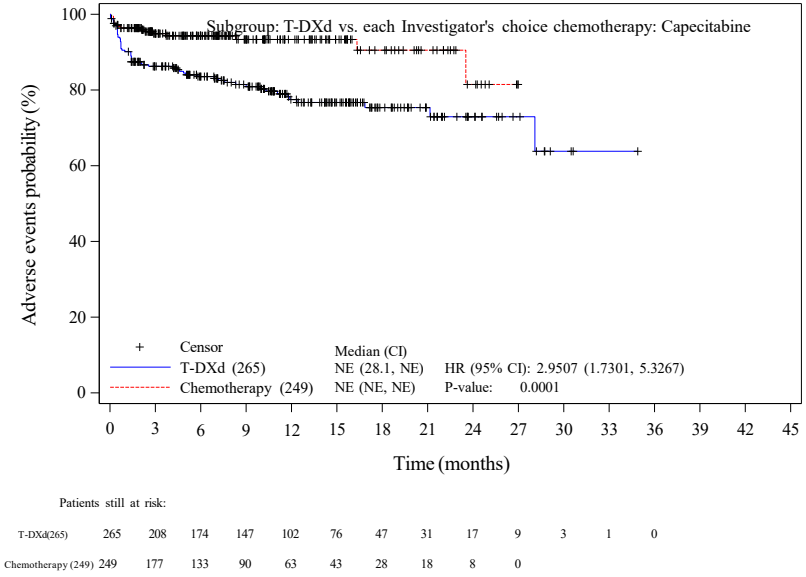
Figure 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence ≥ 5% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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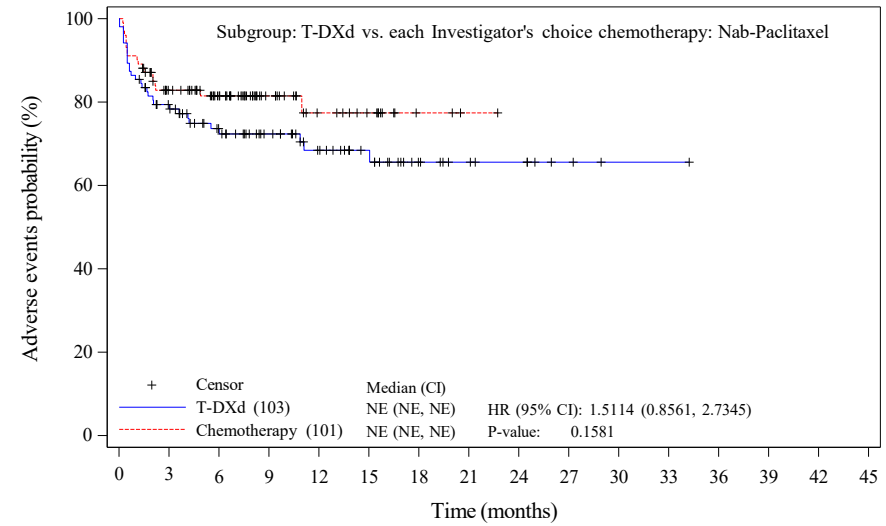
Figure 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence ≥ 5% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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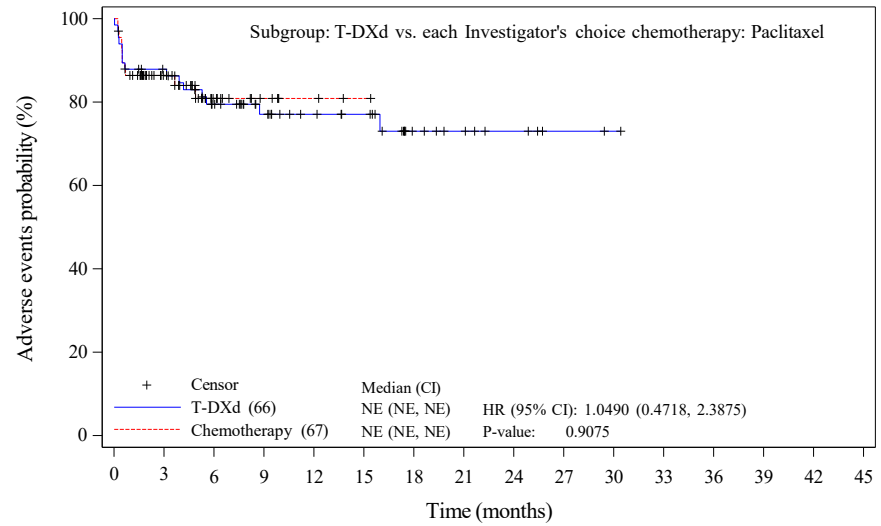
Figure 2.32.2 Adverse events with CTCAE grade 3 or higher by SOC and PT with incidence ≥ 5% in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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Tabelle 2.33.1 Unerwünschte Ereignisse mit CTCAE-Grad 3 oder höher nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – SAF

Table 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations						
All (any PT)	101 (23.3)	NE [NE; NE]	46 (11.0)	NE [NE; NE]	1.8843 [1.3354; 2.6994] 0.0004	0.0003
PT: Neutrophil count decreased	60 (13.8)	NE [NE; NE]	36 (8.6)	NE [NE; NE]	1.3917 [0.9216; 2.1301] 0.1207	0.1210
PT: White blood cell count decreased	25 (5.8)	NE [NE; NE]	20 (4.8)	NE [NE; NE]	1.0409 [0.5773; 1.9008] 0.8943	0.8943
PT: Platelet count decreased	18 (4.1)	NE [NE; NE]	0 (0.0)	NE [NE; NE]	NE [NE; NE]	0.0001
PT: Gamma-glutamyltransferase increased	10 (2.3)	NE [NE; NE]	2 (0.5)	NE [NE; NE]	3.3643 [0.8713; 22.0845] 0.1206	0.1004
PT: Lymphocyte count decreased	10 (2.3)	NE [NE; NE]	2 (0.5)	NE [NE; NE]	3.8486 [1.0100; 25.0963] 0.0826	0.0617
SOC: Blood and lymphatic system disorders						
All (any PT)	72 (16.6)	NE [NE; NE]	53 (12.7)	NE [NE; NE]	1.1399 [0.7999; 1.6345] 0.4715	0.4719
PT: Anaemia	38 (8.8)	NE [NE; NE]	18 (4.3)	NE [NE; NE]	1.7305 [0.9992; 3.1109] 0.0567	0.0537

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Neutropenia	37 (8.5)	NE [NE; NE]	35 (8.4)	NE [NE; NE]	0.8942 [0.5620; 1.4268] 0.6366	0.6396
PT: Leukopenia	6 (1.4)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	0.8981 [0.2667; 3.1532] 0.8608	0.8607
SOC: Metabolism and nutrition disorders						
All (any PT)	33 (7.6)	NE [NE; NE]	13 (3.1)	NE [NE; NE]	1.9505 [1.0451; 3.8638] 0.0433	0.0396
PT: Hypokalaemia	19 (4.4)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	2.8022 [1.1169; 8.4995] 0.0419	0.0338
SOC: Gastrointestinal disorders						
All (any PT)	31 (7.1)	NE [NE; NE]	23 (5.5)	NE [NE; NE]	1.1409 [0.6655; 1.9835] 0.6341	0.6339
PT: Diarrhoea	10 (2.3)	NE [NE; NE]	11 (2.6)	NE [NE; NE]	0.7726 [0.3203; 1.8409] 0.5572	0.5564
PT: Nausea	9 (2.1)	NE [NE; NE]	2 (0.5)	NE [NE; NE]	4.0443 [1.0390; 26.5669] 0.0743	0.0534

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Infections and infestations						
All (any PT)	27 (6.2)	NE [NE; NE]	25 (6.0)	NE [23.3; NE]	0.6700 [0.3847; 1.1707] 0.1560	0.1536
SOC: General disorders and administration site conditions						
All (any PT)	24 (5.5)	NE [NE; NE]	14 (3.4)	NE [NE; NE]	1.4130 [0.7369; 2.8134] 0.3074	0.3054
PT: Asthenia	10 (2.3)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	1.6517 [0.5817; 5.3361] 0.3632	0.3584
PT: Fatigue	9 (2.1)	NE [NE; NE]	6 (1.4)	NE [NE; NE]	1.1783 [0.4203; 3.5448] 0.7579	0.7579
SOC: Respiratory, thoracic and mediastinal disorders						
All (any PT)	15 (3.5)	NE [NE; NE]	11 (2.6)	NE [NE; NE]	0.9939 [0.4544; 2.2384] 0.9879	0.9879
SOC: Vascular disorders						
All (any PT)	15 (3.5)	NE [NE; NE]	14 (3.4)	NE [NE; NE]	0.8474 [0.4048; 1.7842] 0.6583	0.6580

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Table 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Hypertension	12 (2.8)	NE [NE; NE]	11 (2.6)	NE [NE; NE]	0.8468 [0.3689; 1.9623] 0.6926	0.6923
SOC: Nervous system disorders						
All (any PT)	9 (2.1)	NE [NE; NE]	16 (3.8)	NE [NE; NE]	0.3986 [0.1660; 0.8982] 0.0305	0.0255
SOC: Hepatobiliary disorders						
All (any PT)	8 (1.8)	NE [NE; NE]	4 (1.0)	NE [NE; NE]	1.3690 [0.4261; 5.1743] 0.6114	0.6100
SOC: Injury, poisoning and procedural complications						
All (any PT)	5 (1.2)	NE [NE; NE]	5 (1.2)	NE [NE; NE]	0.6803 [0.1847; 2.4989] 0.5504	0.5485
SOC: Musculoskeletal and connective tissue disorders						
All (any PT)	4 (0.9)	NE [NE; NE]	10 (2.4)	NE [26.5; NE]	0.2628 [0.0709; 0.8011] 0.0263	0.0176

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders						
All (any PT)	0 (0.0)	NE [NE; NE]	36 (8.6)	NE [NE; NE]	NE [NE; NE]	<.0001
PT: Palmar-plantar erythrodysaesthesia syndrome	0 (0.0)	NE [NE; NE]	31 (7.4)	NE [NE; NE]	NE [NE; NE]	<.0001

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Confidence limits are based on the profile-likelihood approach. p-value is two-sided and based on the profile-likelihood approach.
c. Two-sided p-value from unstratified log-rank test.
Includes Adverse Events with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 11DEC2024 6:50; Program name: T.2.33.1_GR310SRTEAE_SAF.sas; Output name: T.2.33.1_GR310SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Tabelle 2.33.2 Unerwünschte Ereignisse mit CTCAE-Grad 3 oder höher nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Subgruppenanalyse – SAF

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: All (any PT)						
Age at randomization						0.5705
<65 years of age	72 / 301 (23.9)	NE [NE; NE]	34 / 285 (11.9)	NE [23.5; NE]	1.8032 [1.2058; 2.7503] 0.0044	
>=65 years of age	29 / 133 (21.8)	28.1 [28.1; NE]	12 / 132 (9.1)	NE [NE; NE]	2.1207 [1.1033; 4.3374] 0.0258	
Race						0.1230
Asian	62 / 153 (40.5)	28.1 [11.9; NE]	31 / 147 (21.1)	NE [23.5; NE]	1.8532 [1.2111; 2.8940] 0.0047	
White	33 / 231 (14.3)	NE [NE; NE]	15 / 223 (6.7)	NE [NE; NE]	1.7612 [0.9705; 3.3481] 0.0671	
Other	6 / 50 (12.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.7452
Asia	59 / 148 (39.9)	28.1 [11.9; NE]	31 / 144 (21.5)	NE [23.5; NE]	1.7850 [1.1617; 2.7960] 0.0085	
Europe	34 / 227 (15.0)	NE [NE; NE]	11 / 206 (5.3)	NE [NE; NE]	2.3419 [1.2195; 4.8633] 0.0121	
Rest of the World	8 / 59 (13.6)	NE [NE; NE]	4 / 67 (6.0)	NE [NE; NE]	1.9303 [0.6017; 7.2852] 0.2809	
HER2 IHC expression						0.4660
IHC 1+	54 / 239 (22.6)	NE [28.1; NE]	28 / 226 (12.4)	NE [NE; NE]	1.6202 [1.0318; 2.5993] 0.0375	
IHC 2+/ISH-	29 / 116 (25.0)	NE [NE; NE]	9 / 115 (7.8)	NE [NE; NE]	2.8171 [1.3795; 6.3429] 0.0050	
IHC >0 <1+	17 / 76 (22.4)	NE [21.2; NE]	9 / 74 (12.2)	NE [23.5; NE]	1.8281 [0.8326; 4.2959] 0.1381	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.5264
Yes	88 / 393 (22.4)	NE [NE; NE]	41 / 377 (10.9)	NE [NE; NE]	1.8073 [1.2529; 2.6505] 0.0016	
No	13 / 41 (31.7)	NE [11.8; NE]	5 / 40 (12.5)	NE [NE; NE]	2.6620 [1.0034; 8.2998] 0.0532	
Prior Taxane Use In The Non-Metastatic Setting						0.6865
Yes	46 / 177 (26.0)	NE [NE; NE]	20 / 172 (11.6)	NE [NE; NE]	2.1214 [1.2708; 3.6734] 0.0043	
No	55 / 257 (21.4)	NE [28.1; NE]	26 / 245 (10.6)	NE [23.5; NE]	1.7234 [1.0879; 2.8005] 0.0217	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4477
1	14 / 65 (21.5)	NE [NE; NE]	5 / 79 (6.3)	NE [16.3; NE]	3.1501 [1.1843; 9.8464] 0.0225	
2	64 / 293 (21.8)	NE [NE; NE]	32 / 281 (11.4)	NE [NE; NE]	1.6878 [1.1108; 2.6162] 0.0150	
>=3	22 / 75 (29.3)	NE [28.1; NE]	9 / 56 (16.1)	23.5 [NE; NE]	1.5951 [0.7506; 3.6779] 0.2447	
ER/PR status I						0.4933
ER+, PR+	52 / 252 (20.6)	NE [NE; NE]	25 / 234 (10.7)	NE [23.5; NE]	1.6940 [1.0608; 2.7781] 0.0288	
ER+, PR-	46 / 166 (27.7)	NE [28.1; NE]	20 / 171 (11.7)	NE [NE; NE]	2.1594 [1.2879; 3.7508] 0.0037	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.5322
ER <=10%	6 / 21 (28.6)	NE [4.9; NE]	1 / 14 (7.1)	NE [NE; NE]	4.1454 [0.7056; 78.4118] 0.1577	
ER >10%	82 / 362 (22.7)	NE [NE; NE]	35 / 343 (10.2)	NE [NE; NE]	2.0161 [1.3661; 3.0389] 0.0004	
Positive	13 / 51 (25.5)	21.2 [16.9; NE]	10 / 60 (16.7)	NE [NE; NE]	1.2833 [0.5631; 3.0130] 0.5452	
Endocrine Resistance						0.7093
Primary	28 / 127 (22.0)	NE [NE; NE]	16 / 137 (11.7)	NE [NE; NE]	1.7034 [0.9282; 3.2327] 0.0885	
Secondary	73 / 307 (23.8)	NE [28.1; NE]	30 / 279 (10.8)	NE [23.5; NE]	1.9678 [1.2972; 3.0620] 0.0016	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0477
Capecitabine	56 / 265 (21.1)	NE [28.1; NE]	16 / 249 (6.4)	NE [NE; NE]	2.9507 [1.7301; 5.3267] 0.0001	
Nab-Paclitaxel	30 / 103 (29.1)	NE [NE; NE]	19 / 101 (18.8)	NE [NE; NE]	1.5114 [0.8561; 2.7345] 0.1581	
Paclitaxel	15 / 66 (22.7)	NE [NE; NE]	11 / 67 (16.4)	NE [NE; NE]	1.0490 [0.4718; 2.3875] 0.9075	
Prior anthracycline use						0.3441
Yes	45 / 197 (22.8)	NE [NE; NE]	25 / 198 (12.6)	NE [NE; NE]	1.6324 [1.0072; 2.7059] 0.0486	
No	56 / 237 (23.6)	NE [28.1; NE]	21 / 219 (9.6)	NE [23.5; NE]	2.1856 [1.3403; 3.7004] 0.0019	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.3421
Yes	69 / 294 (23.5)	NE [NE; NE]	27 / 275 (9.8)	NE [NE; NE]	2.2208 [1.4386; 3.5282] 0.0003	
No	32 / 140 (22.9)	28.1 [28.1; NE]	19 / 142 (13.4)	NE [23.5; NE]	1.4175 [0.8050; 2.5613] 0.2327	
ECOG						0.3799
0	53 / 251 (21.1)	NE [28.1; NE]	21 / 246 (8.5)	NE [NE; NE]	2.1972 [1.3405; 3.7335] 0.0019	
>=1	48 / 178 (27.0)	NE [21.2; NE]	24 / 163 (14.7)	NE [NE; NE]	1.6455 [1.0166; 2.7351] 0.0450	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: Platelet count decreased						
Age at randomization						0.9998
<65 years of age	14 / 301 (4.7)	NE [NE; NE]	0 / 285 (0.0)	NE [NE; NE]	NE [NE; NE]	
>=65 years of age	4 / 133 (3.0)	NE [NE; NE]	0 / 132 (0.0)	NE [NE; NE]	NE [NE; NE]	
Race						NE
Asian	15 / 153 (9.8)	NE [NE; NE]	0 / 147 (0.0)	NE [NE; NE]	NE [NE; NE]	
White	3 / 231 (1.3)	NE [NE; NE]	0 / 223 (0.0)	NE [NE; NE]	NE [NE; NE]	
Other	0 / 50 (0.0)	NE [NE; NE]	0 / 47 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						NE
Asia	16 / 148 (10.8)	NE [NE; NE]	0 / 144 (0.0)	NE [NE; NE]	NE [NE; NE]	
Europe	2 / 227 (0.9)	NE [NE; NE]	0 / 206 (0.0)	NE [NE; NE]	NE [NE; NE]	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
HER2 IHC expression						1.0000
IHC 1+	8 / 239 (3.3)	NE [NE; NE]	0 / 226 (0.0)	NE [NE; NE]	NE [NE; NE]	
IHC 2+/ISH-	5 / 116 (4.3)	NE [NE; NE]	0 / 115 (0.0)	NE [NE; NE]	NE [NE; NE]	
IHC >0 <1+	5 / 76 (6.6)	NE [NE; NE]	0 / 74 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9996
Yes	15 / 393 (3.8)	NE [NE; NE]	0 / 377 (0.0)	NE [NE; NE]	NE [NE; NE]	
No	3 / 41 (7.3)	NE [NE; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.9999
Yes	8 / 177 (4.5)	NE [NE; NE]	0 / 172 (0.0)	NE [NE; NE]	NE [NE; NE]	
No	10 / 257 (3.9)	NE [NE; NE]	0 / 245 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						1.0000
1	2 / 65 (3.1)	NE [NE; NE]	0 / 79 (0.0)	NE [NE; NE]	NE [NE; NE]	
2	13 / 293 (4.4)	NE [NE; NE]	0 / 281 (0.0)	NE [NE; NE]	NE [NE; NE]	
>=3	2 / 75 (2.7)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.9999
ER+, PR+	10 / 252 (4.0)	NE [NE; NE]	0 / 234 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER+, PR-	8 / 166 (4.8)	NE [NE; NE]	0 / 171 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						1.0000
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	17 / 362 (4.7)	NE [NE; NE]	0 / 343 (0.0)	NE [NE; NE]	NE [NE; NE]	
Positive	1 / 51 (2.0)	NE [NE; NE]	0 / 60 (0.0)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						1.0000
Primary	5 / 127 (3.9)	NE [NE; NE]	0 / 137 (0.0)	NE [NE; NE]	NE [NE; NE]	
Secondary	13 / 307 (4.2)	NE [NE; NE]	0 / 279 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						NE
Capecitabine	7 / 265 (2.6)	NE [NE; NE]	0 / 249 (0.0)	NE [NE; NE]	NE [NE; NE]	
Nab-Paclitaxel	9 / 103 (8.7)	NE [NE; NE]	0 / 101 (0.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	2 / 66 (3.0)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.9997
Yes	10 / 197 (5.1)	NE [NE; NE]	0 / 198 (0.0)	NE [NE; NE]	NE [NE; NE]	
No	8 / 237 (3.4)	NE [NE; NE]	0 / 219 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9997
Yes	14 / 294 (4.8)	NE [NE; NE]	0 / 275 (0.0)	NE [NE; NE]	NE [NE; NE]	
No	4 / 140 (2.9)	NE [NE; NE]	0 / 142 (0.0)	NE [NE; NE]	NE [NE; NE]	
ECOG						1.0000
0	11 / 251 (4.4)	NE [NE; NE]	0 / 246 (0.0)	NE [NE; NE]	NE [NE; NE]	
>=1	7 / 178 (3.9)	NE [NE; NE]	0 / 163 (0.0)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: All (any PT)						
Age at randomization						0.5863
<65 years of age	17 / 301 (5.6)	NE [NE; NE]	5 / 285 (1.8)	NE [NE; NE]	2.3474 [0.9156; 7.2062] 0.0882	
>=65 years of age	16 / 133 (12.0)	NE [NE; NE]	8 / 132 (6.1)	NE [NE; NE]	1.7780 [0.7790; 4.3987] 0.1794	
Race						0.2707
Asian	19 / 153 (12.4)	NE [NE; NE]	7 / 147 (4.8)	NE [NE; NE]	2.1761 [0.9495; 5.5974] 0.0736	
White	13 / 231 (5.6)	NE [NE; NE]	4 / 223 (1.8)	NE [NE; NE]	2.5856 [0.9055; 9.2384] 0.0875	
Other	1 / 50 (2.0)	NE [NE; NE]	2 / 47 (4.3)	NE [NE; NE]	0.2343 [0.0095; 2.9270] 0.2556	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.2286
Asia	19 / 148 (12.8)	NE [NE; NE]	7 / 144 (4.9)	NE [NE; NE]	2.2133 [0.9667; 5.6895] 0.0670	
Europe	11 / 227 (4.8)	NE [NE; NE]	6 / 206 (2.9)	NE [NE; NE]	1.3981 [0.5252; 4.0946] 0.5114	
Rest of the World	3 / 59 (5.1)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
HER2 IHC expression						0.8156
IHC 1+	18 / 239 (7.5)	NE [NE; NE]	7 / 226 (3.1)	NE [NE; NE]	1.9344 [0.8342; 5.0143] 0.1355	
IHC 2+/ISH-	8 / 116 (6.9)	NE [NE; NE]	4 / 115 (3.5)	NE [NE; NE]	1.4480 [0.4432; 5.5286] 0.5517	
IHC >0 <1+	7 / 76 (9.2)	NE [NE; NE]	2 / 74 (2.7)	NE [NE; NE]	3.0119 [0.7238; 20.2700] 0.1497	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.6231
Yes	29 / 393 (7.4)	NE [NE; NE]	12 / 377 (3.2)	NE [NE; NE]	1.8642 [0.9687; 3.8181] 0.0678	
No	4 / 41 (9.8)	NE [25.8; NE]	1 / 40 (2.5)	NE [NE; NE]	2.5939 [0.3289; 52.6461] 0.3935	
Prior Taxane Use In The Non-Metastatic Setting						0.0727
Yes	11 / 177 (6.2)	NE [NE; NE]	8 / 172 (4.7)	NE [NE; NE]	1.1178 [0.4478; 2.9100] 0.8112	
No	22 / 257 (8.6)	NE [NE; NE]	5 / 245 (2.0)	NE [NE; NE]	3.3244 [1.3529; 9.9738] 0.0107	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.1481
1	3 / 65 (4.6)	NE [NE; NE]	2 / 79 (2.5)	NE [NE; NE]	1.5314 [0.2482; 11.7891] 0.6421	
2	24 / 293 (8.2)	NE [NE; NE]	11 / 281 (3.9)	NE [NE; NE]	1.6434 [0.8178; 3.5143] 0.1726	
>=3	6 / 75 (8.0)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.0534
ER+, PR+	23 / 252 (9.1)	NE [NE; NE]	5 / 234 (2.1)	NE [NE; NE]	3.5004 [1.4343; 10.4627] 0.0072	
ER+, PR-	8 / 166 (4.8)	NE [NE; NE]	7 / 171 (4.1)	NE [NE; NE]	0.8771 [0.3052; 2.5572] 0.8050	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.0558
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	30 / 362 (8.3)	NE [NE; NE]	8 / 343 (2.3)	NE [NE; NE]	2.8790 [1.3754; 6.7734] 0.0059	
Positive	2 / 51 (3.9)	NE [NE; NE]	5 / 60 (8.3)	NE [NE; NE]	0.3592 [0.0510; 1.6895] 0.2059	
Endocrine Resistance						0.6138
Primary	9 / 127 (7.1)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	1.5014 [0.5120; 4.9335] 0.4675	
Secondary	24 / 307 (7.8)	NE [NE; NE]	8 / 279 (2.9)	NE [NE; NE]	2.2309 [1.0384; 5.3303] 0.0454	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.0957
Capecitabine	23 / 265 (8.7)	NE [NE; NE]	10 / 249 (4.0)	NE [NE; NE]	1.7509 [0.8529; 3.8656] 0.1362	
Nab-Paclitaxel	9 / 103 (8.7)	NE [25.8; NE]	1 / 101 (1.0)	NE [NE; NE]	6.7954 [1.2246; 126.6960] 0.0379	
Paclitaxel	1 / 66 (1.5)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	0.4813 [0.0224; 5.0318] 0.5419	
Prior anthracycline use						0.4113
Yes	13 / 197 (6.6)	NE [NE; NE]	7 / 198 (3.5)	NE [NE; NE]	1.4812 [0.5990; 3.9773] 0.4041	
No	20 / 237 (8.4)	NE [NE; NE]	6 / 219 (2.7)	NE [NE; NE]	2.5011 [1.0566; 6.8771] 0.0433	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.4703
Yes	20 / 294 (6.8)	NE [NE; NE]	9 / 275 (3.3)	NE [NE; NE]	1.6537 [0.7678; 3.8483] 0.2104	
No	13 / 140 (9.3)	NE [NE; NE]	4 / 142 (2.8)	NE [NE; NE]	2.6963 [0.9454; 9.6266] 0.0731	
ECOG						0.3295
0	15 / 251 (6.0)	NE [NE; NE]	4 / 246 (1.6)	NE [NE; NE]	2.6215 [0.9410; 9.2609] 0.0782	
>=1	17 / 178 (9.6)	NE [NE; NE]	8 / 163 (4.9)	NE [NE; NE]	1.7069 [0.7558; 4.1983] 0.2090	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: Hypokalaemia						
Age at randomization						0.2393
<65 years of age	10 / 301 (3.3)	NE [NE; NE]	1 / 285 (0.4)	NE [NE; NE]	6.4879 [1.2188; 119.7412] 0.0423	
>=65 years of age	9 / 133 (6.8)	NE [NE; NE]	4 / 132 (3.0)	NE [NE; NE]	1.9682 [0.6395; 7.2783] 0.2510	
Race						0.0073
Asian	13 / 153 (8.5)	NE [NE; NE]	3 / 147 (2.0)	NE [NE; NE]	3.3330 [1.0646; 14.6041] 0.0476	
White	6 / 231 (2.6)	NE [NE; NE]	0 / 223 (0.0)	NE [NE; NE]	NE [NE; NE]	
Other	0 / 50 (0.0)	NE [NE; NE]	2 / 47 (4.3)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.4035
Asia	13 / 148 (8.8)	NE [NE; NE]	3 / 144 (2.1)	NE [NE; NE]	3.3930 [1.0857; 14.8543] 0.0438	
Europe	4 / 227 (1.8)	NE [NE; NE]	2 / 206 (1.0)	NE [NE; NE]	1.5787 [0.3036; 11.4814] 0.5968	
Rest of the World	2 / 59 (3.4)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
HER2 IHC expression						0.9307
IHC 1+	13 / 239 (5.4)	NE [NE; NE]	3 / 226 (1.3)	NE [NE; NE]	3.0871 [0.9817; 13.5582] 0.0664	
IHC 2+/ISH-	3 / 116 (2.6)	NE [NE; NE]	1 / 115 (0.9)	NE [NE; NE]	2.1904 [0.2692; 45.0111] 0.4931	
IHC >0 <1+	3 / 76 (3.9)	NE [NE; NE]	1 / 74 (1.4)	NE [NE; NE]	2.6324 [0.3369; 53.2130] 0.3838	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.1341
Yes	15 / 393 (3.8)	NE [NE; NE]	5 / 377 (1.3)	NE [NE; NE]	2.2491 [0.8643; 6.9525] 0.1094	
No	4 / 41 (9.8)	NE [25.8; NE]	0 / 40 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.0714
Yes	7 / 177 (4.0)	NE [NE; NE]	4 / 172 (2.3)	NE [NE; NE]	1.5553 [0.4692; 5.9424] 0.4770	
No	12 / 257 (4.7)	NE [NE; NE]	1 / 245 (0.4)	NE [NE; NE]	7.9597 [1.5533; 145.3948] 0.0186	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.2724
1	1 / 65 (1.5)	NE [NE; NE]	0 / 79 (0.0)	NE [NE; NE]	NE [NE; NE]	
2	14 / 293 (4.8)	NE [NE; NE]	5 / 281 (1.8)	NE [NE; NE]	2.0248 [0.7672; 6.3061] 0.1706	
>=3	4 / 75 (5.3)	NE [NE; NE]	0 / 56 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.6497
ER+, PR+	13 / 252 (5.2)	NE [NE; NE]	3 / 234 (1.3)	NE [NE; NE]	3.1507 [1.0079; 13.7994] 0.0601	
ER+, PR-	5 / 166 (3.0)	NE [NE; NE]	2 / 171 (1.2)	NE [NE; NE]	1.7065 [0.3473; 12.2335] 0.5290	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.4353
ER <=10%	1 / 21 (4.8)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	16 / 362 (4.4)	NE [NE; NE]	3 / 343 (0.9)	NE [NE; NE]	3.9557 [1.3041; 17.0997] 0.0193	
Positive	2 / 51 (3.9)	NE [NE; NE]	2 / 60 (3.3)	NE [NE; NE]	0.8341 [0.0992; 7.0136] 0.8567	
Endocrine Resistance						0.8480
Primary	4 / 127 (3.1)	NE [NE; NE]	1 / 137 (0.7)	NE [NE; NE]	3.5378 [0.5166; 69.5088] 0.2305	
Secondary	15 / 307 (4.9)	NE [NE; NE]	4 / 279 (1.4)	NE [NE; NE]	2.6184 [0.9415; 9.2380] 0.0779	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1646
Capecitabine	13 / 265 (4.9)	NE [NE; NE]	5 / 249 (2.0)	NE [NE; NE]	1.9262 [0.7231; 6.0282] 0.2063	
Nab-Paclitaxel	6 / 103 (5.8)	NE [25.8; NE]	0 / 101 (0.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.1910
Yes	9 / 197 (4.6)	NE [NE; NE]	4 / 198 (2.0)	NE [NE; NE]	1.9024 [0.6154; 7.0534] 0.2782	
No	10 / 237 (4.2)	NE [NE; NE]	1 / 219 (0.5)	NE [NE; NE]	6.5762 [1.2444; 121.1071] 0.0397	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.8586
Yes	9 / 294 (3.1)	NE [NE; NE]	2 / 275 (0.7)	NE [NE; NE]	2.9586 [0.7505; 19.5634] 0.1493	
No	10 / 140 (7.1)	NE [NE; NE]	3 / 142 (2.1)	NE [NE; NE]	2.8396 [0.8597; 12.7326] 0.0997	
ECOG						0.9848
0	11 / 251 (4.4)	NE [NE; NE]	3 / 246 (1.2)	NE [NE; NE]	2.6523 [0.8186; 11.8055] 0.1227	
>=1	8 / 178 (4.5)	NE [NE; NE]	2 / 163 (1.2)	NE [NE; NE]	3.0570 [0.7608; 20.3229] 0.1385	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders; PT: All (any PT)						
Age at randomization						0.0701
<65 years of age	9 / 301 (3.0)	NE [29.8; NE]	12 / 285 (4.2)	NE [NE; NE]	0.4965 [0.1922; 1.2145] 0.1232	
>=65 years of age	0 / 133 (0.0)	NE [NE; NE]	4 / 132 (3.0)	NE [NE; NE]	NE [NE; NE]	
Race						0.7468
Asian	2 / 153 (1.3)	NE [NE; NE]	6 / 147 (4.1)	NE [NE; NE]	0.2504 [0.0364; 1.1016] 0.0699	
White	5 / 231 (2.2)	NE [29.8; NE]	8 / 223 (3.6)	NE [NE; NE]	0.3851 [0.1021; 1.2325] 0.1086	
Other	2 / 50 (4.0)	NE [NE; NE]	2 / 47 (4.3)	NE [NE; NE]	0.6717 [0.0735; 5.9534] 0.7026	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.1490
Asia	2 / 148 (1.4)	NE [NE; NE]	6 / 144 (4.2)	NE [NE; NE]	0.2531 [0.0368; 1.1133] 0.0723	
Europe	3 / 227 (1.3)	NE [NE; NE]	8 / 206 (3.9)	NE [NE; NE]	0.2751 [0.0599; 0.9581] 0.0428	
Rest of the World	4 / 59 (6.8)	29.8 [29.8; NE]	2 / 67 (3.0)	NE [NE; NE]	1.2234 [0.1945; 9.5657] 0.8289	
HER2 IHC expression						0.9411
IHC 1+	5 / 239 (2.1)	NE [NE; NE]	10 / 226 (4.4)	NE [NE; NE]	0.3457 [0.1066; 0.9846] 0.0451	
IHC 2+/ISH-	3 / 116 (2.6)	NE [29.8; NE]	4 / 115 (3.5)	NE [NE; NE]	0.5539 [0.1035; 2.6123] 0.4489	
IHC >0 <1+	1 / 76 (1.3)	NE [NE; NE]	2 / 74 (2.7)	NE [NE; NE]	0.4443 [0.0207; 4.6411] 0.4963	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2207
Yes	6 / 393 (1.5)	NE [29.8; NE]	14 / 377 (3.7)	NE [NE; NE]	0.3162 [0.1104; 0.7998] 0.0146	
No	3 / 41 (7.3)	NE [NE; NE]	2 / 40 (5.0)	NE [NE; NE]	1.1296 [0.1854; 8.6447] 0.8944	
Prior Taxane Use In The Non-Metastatic Setting						0.8172
Yes	3 / 177 (1.7)	NE [NE; NE]	6 / 172 (3.5)	NE [NE; NE]	0.3755 [0.0774; 1.4603] 0.1594	
No	6 / 257 (2.3)	NE [29.8; NE]	10 / 245 (4.1)	NE [NE; NE]	0.4100 [0.1362; 1.1280] 0.0823	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.3140
1	2 / 65 (3.1)	NE [NE; NE]	1 / 79 (1.3)	NE [NE; NE]	2.4805 [0.2377; 53.3422] 0.4428	
2	6 / 293 (2.0)	NE [29.8; NE]	12 / 281 (4.3)	NE [NE; NE]	0.3332 [0.1145; 0.8714] 0.0235	
>=3	1 / 75 (1.3)	NE [NE; NE]	3 / 56 (5.4)	NE [NE; NE]	0.2166 [0.0107; 1.6930] 0.1452	
ER/PR status I						0.9417
ER+, PR+	4 / 252 (1.6)	NE [NE; NE]	7 / 234 (3.0)	NE [NE; NE]	0.4451 [0.1159; 1.4838] 0.1875	
ER+, PR-	5 / 166 (3.0)	NE [29.8; NE]	9 / 171 (5.3)	NE [NE; NE]	0.3735 [0.1109; 1.1187] 0.0772	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2046
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	2 / 14 (14.3)	NE [5.1; NE]	NE [NE; NE]	
ER >10%	8 / 362 (2.2)	NE [NE; NE]	13 / 343 (3.8)	NE [NE; NE]	0.4077 [0.1566; 0.9923] 0.0464	
Positive	1 / 51 (2.0)	NE [NE; NE]	1 / 60 (1.7)	NE [NE; NE]	1.0585 [0.0418; 26.8114] 0.9680	
Endocrine Resistance						0.7850
Primary	2 / 127 (1.6)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	0.3761 [0.0532; 1.7734] 0.2300	
Secondary	7 / 307 (2.3)	NE [29.8; NE]	11 / 279 (3.9)	NE [NE; NE]	0.4117 [0.1491; 1.0619] 0.0631	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1336
Capecitabine	5 / 265 (1.9)	NE [29.8; NE]	4 / 249 (1.6)	NE [NE; NE]	0.8520 [0.2200; 3.5100] 0.8145	
Nab-Paclitaxel	3 / 103 (2.9)	NE [NE; NE]	6 / 101 (5.9)	NE [NE; NE]	0.3860 [0.0800; 1.4934] 0.1702	
Paclitaxel	1 / 66 (1.5)	NE [NE; NE]	6 / 67 (9.0)	NE [NE; NE]	0.1218 [0.0064; 0.7168] 0.0204	
Prior anthracycline use						0.0526
Yes	2 / 197 (1.0)	NE [NE; NE]	10 / 198 (5.1)	NE [NE; NE]	0.1535 [0.0234; 0.5918] 0.0062	
No	7 / 237 (3.0)	NE [29.8; NE]	6 / 219 (2.7)	NE [NE; NE]	0.7756 [0.2507; 2.4589] 0.6544	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.7468
Yes	7 / 294 (2.4)	NE [29.8; NE]	11 / 275 (4.0)	NE [NE; NE]	0.3828 [0.1304; 1.0191] 0.0530	
No	2 / 140 (1.4)	NE [NE; NE]	5 / 142 (3.5)	NE [NE; NE]	0.3489 [0.0497; 1.6333] 0.1908	
ECOG						0.5052
0	5 / 251 (2.0)	NE [29.8; NE]	7 / 246 (2.8)	NE [NE; NE]	0.4564 [0.1298; 1.4789] 0.1854	
>=1	4 / 178 (2.2)	NE [NE; NE]	9 / 163 (5.5)	NE [NE; NE]	0.3431 [0.0925; 1.0601] 0.0637	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)						
Age at randomization						0.2633
<65 years of age	4 / 301 (1.3)	NE [NE; NE]	8 / 285 (2.8)	NE [26.5; NE]	0.3119 [0.0817; 1.0119] 0.0495	
>=65 years of age	0 / 133 (0.0)	NE [NE; NE]	2 / 132 (1.5)	NE [NE; NE]	NE [NE; NE]	
Race						0.3706
Asian	1 / 153 (0.7)	NE [NE; NE]	1 / 147 (0.7)	NE [NE; NE]	0.7968 [0.0315; 20.1374] 0.8721	
White	1 / 231 (0.4)	NE [NE; NE]	7 / 223 (3.1)	NE [26.5; NE]	0.0891 [0.0047; 0.5167] 0.0058	
Other	2 / 50 (4.0)	NE [NE; NE]	2 / 47 (4.3)	NE [NE; NE]	0.4598 [0.0497; 4.2386] 0.4588	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						0.3570
Asia	2 / 148 (1.4)	NE [NE; NE]	2 / 144 (1.4)	NE [26.5; NE]	0.5975 [0.0701; 5.0808] 0.6077	
Europe	1 / 227 (0.4)	NE [NE; NE]	6 / 206 (2.9)	NE [NE; NE]	0.1042 [0.0055; 0.6257] 0.0122	
Rest of the World	1 / 59 (1.7)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	0.5116 [0.0238; 5.3519] 0.5776	
HER2 IHC expression						0.4820
IHC 1+	2 / 239 (0.8)	NE [NE; NE]	4 / 226 (1.8)	NE [NE; NE]	0.3619 [0.0497; 1.8748] 0.2246	
IHC 2+/ISH-	2 / 116 (1.7)	NE [NE; NE]	4 / 115 (3.5)	NE [NE; NE]	0.3635 [0.0492; 1.9184] 0.2335	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	2 / 74 (2.7)	26.5 [26.5; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.2277
Yes	4 / 393 (1.0)	NE [NE; NE]	8 / 377 (2.1)	NE [26.5; NE]	0.3465 [0.0911; 1.1193] 0.0752	
No	0 / 41 (0.0)	NE [NE; NE]	2 / 40 (5.0)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.3665
Yes	1 / 177 (0.6)	NE [NE; NE]	5 / 172 (2.9)	NE [NE; NE]	0.1667 [0.0087; 1.0396] 0.0636	
No	3 / 257 (1.2)	NE [NE; NE]	5 / 245 (2.0)	NE [26.5; NE]	0.3550 [0.0715; 1.4788] 0.1461	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						0.4698
1	0 / 65 (0.0)	NE [NE; NE]	1 / 79 (1.3)	NE [NE; NE]	NE [NE; NE]	
2	4 / 293 (1.4)	NE [NE; NE]	8 / 281 (2.8)	NE [26.5; NE]	0.3200 [0.0845; 1.0306] 0.0532	
>=3	0 / 75 (0.0)	NE [NE; NE]	1 / 56 (1.8)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.1119
ER+, PR+	1 / 252 (0.4)	NE [NE; NE]	7 / 234 (3.0)	NE [26.5; NE]	0.0925 [0.0049; 0.5292] 0.0062	
ER+, PR-	3 / 166 (1.8)	NE [NE; NE]	3 / 171 (1.8)	NE [NE; NE]	0.7597 [0.1387; 4.1583] 0.7382	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						0.2818
ER <=10%	1 / 21 (4.8)	NE [14.5; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	3 / 362 (0.8)	NE [NE; NE]	8 / 343 (2.3)	NE [26.5; NE]	0.2407 [0.0517; 0.8517] 0.0258	
Positive	0 / 51 (0.0)	NE [NE; NE]	2 / 60 (3.3)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						0.0932
Primary	2 / 127 (1.6)	NE [NE; NE]	1 / 137 (0.7)	NE [NE; NE]	1.2035 [0.1129; 26.1812] 0.8806	
Secondary	2 / 307 (0.7)	NE [NE; NE]	9 / 279 (3.2)	NE [26.5; NE]	0.1477 [0.0223; 0.5828] 0.0054	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						0.1510
Capecitabine	4 / 265 (1.5)	NE [NE; NE]	6 / 249 (2.4)	NE [26.5; NE]	0.4372 [0.1109; 1.5443] 0.1911	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	2 / 101 (2.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.2903
Yes	2 / 197 (1.0)	NE [NE; NE]	8 / 198 (4.0)	NE [NE; NE]	0.1946 [0.0292; 0.7858] 0.0225	
No	2 / 237 (0.8)	NE [NE; NE]	2 / 219 (0.9)	NE [26.5; NE]	0.5226 [0.0610; 4.4887] 0.5176	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.6678
Yes	2 / 294 (0.7)	NE [NE; NE]	6 / 275 (2.2)	NE [26.5; NE]	0.2076 [0.0296; 0.9343] 0.0397	
No	2 / 140 (1.4)	NE [NE; NE]	4 / 142 (2.8)	NE [NE; NE]	0.3457 [0.0471; 1.8143] 0.2072	
ECOG						0.1022
0	4 / 251 (1.6)	NE [NE; NE]	7 / 246 (2.8)	NE [26.5; NE]	0.3950 [0.1025; 1.3237] 0.1291	
>=1	0 / 178 (0.0)	NE [NE; NE]	3 / 163 (1.8)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)						
Age at randomization						0.9993
<65 years of age	0 / 301 (0.0)	NE [NE; NE]	19 / 285 (6.7)	NE [NE; NE]	NE [NE; NE]	
>=65 years of age	0 / 133 (0.0)	NE [NE; NE]	17 / 132 (12.9)	NE [NE; NE]	NE [NE; NE]	
Race						1.0000
Asian	0 / 153 (0.0)	NE [NE; NE]	11 / 147 (7.5)	NE [NE; NE]	NE [NE; NE]	
White	0 / 231 (0.0)	NE [NE; NE]	21 / 223 (9.4)	NE [NE; NE]	NE [NE; NE]	
Other	0 / 50 (0.0)	NE [NE; NE]	4 / 47 (8.5)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						1.0000
Asia	0 / 148 (0.0)	NE [NE; NE]	12 / 144 (8.3)	NE [NE; NE]	NE [NE; NE]	
Europe	0 / 227 (0.0)	NE [NE; NE]	15 / 206 (7.3)	NE [NE; NE]	NE [NE; NE]	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	9 / 67 (13.4)	NE [14.4; NE]	NE [NE; NE]	
HER2 IHC expression						1.0000
IHC 1+	0 / 239 (0.0)	NE [NE; NE]	22 / 226 (9.7)	NE [NE; NE]	NE [NE; NE]	
IHC 2+/ISH-	0 / 116 (0.0)	NE [NE; NE]	6 / 115 (5.2)	NE [NE; NE]	NE [NE; NE]	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	8 / 74 (10.8)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9998
Yes	0 / 393 (0.0)	NE [NE; NE]	33 / 377 (8.8)	NE [NE; NE]	NE [NE; NE]	
No	0 / 41 (0.0)	NE [NE; NE]	3 / 40 (7.5)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.9999
Yes	0 / 177 (0.0)	NE [NE; NE]	16 / 172 (9.3)	NE [NE; NE]	NE [NE; NE]	
No	0 / 257 (0.0)	NE [NE; NE]	20 / 245 (8.2)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						1.0000
1	0 / 65 (0.0)	NE [NE; NE]	6 / 79 (7.6)	NE [NE; NE]	NE [NE; NE]	
2	0 / 293 (0.0)	NE [NE; NE]	26 / 281 (9.3)	NE [NE; NE]	NE [NE; NE]	
>=3	0 / 75 (0.0)	NE [NE; NE]	4 / 56 (7.1)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						0.9998
ER+, PR+	0 / 252 (0.0)	NE [NE; NE]	18 / 234 (7.7)	NE [NE; NE]	NE [NE; NE]	
ER+, PR-	0 / 166 (0.0)	NE [NE; NE]	17 / 171 (9.9)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
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Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						1.0000
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	0 / 362 (0.0)	NE [NE; NE]	28 / 343 (8.2)	NE [NE; NE]	NE [NE; NE]	
Positive	0 / 51 (0.0)	NE [NE; NE]	8 / 60 (13.3)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						0.9993
Primary	0 / 127 (0.0)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	NE [NE; NE]	
Secondary	0 / 307 (0.0)	NE [NE; NE]	31 / 279 (11.1)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						NE
Capecitabine	0 / 265 (0.0)	NE [NE; NE]	33 / 249 (13.3)	NE [NE; NE]	NE [NE; NE]	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	1 / 101 (1.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	2 / 67 (3.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.9998
Yes	0 / 197 (0.0)	NE [NE; NE]	19 / 198 (9.6)	NE [NE; NE]	NE [NE; NE]	
No	0 / 237 (0.0)	NE [NE; NE]	17 / 219 (7.8)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9997
Yes	0 / 294 (0.0)	NE [NE; NE]	26 / 275 (9.5)	NE [NE; NE]	NE [NE; NE]	
No	0 / 140 (0.0)	NE [NE; NE]	10 / 142 (7.0)	NE [NE; NE]	NE [NE; NE]	
ECOG						0.9996
0	0 / 251 (0.0)	NE [NE; NE]	25 / 246 (10.2)	NE [NE; NE]	NE [NE; NE]	
>=1	0 / 178 (0.0)	NE [NE; NE]	11 / 163 (6.7)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
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CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome						
Age at randomization						NE
<65 years of age	0 / 301 (0.0)	NE [NE; NE]	15 / 285 (5.3)	NE [NE; NE]	NE [NE; NE]	
>=65 years of age	0 / 133 (0.0)	NE [NE; NE]	16 / 132 (12.1)	NE [NE; NE]	NE [NE; NE]	
Race						1.0000
Asian	0 / 153 (0.0)	NE [NE; NE]	10 / 147 (6.8)	NE [NE; NE]	NE [NE; NE]	
White	0 / 231 (0.0)	NE [NE; NE]	18 / 223 (8.1)	NE [NE; NE]	NE [NE; NE]	
Other	0 / 50 (0.0)	NE [NE; NE]	3 / 47 (6.4)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Region						NE
Asia	0 / 148 (0.0)	NE [NE; NE]	11 / 144 (7.6)	NE [NE; NE]	NE [NE; NE]	
Europe	0 / 227 (0.0)	NE [NE; NE]	11 / 206 (5.3)	NE [NE; NE]	NE [NE; NE]	
Rest of the World	0 / 59 (0.0)	NE [NE; NE]	9 / 67 (13.4)	NE [14.4; NE]	NE [NE; NE]	
HER2 IHC expression						1.0000
IHC 1+	0 / 239 (0.0)	NE [NE; NE]	19 / 226 (8.4)	NE [NE; NE]	NE [NE; NE]	
IHC 2+/ISH-	0 / 116 (0.0)	NE [NE; NE]	5 / 115 (4.3)	NE [NE; NE]	NE [NE; NE]	
IHC >0 <1+	0 / 76 (0.0)	NE [NE; NE]	7 / 74 (9.5)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Prior CDK4/6 inhibitor use						0.9999
Yes	0 / 393 (0.0)	NE [NE; NE]	28 / 377 (7.4)	NE [NE; NE]	NE [NE; NE]	
No	0 / 41 (0.0)	NE [NE; NE]	3 / 40 (7.5)	NE [NE; NE]	NE [NE; NE]	
Prior Taxane Use In The Non-Metastatic Setting						0.9998
Yes	0 / 177 (0.0)	NE [NE; NE]	14 / 172 (8.1)	NE [NE; NE]	NE [NE; NE]	
No	0 / 257 (0.0)	NE [NE; NE]	17 / 245 (6.9)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Number of prior lines of endocrine therapy in the metastatic setting						1.0000
1	0 / 65 (0.0)	NE [NE; NE]	5 / 79 (6.3)	NE [NE; NE]	NE [NE; NE]	
2	0 / 293 (0.0)	NE [NE; NE]	22 / 281 (7.8)	NE [NE; NE]	NE [NE; NE]	
>=3	0 / 75 (0.0)	NE [NE; NE]	4 / 56 (7.1)	NE [NE; NE]	NE [NE; NE]	
ER/PR status I						1.0000
ER+, PR+	0 / 252 (0.0)	NE [NE; NE]	17 / 234 (7.3)	NE [NE; NE]	NE [NE; NE]	
ER+, PR-	0 / 166 (0.0)	NE [NE; NE]	13 / 171 (7.6)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 16JAN2025 11:56; Program name: T.2.33.2_GR310SRTEAE_SAF_SUB.sas; Output name: T.2.33.2_GR310SRTEAE_SAF_SUB.rtf; DI-EG project ID: D9670C00001;

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
ER/PR status II						1.0000
ER <=10%	0 / 21 (0.0)	NE [NE; NE]	0 / 14 (0.0)	NE [NE; NE]	NE [NE; NE]	
ER >10%	0 / 362 (0.0)	NE [NE; NE]	24 / 343 (7.0)	NE [NE; NE]	NE [NE; NE]	
Positive	0 / 51 (0.0)	NE [NE; NE]	7 / 60 (11.7)	NE [NE; NE]	NE [NE; NE]	
Endocrine Resistance						0.9994
Primary	0 / 127 (0.0)	NE [NE; NE]	5 / 137 (3.6)	NE [NE; NE]	NE [NE; NE]	
Secondary	0 / 307 (0.0)	NE [NE; NE]	26 / 279 (9.3)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
T-DXd vs. each Investigator's choice chemotherapy						NE
Capecitabine	0 / 265 (0.0)	NE [NE; NE]	31 / 249 (12.4)	NE [NE; NE]	NE [NE; NE]	
Nab-Paclitaxel	0 / 103 (0.0)	NE [NE; NE]	0 / 101 (0.0)	NE [NE; NE]	NE [NE; NE]	
Paclitaxel	0 / 66 (0.0)	NE [NE; NE]	0 / 67 (0.0)	NE [NE; NE]	NE [NE; NE]	
Prior anthracycline use						0.9997
Yes	0 / 197 (0.0)	NE [NE; NE]	17 / 198 (8.6)	NE [NE; NE]	NE [NE; NE]	
No	0 / 237 (0.0)	NE [NE; NE]	14 / 219 (6.4)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Table 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Liver metastases						0.9998
Yes	0 / 294 (0.0)	NE [NE; NE]	22 / 275 (8.0)	NE [NE; NE]	NE [NE; NE]	
No	0 / 140 (0.0)	NE [NE; NE]	9 / 142 (6.3)	NE [NE; NE]	NE [NE; NE]	
ECOG						0.9995
0	0 / 251 (0.0)	NE [NE; NE]	23 / 246 (9.3)	NE [NE; NE]	NE [NE; NE]	
>=1	0 / 178 (0.0)	NE [NE; NE]	8 / 163 (4.9)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Tabelle 2.33.3 Unerwünschte Ereignisse mit CTCAE-Grad 3 oder höher nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Subgruppenanalyse – Interaktions-p-Wert <0,05 – SAF

Table 2.33.3 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Investigations; PT: All (any PT)						
T-DXd vs. each Investigator's choice chemotherapy						0.0477
Capecitabine	56 / 265 (21.1)	NE [28.1; NE]	16 / 249 (6.4)	NE [NE; NE]	2.9507 [1.7301; 5.3267] 0.0001	
Nab-Paclitaxel	30 / 103 (29.1)	NE [NE; NE]	19 / 101 (18.8)	NE [NE; NE]	1.5114 [0.8561; 2.7345] 0.1581	
Paclitaxel	15 / 66 (22.7)	NE [NE; NE]	11 / 67 (16.4)	NE [NE; NE]	1.0490 [0.4718; 2.3875] 0.9075	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
Program Location: DS8201_az_transfers_wks_bdmprog/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_internal/20240611_AMNOG_01/programs/tlf/Primary
Run date: 10DEC2024 5:42; Program name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.sas; Output name: T.2.33.3_GR310SRTEAE_SAF_SUB_SIG.rtf; DI-EG project ID: D9670C00001;

Table 2.33.3 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Subgroup Analysis - interaction p-value < 0.05 - Safety Analysis Set

DESTINY Breast-06	T-DXd N=434		Chemotherapy N=417		T-DXd vs. Chemotherapy	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Metabolism and nutrition disorders; PT: Hypokalaemia						
Race						0.0073
Asian	13 / 153 (8.5)	NE [NE; NE]	3 / 147 (2.0)	NE [NE; NE]	3.3330 [1.0646; 14.6041] 0.0476	
White	6 / 231 (2.6)	NE [NE; NE]	0 / 223 (0.0)	NE [NE; NE]	NE [NE; NE]	
Other	0 / 50 (0.0)	NE [NE; NE]	2 / 47 (4.3)	NE [NE; NE]	NE [NE; NE]	

Subgroup analyses conducted for the SOC and PT identified as relevant on safety analysis set level.
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category;
a. Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the log-log transformation.
b. Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. Two-sided p-value from unstratified log-rank test.
c. Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment-by-subgroup interaction as categorical variables in the model. The p-value is based on the profile-likelihood approach.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Tabelle 14.3.5.1.1.2 Unerwünschte Ereignisse nach SOC und PT, die zum Therapieabbruch führten

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Table 14.3.5.1.1.2
Number of patients with adverse events leading to discontinuation of investigational product,
by system organ class and preferred term
Safety analysis set

System organ class / Preferred term	Number (%) of patients[a] T-DXd (N=434)	Chemotherapy (N=417)
Patients with any AE leading to discontinuation of IP[b]	62 (14.3)	39 (9.4)
Infections and infestations	2 (0.5)	0
Pneumocystis jirovecii pneumonia	1 (0.2)	0
Pneumonia	1 (0.2)	0
Blood and lymphatic system disorders	2 (0.5)	0
Anaemia	1 (0.2)	0
Pancytopenia	1 (0.2)	0
Immune system disorders	0	2 (0.5)
Anaphylactic shock	0	1 (0.2)
Hypersensitivity	0	1 (0.2)
Metabolism and nutrition disorders	3 (0.7)	0
Decreased appetite	1 (0.2)	0
Hypokalaemia	2 (0.5)	0
Nervous system disorders	2 (0.5)	12 (2.9)
Dysaesthesia	0	1 (0.2)
Dysgeusia	1 (0.2)	0
Leukoencephalopathy	1 (0.2)	0
Neuromuscular toxicity	0	1 (0.2)

[a] Number (%) of patients with AEs leading to discontinuation of IP, sorted by international order for system organ class and alphabetically for preferred term. Patients with multiple events in the same preferred term are counted only once in that preferred term. Patients with events in more than one preferred term are counted once in each of those preferred terms. Patients with events in more than one preferred term within the same system organ class are counted only once in that system organ class.
[b] Action taken = Drug permanently discontinued.
Includes AEs with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
MedDRA version 26.1.
IP = investigational product. T-DXd = trastuzumab deruxtecan.
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Table 14.3.5.1.1.2
Number of patients with adverse events leading to discontinuation of investigational product, by system organ class and preferred term
Safety analysis set

System organ class / Preferred term	Number (%) of patients[a] T-DXd (N=434)	Chemotherapy (N=417)
Nervous system disorders (continued)		
Neuropathy peripheral	0	2 (0.5)
Peripheral motor neuropathy	0	1 (0.2)
Peripheral sensory neuropathy	0	6 (1.4)
Spinal cord compression	0	1 (0.2)
Cardiac disorders	1 (0.2)	5 (1.2)
Angina pectoris	0	3 (0.7)
Atrial fibrillation	0	1 (0.2)
Left ventricular dysfunction	1 (0.2)	0
Ventricular tachycardia	0	1 (0.2)
Vascular disorders	0	1 (0.2)
Lymphoedema	0	1 (0.2)
Respiratory, thoracic and mediastinal disorders	39 (9.0)	1 (0.2)
Interstitial lung disease	15 (3.5)	0
Nasal inflammation	0	1 (0.2)
Pneumonitis	23 (5.3)	0
Pulmonary embolism	1 (0.2)	0
Gastrointestinal disorders	1 (0.2)	4 (1.0)
Ascites	1 (0.2)	0

[a] Number (%) of patients with AEs leading to discontinuation of IP, sorted by international order for system organ class and alphabetically for preferred term. Patients with multiple events in the same preferred term are counted only once in that preferred term. Patients with events in more than one preferred term are counted once in each of those preferred terms. Patients with events in more than one preferred term within the same system organ class are counted only once in that system organ class.
[b] Action taken = Drug permanently discontinued.
Includes AEs with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
MedDRA version 26.1.
IP = investigational product. T-DXd = trastuzumab deruxtecan.
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Table 14.3.5.1.1.2
Number of patients with adverse events leading to discontinuation of investigational product, by system organ class and preferred term
Safety analysis set

System organ class / Preferred term	Number (%) of patients[a] T-DXd (N=434)	Chemotherapy (N=417)
Gastrointestinal disorders (continued)		
Colitis	0	3 (0.7)
Mouth ulceration	0	1 (0.2)
Hepatobiliary disorders	2 (0.5)	1 (0.2)
Acute hepatic failure	1 (0.2)	0
Drug-induced liver injury	0	1 (0.2)
Hepatic cirrhosis	1 (0.2)	0
Skin and subcutaneous tissue disorders	0	5 (1.2)
Nail disorder	0	1 (0.2)
Nail toxicity	0	1 (0.2)
Paraneoplastic dermatomyositis	0	1 (0.2)
Rash	0	1 (0.2)
Skin fissures	0	1 (0.2)
Renal and urinary disorders	0	2 (0.5)
Cystitis interstitial	0	1 (0.2)
Renal colic	0	1 (0.2)
General disorders and administration site conditions	3 (0.7)	7 (1.7)
Asthenia	1 (0.2)	3 (0.7)
Facial pain	0	1 (0.2)

[a] Number (%) of patients with AEs leading to discontinuation of IP, sorted by international order for system organ class and alphabetically for preferred term. Patients with multiple events in the same preferred term are counted only once in that preferred term. Patients with events in more than one preferred term are counted once in each of those preferred terms. Patients with events in more than one preferred term within the same system organ class are counted only once in that system organ class.
[b] Action taken = Drug permanently discontinued.
Includes AEs with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
MedDRA version 26.1.
IP = investigational product. T-DXd = trastuzumab deruxtecan.
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Table 14.3.5.1.1.2
Number of patients with adverse events leading to discontinuation of investigational product, by system organ class and preferred term
Safety analysis set

System organ class / Preferred term	Number (%) of patients[a] T-DXd (N=434)	Chemotherapy (N=417)
General disorders and administration site conditions (continued)		
Fatigue	0	2 (0.5)
General physical health deterioration	2 (0.5)	0
Oedema peripheral	0	1 (0.2)
Investigations	8 (1.8)	1 (0.2)
Blood bilirubin increased	1 (0.2)	0
Ejection fraction decreased	1 (0.2)	0
Gamma-glutamyltransferase increased	1 (0.2)	0
Liver function test increased	1 (0.2)	0
Neutrophil count decreased	0	1 (0.2)
Platelet count decreased	3 (0.7)	0
Pulse abnormal	1 (0.2)	0
Injury, poisoning and procedural complications	1 (0.2)	3 (0.7)
Contusion	0	1 (0.2)
Femur fracture	0	1 (0.2)
Infusion related reaction	1 (0.2)	1 (0.2)

[a] Number (%) of patients with AEs leading to discontinuation of IP, sorted by international order for system organ class and alphabetically for preferred term. Patients with multiple events in the same preferred term are counted only once in that preferred term. Patients with events in more than one preferred term are counted once in each of those preferred terms. Patients with events in more than one preferred term within the same system organ class are counted only once in that system organ class.
[b] Action taken = Drug permanently discontinued.
Includes AEs with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).
MedDRA version 26.1.
IP = investigational product. T-DXd = trastuzumab deruxtecan.
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Abbildung 2.33.1 Unerwünschte Ereignisse mit CTCAE-Grad 3 oder höher nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Kaplan-Meier-Plot – SAF

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Data Intelligence - Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 2024-03-18)

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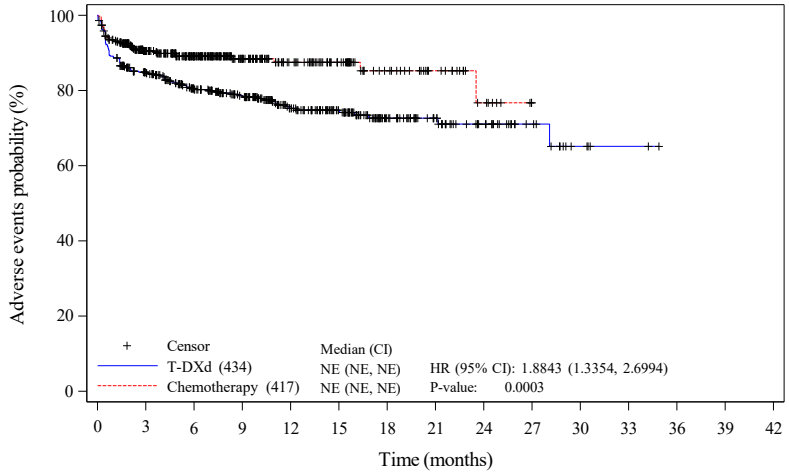
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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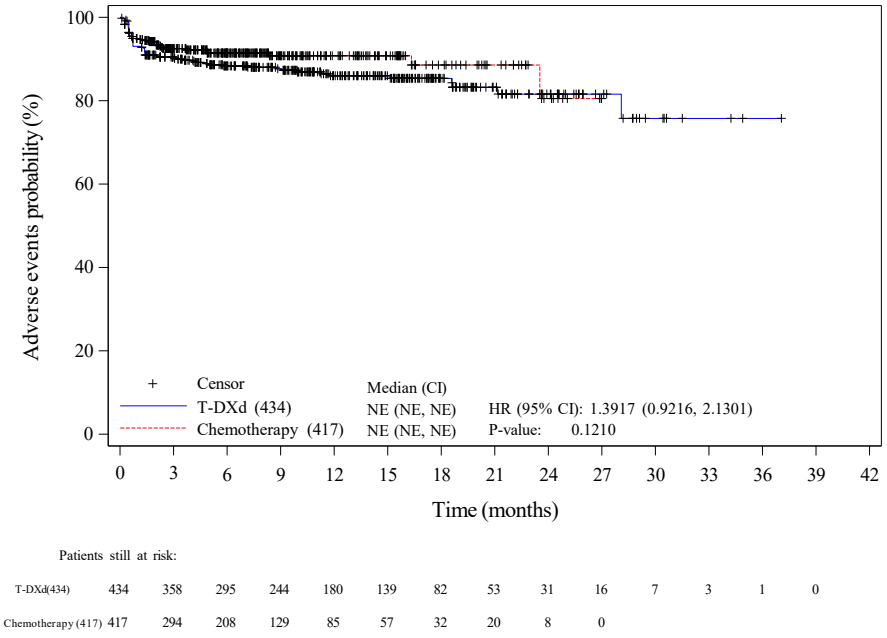
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Neutrophil count decreased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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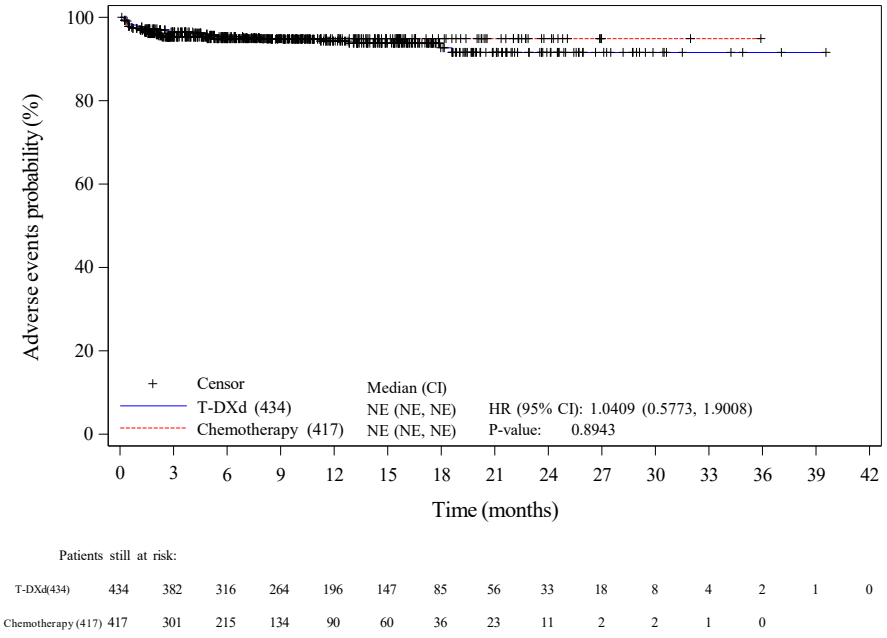
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: White blood cell count decreased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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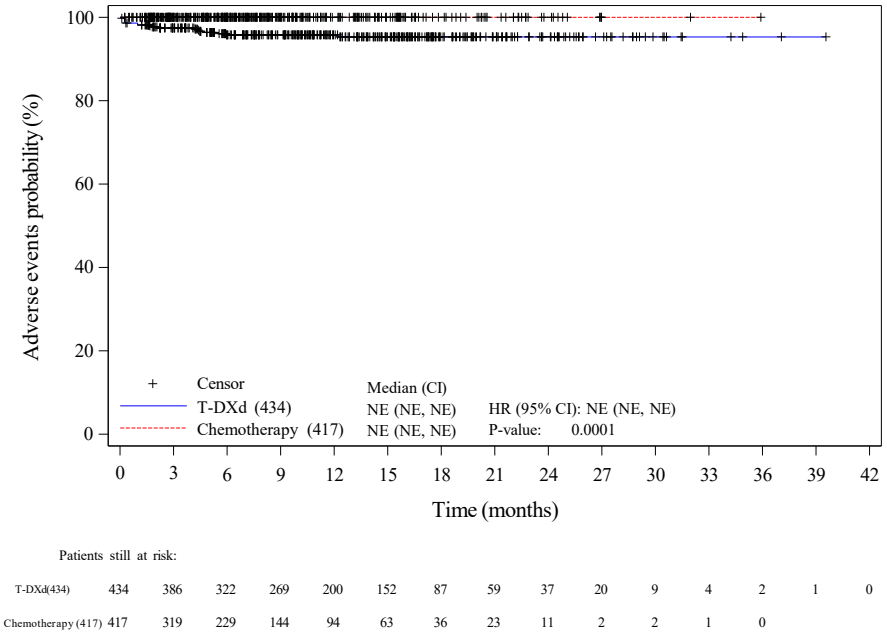
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Platelet count decreased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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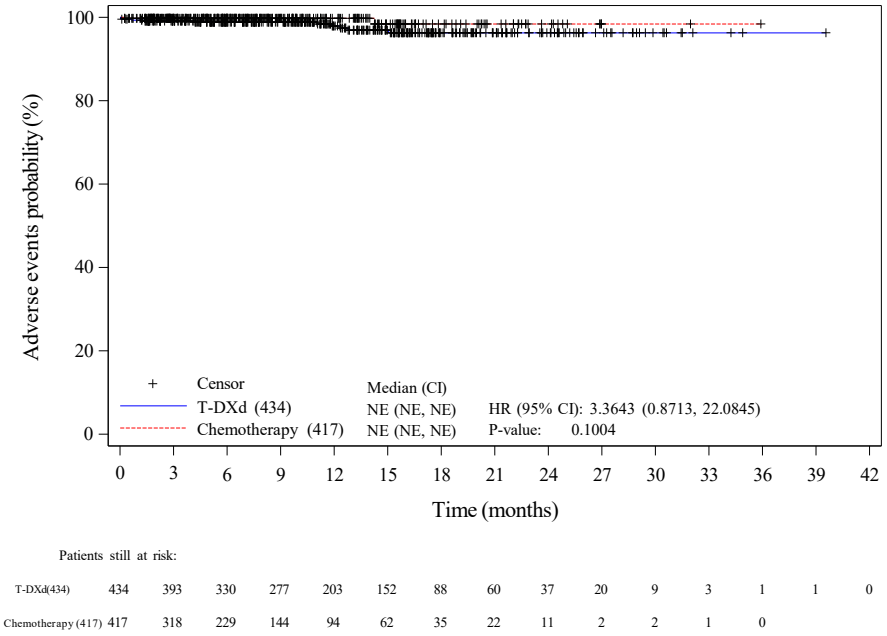
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Gamma-glutamyltransferase increased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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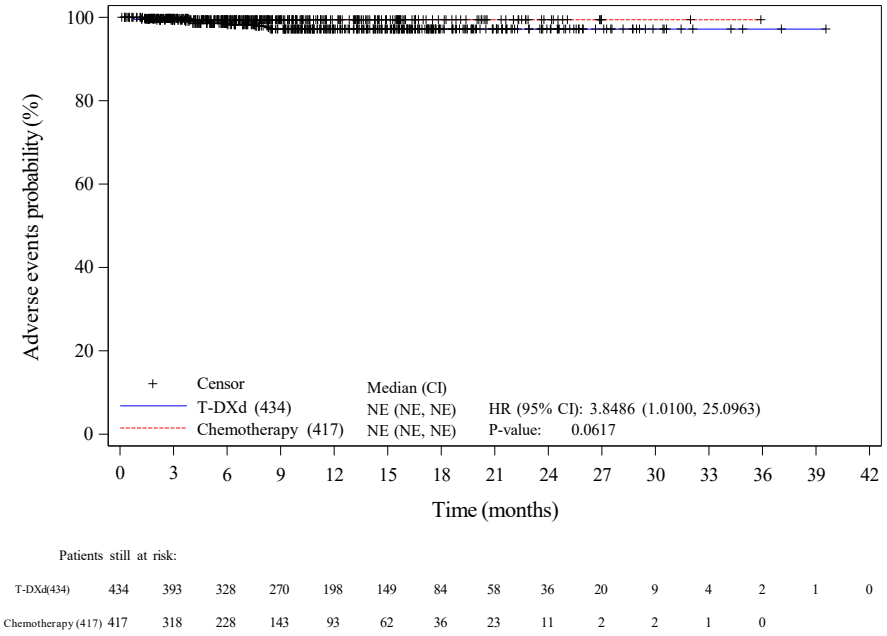
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Investigations; PT: Lymphocyte count decreased



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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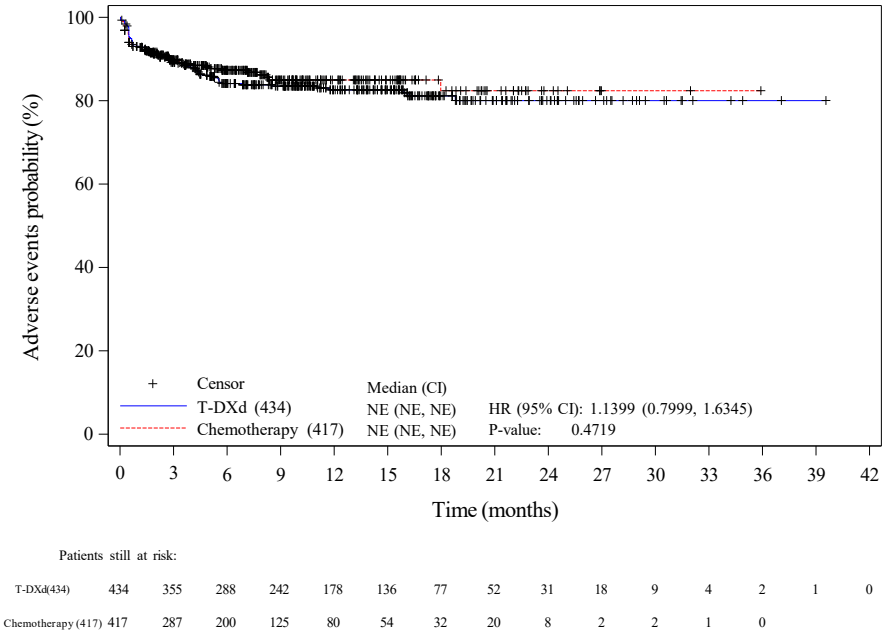
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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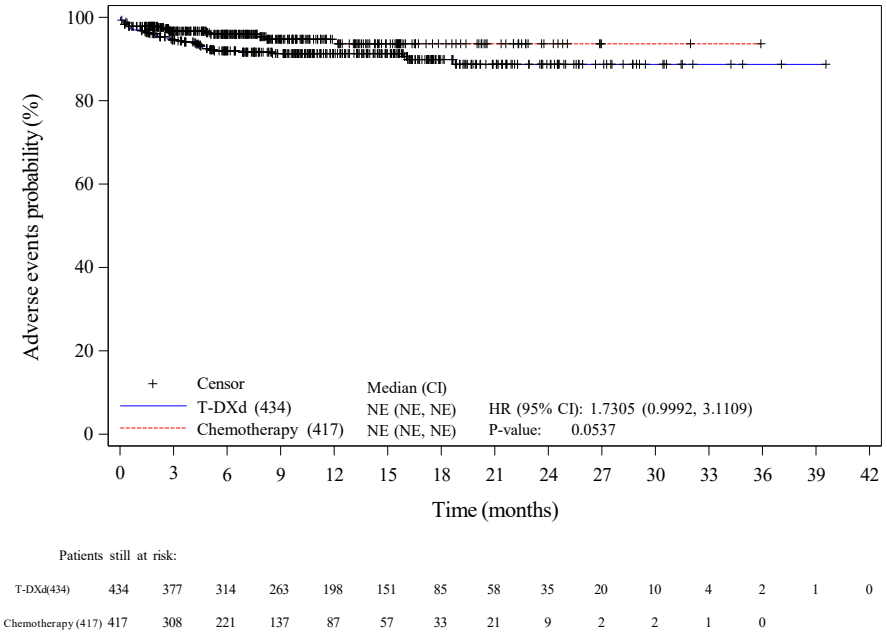
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Anaemia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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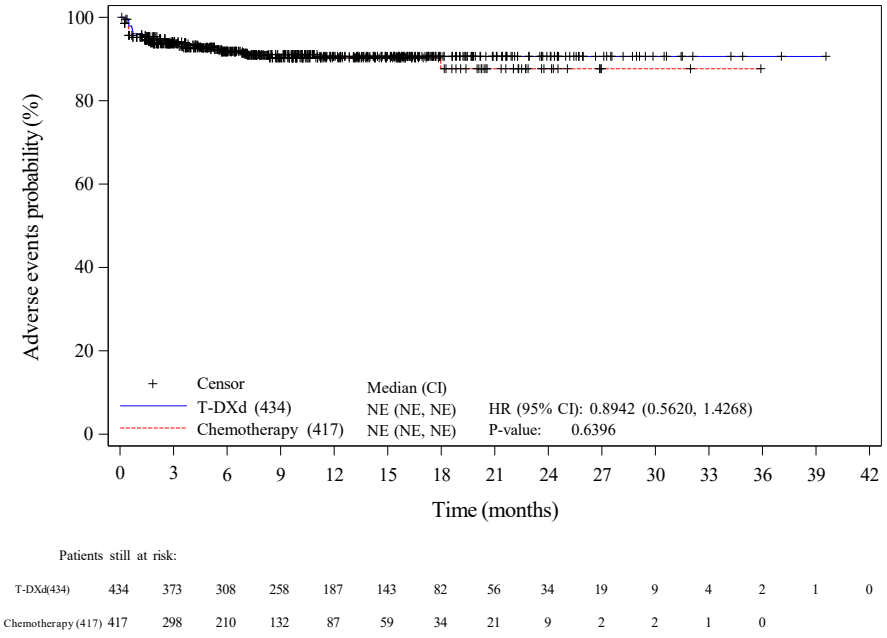
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Neutropenia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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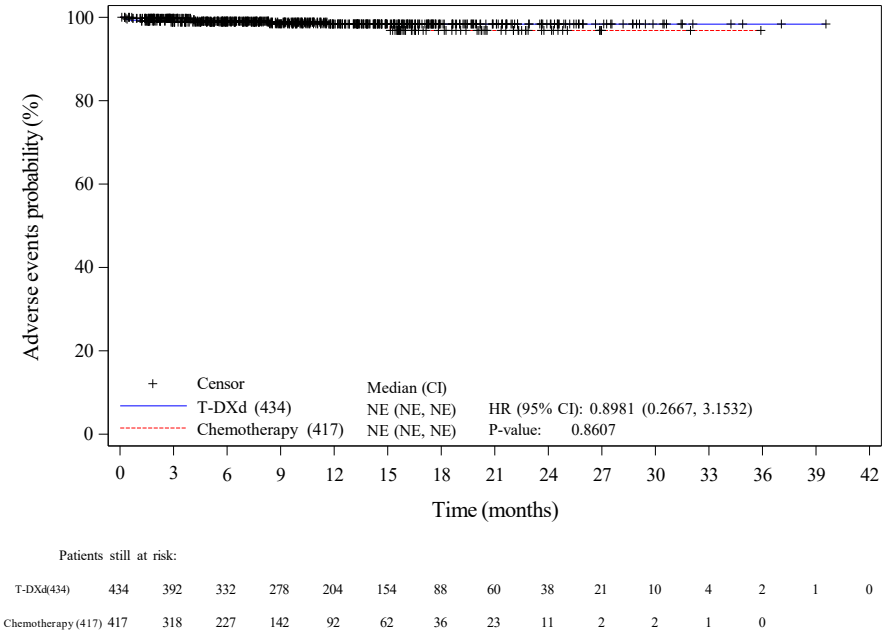
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Blood and lymphatic system disorders; PT: Leukopenia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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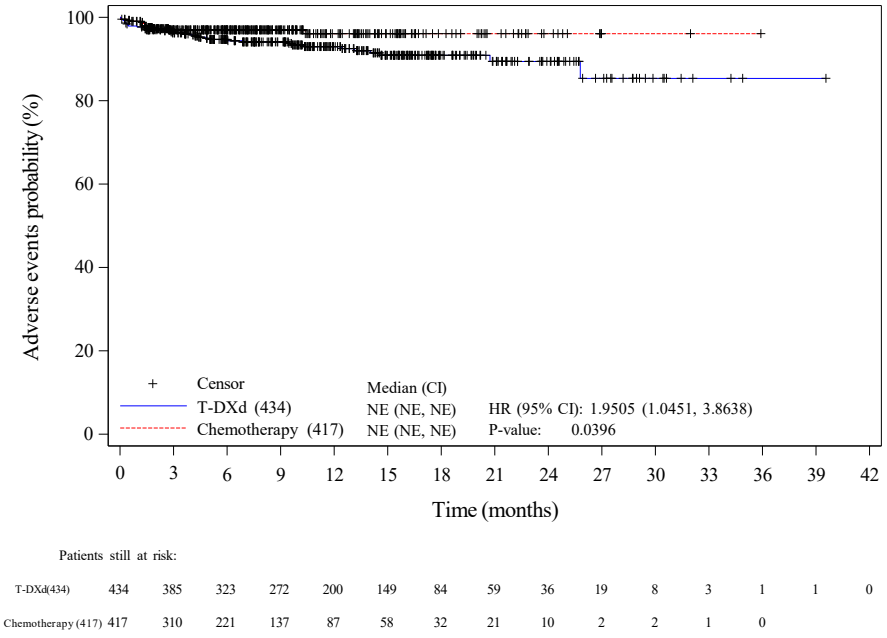
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
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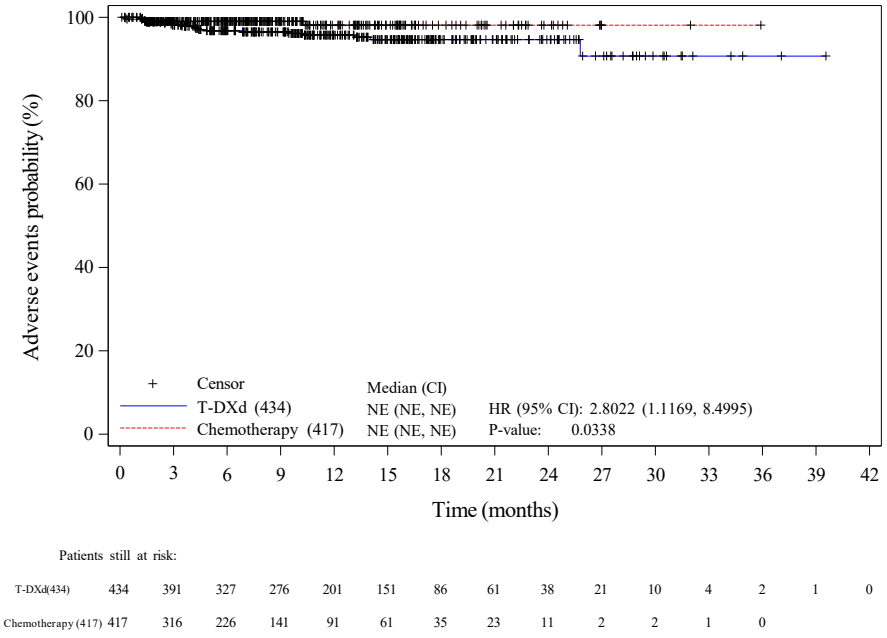
Run date: 10DEC2024 10:04; Program name: F.2.33.1_GR310SRTEAE_SAF.sas; Output name: F.2.33.1_GR310SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hypokalaemia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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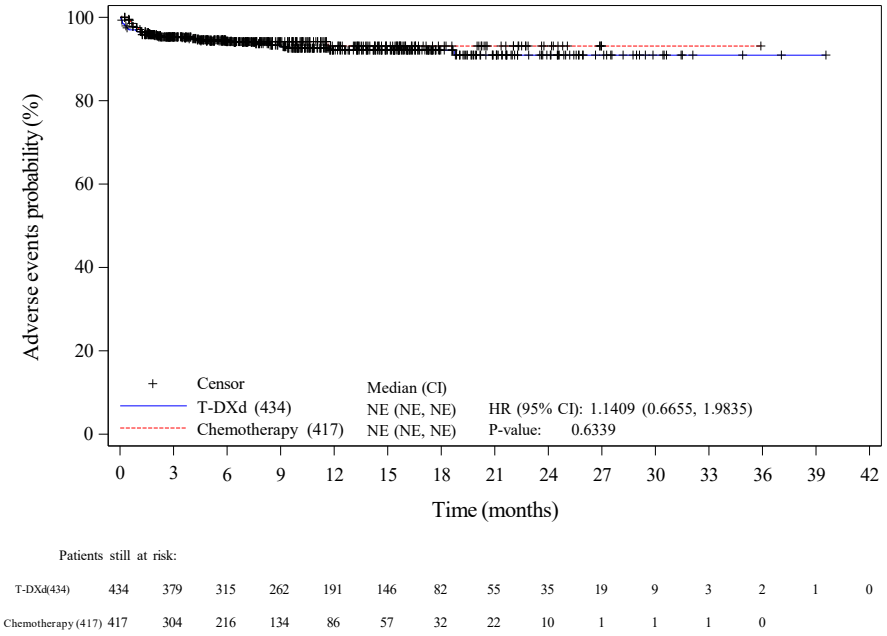
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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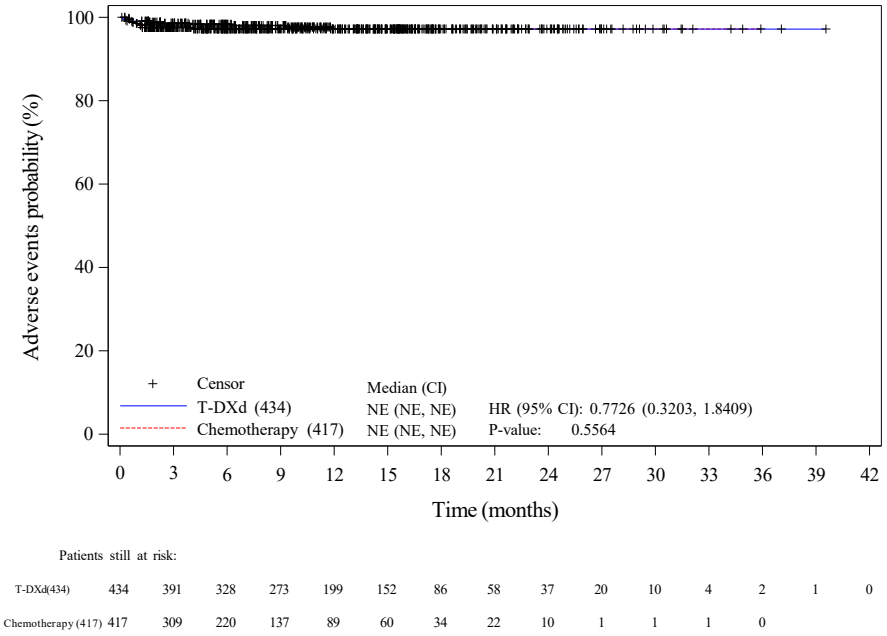
Run date: 10DEC2024 10:04; Program name: F.2.33.1_GR310SRTEAE_SAF.sas; Output name: F.2.33.1_GR310SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Diarrhoea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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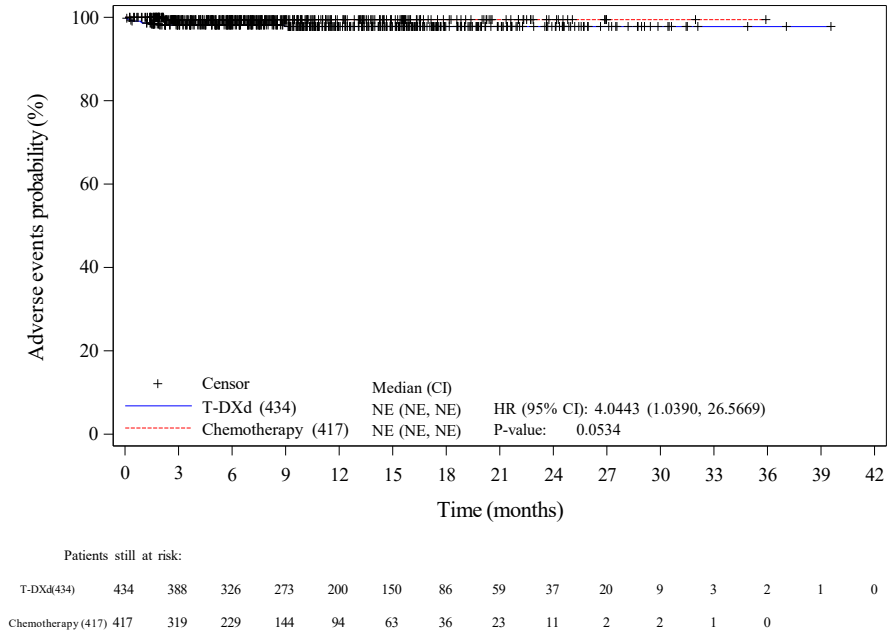
Run date: 10DEC2024 10:04; Program name: F.2.33.1_GR310SRTEAE_SAF.sas; Output name: F.2.33.1_GR310SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Gastrointestinal disorders; PT: Nausea



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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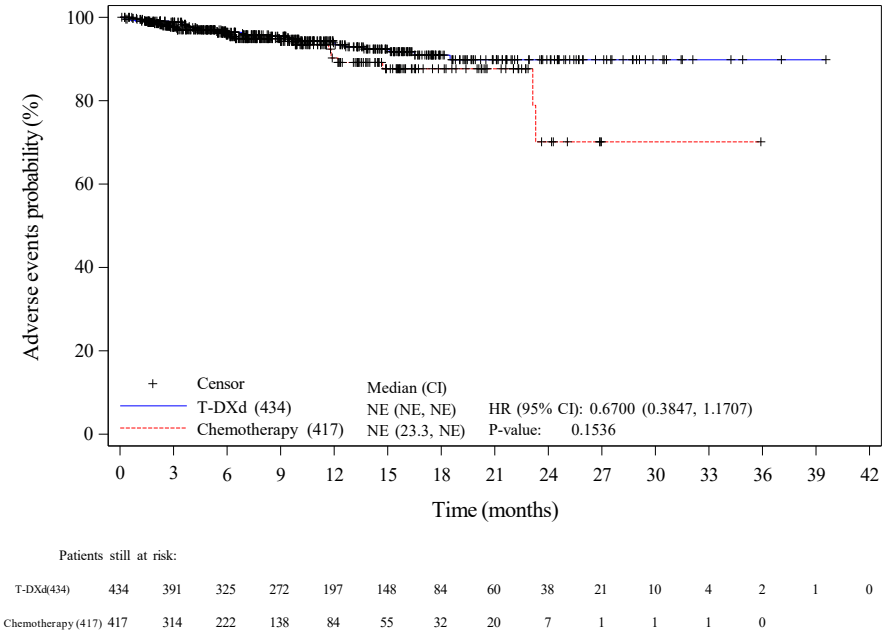
Run date: 10DEC2024 10:04; Program name: F.2.33.1_GR310SRTEAE_SAF.sas; Output name: F.2.33.1_GR310SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Infections and infestations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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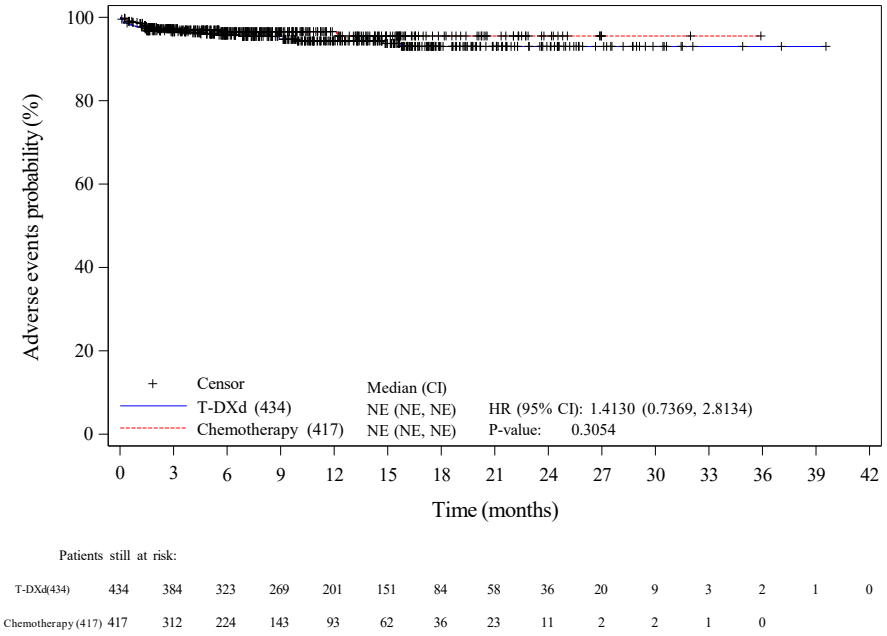
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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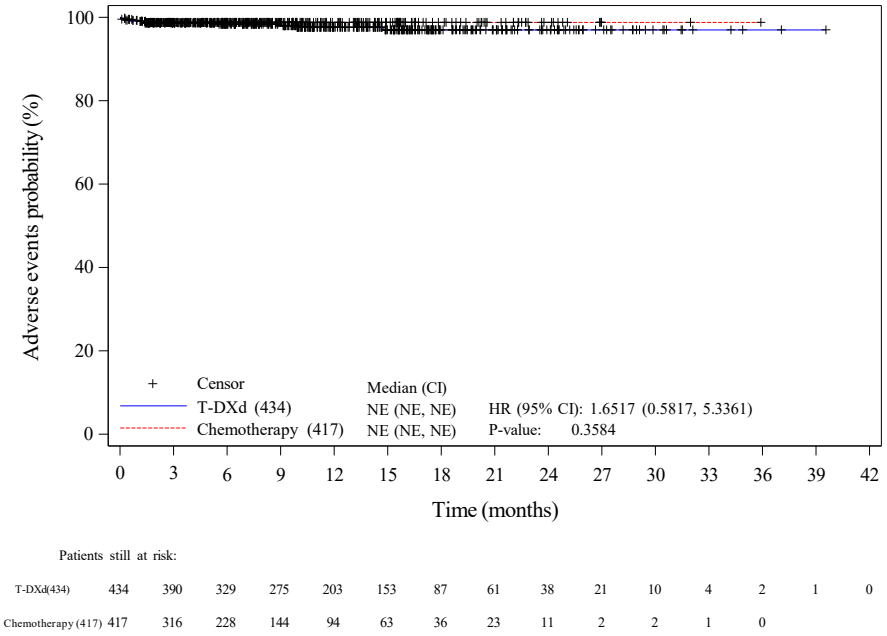
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Asthenia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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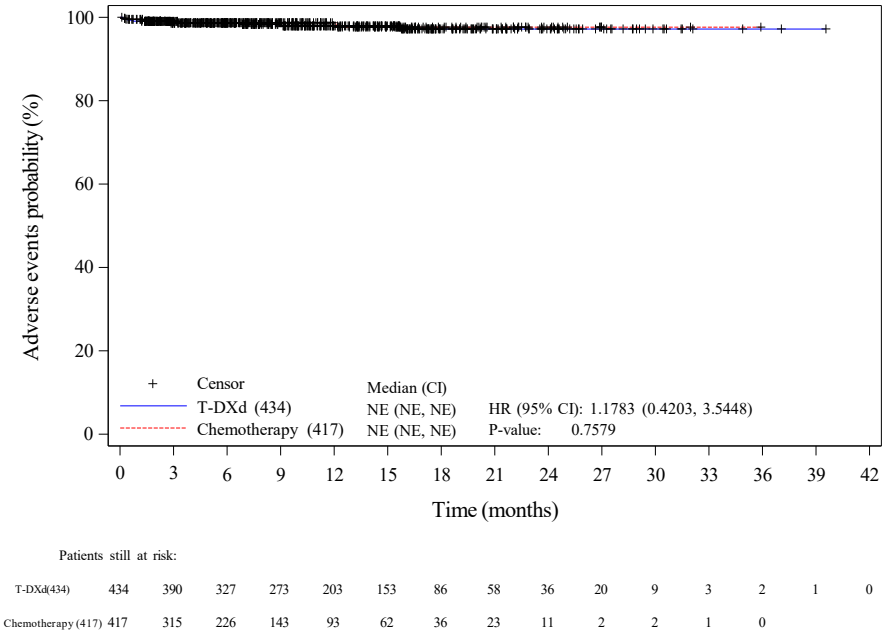
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: General disorders and administration site conditions; PT: Fatigue



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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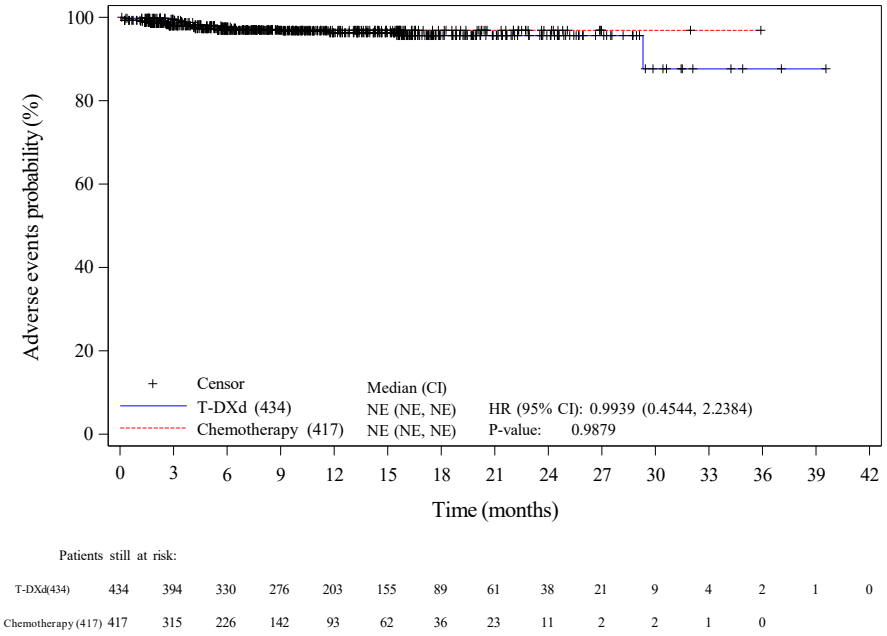
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Respiratory, thoracic and mediastinal disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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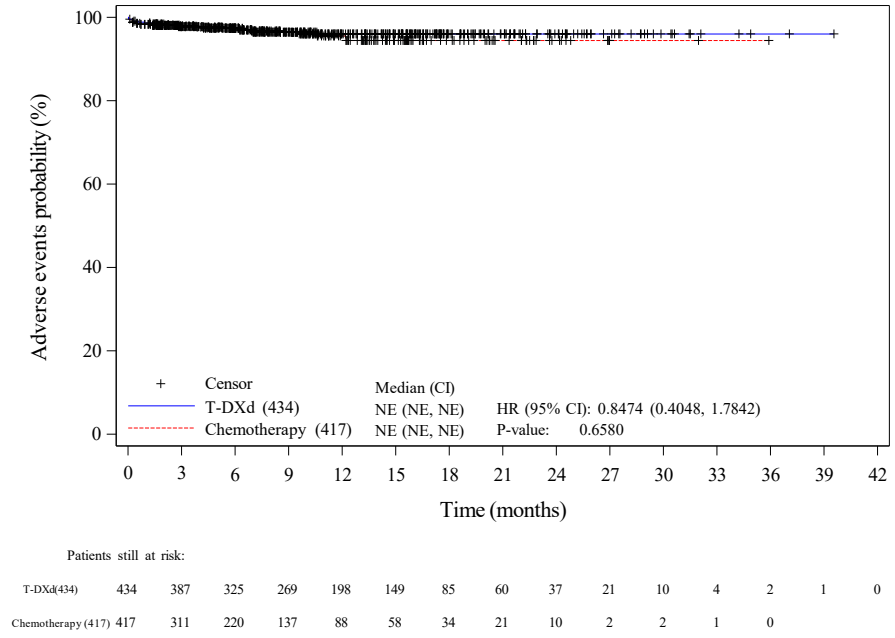
Run date: 10DEC2024 10:04; Program name: F.2.33.1_GR310SRTEAE_SAF.sas; Output name: F.2.33.1_GR310SRTEAE_SAF.rtf; DI-EG project ID: D9670C00001;

Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Vascular disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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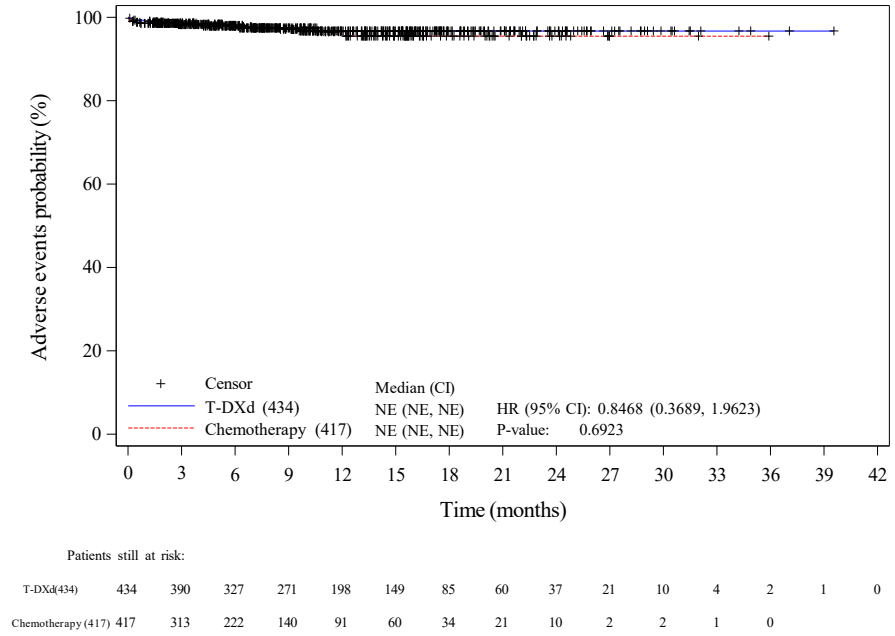
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Vascular disorders; PT: Hypertension



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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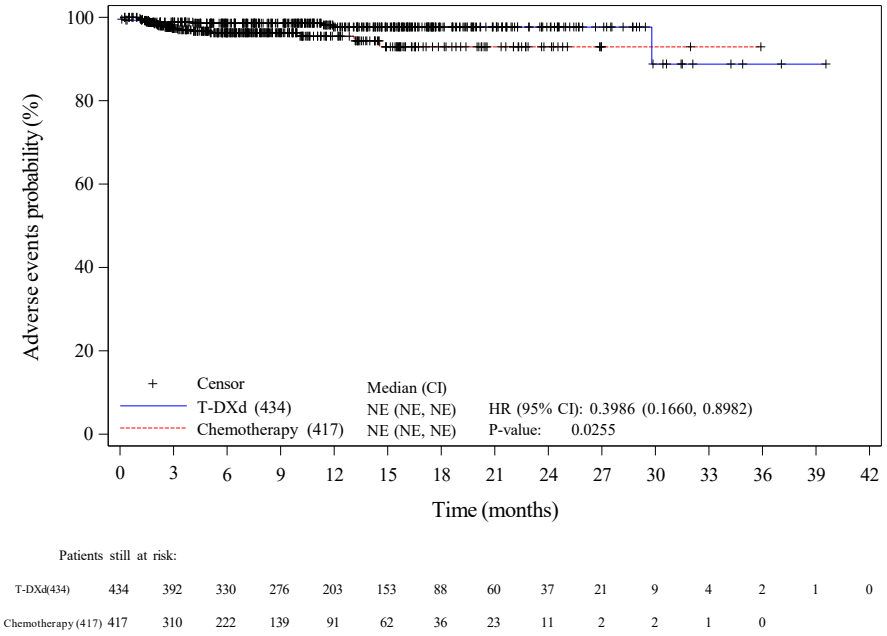
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Nervous system disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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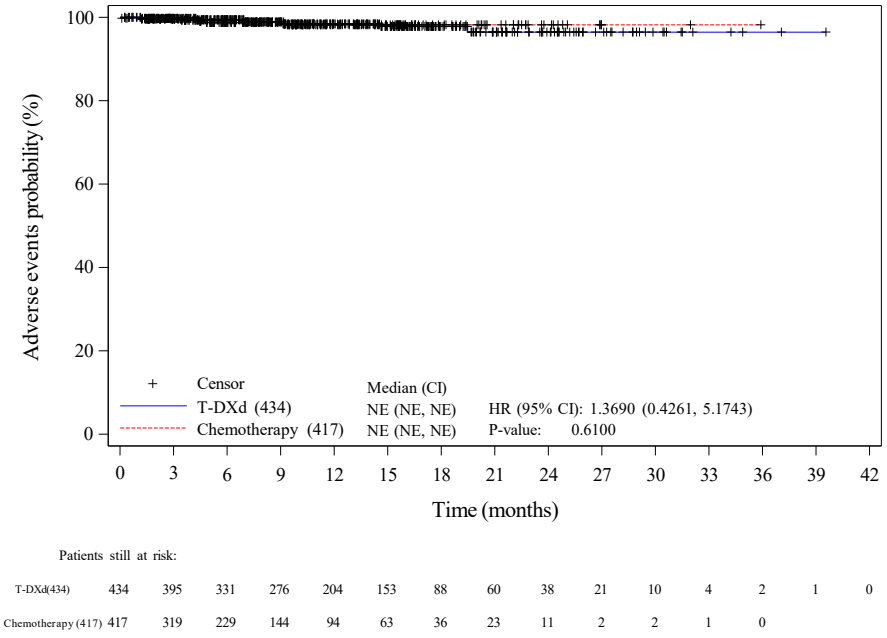
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Hepatobiliary disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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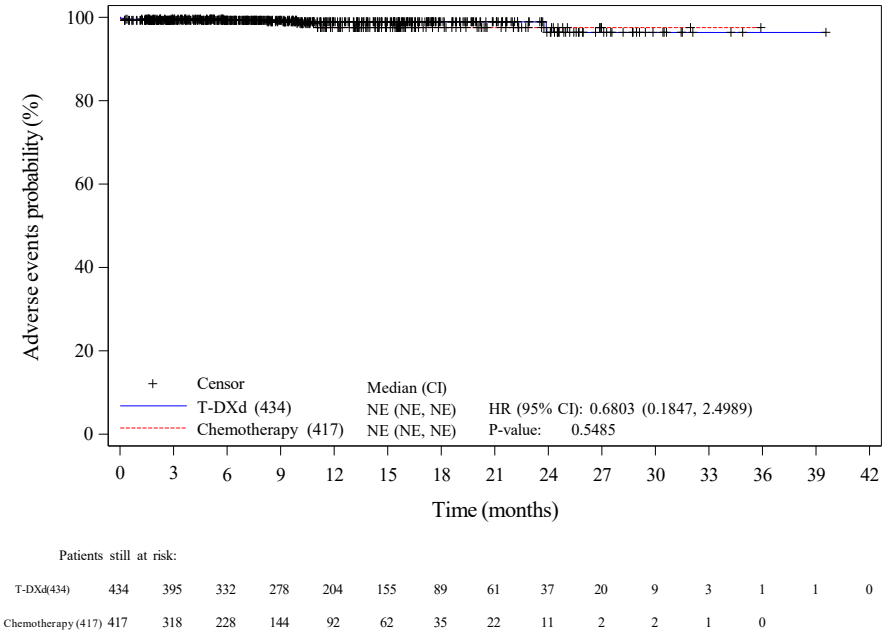
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Injury, poisoning and procedural complications; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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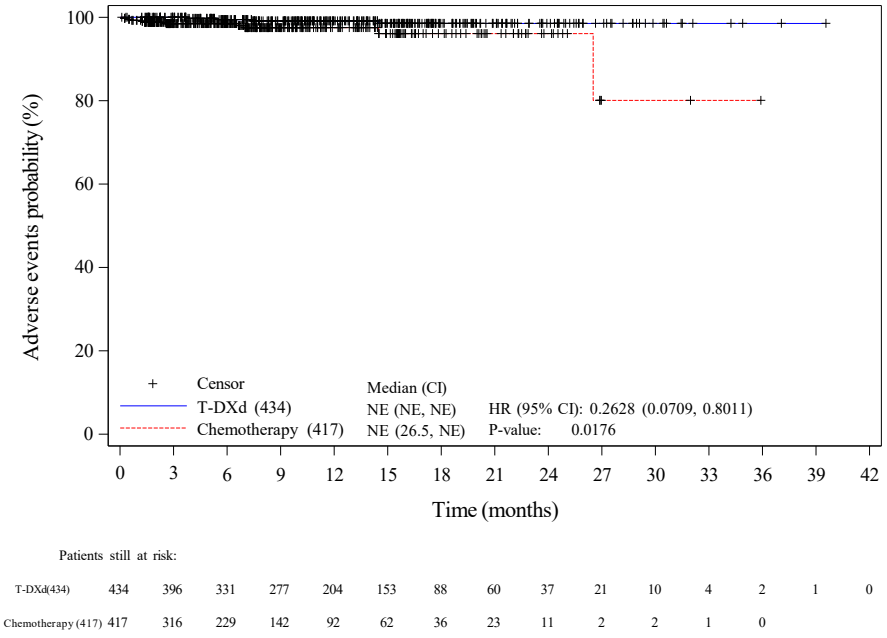
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Musculoskeletal and connective tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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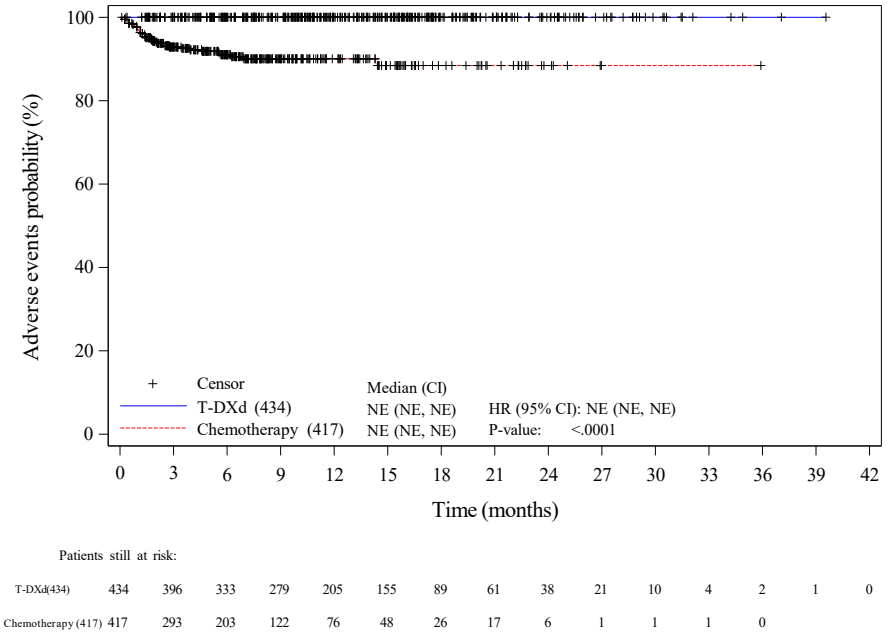
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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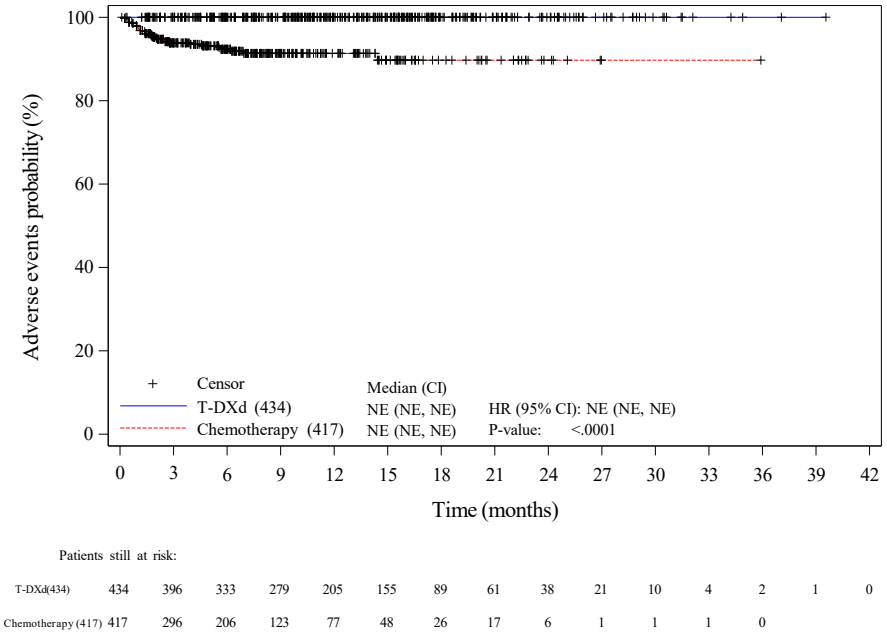
Figure 2.33.1 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for >= 10 patients (in total) and >= 1% of the patients in at least one arm - Kaplan-Meier plot - Safety Analysis Set
SOC: Skin and subcutaneous tissue disorders; PT: Palmar-plantar erythrodysaesthesia syndrome



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Abbildung 2.33.2 Unerwünschte Ereignisse mit CTCAE-Grad 3 oder höher nach SOC und PT beobachtet in ≥10 Patienten (insgesamt) und ≥1 % der Patienten in mindestens einem Arm – Kaplan-Meier-Plot – Analyse nach Subgruppe – SAF

Daiichi Sankyo Europe GmbH
Data Intelligence - Evidence Generation
D9670C00001 - Destiny Breast 06 (DCO 2024-03-18)

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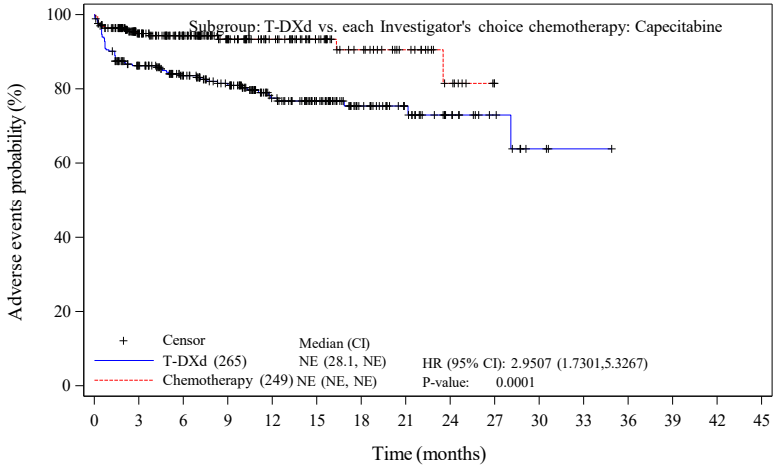
Figure 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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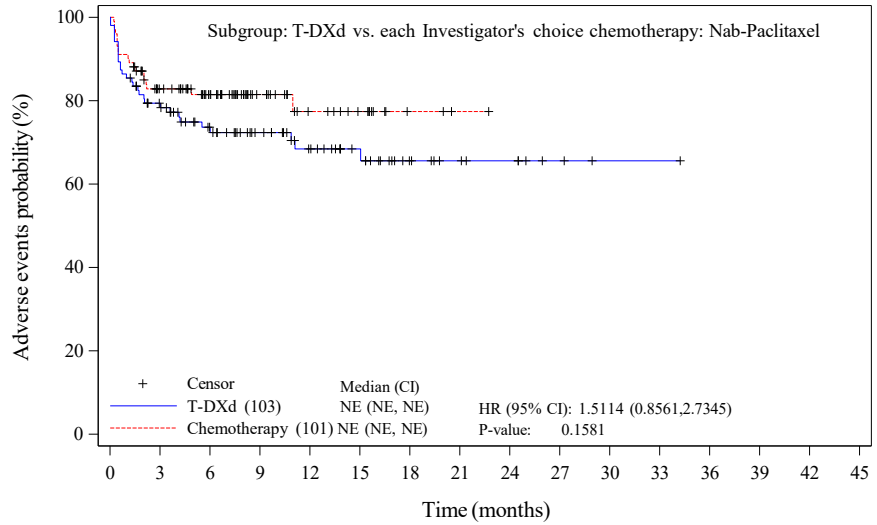
Figure 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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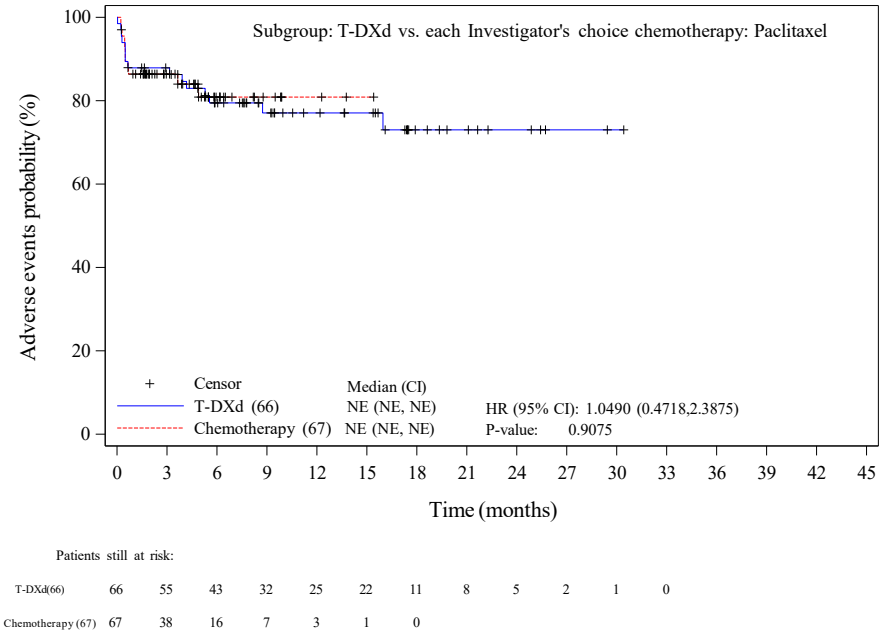
Figure 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Investigations; PT: All (any PT)



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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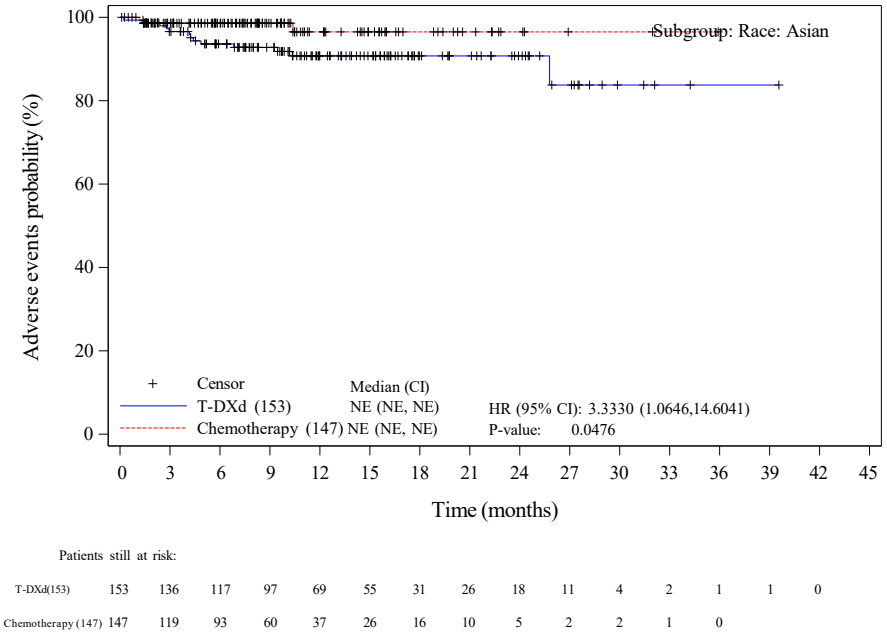
Figure 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hypokalaemia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

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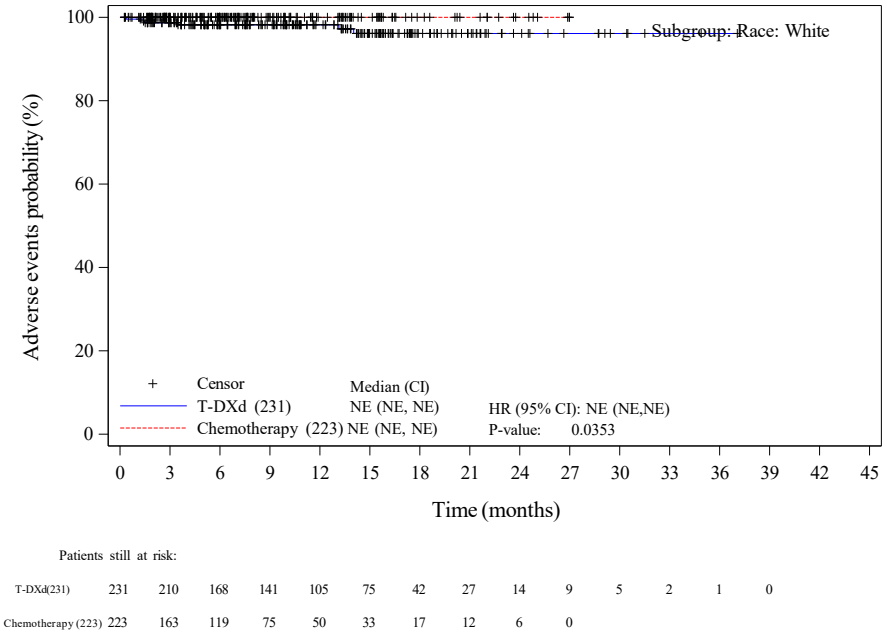
Figure 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hypokalaemia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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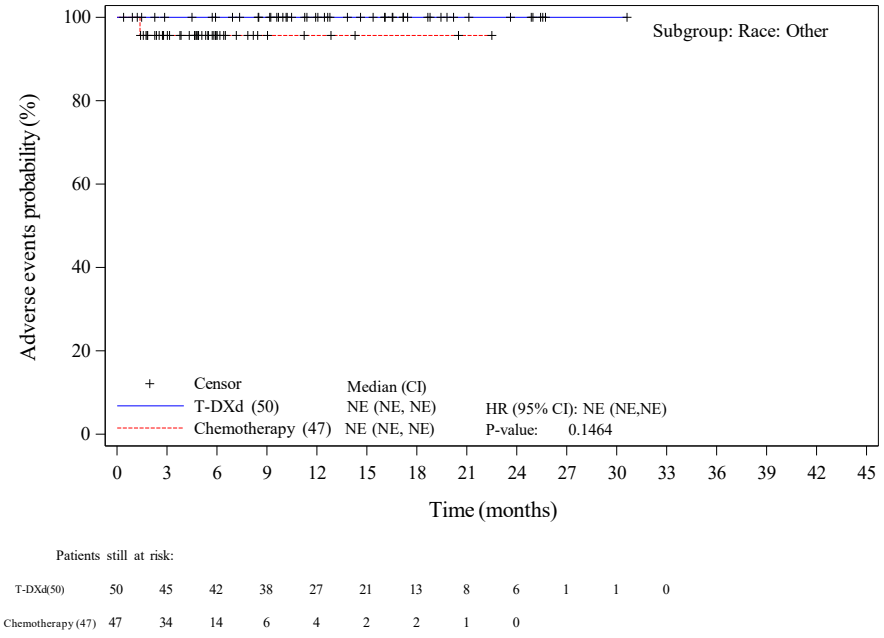
Figure 2.33.2 Adverse events with CTCAE grade 3 or higher by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Kaplan-Meier plot - Analysis by subgroup - Safety Analysis Set
SOC: Metabolism and nutrition disorders; PT: Hypokalaemia



Notes: Hazard ratio (HR) is from unstratified Cox proportional hazards model and two-sided p-value is based on unstratified log-rank test. CI: confidence interval; NE: Not estimable.
Includes AEs with an onset date or worsening on or after the date of first dose and upto and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first).

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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Tabelle 2.34.1 Nicht-Schwerwiegende UE und Nicht-Schwere Unerwünschte Ereignisse von besonderem Interesse – SAF

Table 2.34.1 Non-Serious AE and Non-Severe Adverse Events of Special Interest - Descriptive Summary-Safety Analysis Set

DESTINY Breast-06	T-DXd N=434	Chemotherapy N=417
	n (%)	n (%)
Number of subjects with at least one non-serious AE	428 (98.6)	393 (94.2)
Number of subjects with at least one non-severe AESI of adjudicated drug-related ILD/pneumonitis (NCI CTCAE grade <3)	43 (9.9)	1 (0.2)
Number of subjects with at least one non-severe AESI of ILD/pneumonitis (NCI CTCAE grade <3)	46 (10.6)	1 (0.2)
Number of subjects with at least one non-severe AESI of LVEF decrease (NCI CTCAE grade <3)	32 (7.4)	13 (3.1)

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set; AE:Adverse Event; AESI:Adverse Event of Special Interest; NCI CTCAE: National Cancer Institute-Common Terminology Criteria for Adverse Events

Data source: DS8201_az_transfers/dev/transfer/eg_analysis/DB06_09670C00001/rstrct_DCO20240318_eg/eg_rd_copy/adam/adam
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