Dossier zur Nutzenbewertung gemäß § 35a SGB V

Trastuzumab deruxtecan (Enhertu®)

Daiichi Sankyo Deutschland GmbH

Anhang 4-G

Erwachsene mit fortgeschrittenem HER2-positivem Adenokarzinom des Magens oder des GEJ; nach einer vorhergehenden Trastuzumab-basierten Erstlinientherapie

Analysen für das Nutzendossier

Stand: 30.09.2025

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Anhang 4-G Analysen DESTINY-Gastric04

Anhang 4-G 1 Mortalität – FAS

Anhang 4-G 1.1 Gesamtüberleben

Anhang 4-G 1.1.1 Gesamtüberleben (OS) – FAS

Daiichi Sankyo Europe GmbH
DS8201-A-U306 (DESTINY-GASTRIC04) - DCO 24-OCT-2024

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Final
Statistical analyses for AMNOG (HTA Germany)

Table 9.1.1 Overall survival (OS) - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
	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	124 (50.4)	14.7 [12.1, 16.6]	142 (57.3)	11.4 [9.9, 15.5]	0.7024 [0.5504, 0.8964] 0.0045	0.0044
Subjects with censoring event	122 (49.6)		106 (42.7)			
Alive	117 (47.6)		93 (37.5)			
Withdrawal by Subject	4 (1.6)		12 (4.8)			
Lost to Follow-up	1 (0.4)		1 (0.4)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
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Run date: 23JUN2025 11:01 (CET); Program name: t_tte.sas; Output name: T.9.1.1_OS_FAS.rtf

Anhang 4-G 1.1.2 Gesamtüberleben (OS) – Subgruppenanalyse – FAS

Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.0073
IHC 3+	107 / 207 (51.7)	14.4 [11.9, 16.4]	117 / 208 (56.3)	13.4 [10.8, 16.5]	0.7934 [0.6098, 1.0324] 0.0850 0.0847	
IHC 2+/ISH+	17 / 39 (43.6)	17.7 [9.1, NE]	25 / 40 (62.5)	7.4 [4.5, 10.7]	0.3486 [0.1828, 0.6648] 0.0014 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.1.2_OS_FAS_SUB.rtf

Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.5980
Asia [excluding mainland China]	31 / 57 (54.4)	14.4 [10.5, 19.4]	34 / 60 (56.7)	16.1 [10.8, 18.9]	0.8215 [0.5035, 1.3406] 0.4314 0.4303	
Western Europe	67 / 140 (47.9)	15.7 [11.9, 18.8]	79 / 139 (56.8)	11.1 [8.7, 15.5]	0.6185 [0.4458, 0.8580] 0.0040 0.0037	
Mainland China/Rest of World (ROW)	26 / 49 (53.1)	14.8 [8.7, NE]	29 / 49 (59.2)	9.7 [7.4, 16.0]	0.7808 [0.4590, 1.3282] 0.3613 0.3589	

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

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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.9064
<6 Months	38 / 61 (62.3)	10.2 [8.1, 14.4]	38 / 61 (62.3)	7.3 [5.0, 10.1]	0.7013 [0.4459, 1.1029] 0.1245 0.1232	
≥ 6 Months	86 / 185 (46.5)	16.3 [13.7, 19.4]	104 / 187 (55.6)	13.5 [11.0, 17.6]	0.6843 [0.5134, 0.9122] 0.0097 0.0093	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.7449
<65	69 / 140 (49.3)	15.7 [12.1, 18.1]	75 / 130 (57.7)	11.1 [9.6, 16.1]	0.6750 [0.4856, 0.9383] 0.0193 0.0187	
≥ 65	55 / 106 (51.9)	13.7 [10.5, 17.5]	67 / 118 (56.8)	11.5 [8.9, 16.6]	0.7324 [0.5117, 1.0482] 0.0886 0.0871	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.6344
<75	115 / 222 (51.8)	14.4 [12.0, 16.4]	121 / 212 (57.1)	11.1 [9.7, 15.5]	0.7025 [0.5437, 0.9078] 0.0069 0.0067	
≥ 75	9 / 24 (37.5)	17.5 [10.1, NE]	21 / 36 (58.3)	13.5 [7.3, 18.3]	0.5737 [0.2618, 1.2572] 0.1651 0.1597	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.1270
Male	93 / 187 (49.7)	15.9 [13.6, 18.8]	121 / 205 (59.0)	11.1 [9.6, 15.5]	0.6309 [0.4808, 0.8278] 0.0009 0.0008	
Female	31 / 59 (52.5)	11.5 [8.8, 16.0]	21 / 43 (48.8)	13.4 [9.2, 22.6]	1.0531 [0.6047, 1.8342] 0.8549 0.8509	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.2684
White	59 / 116 (50.9)	13.6 [11.1, 16.4]	74 / 130 (56.9)	10.4 [7.3, 13.4]	0.6855 [0.4861, 0.9666] 0.0313 0.0304	
Asian	53 / 101 (52.5)	14.4 [11.6, 18.1]	55 / 97 (56.7)	14.6 [10.1, 18.2]	0.8442 [0.5782, 1.2327] 0.3805 0.3786	
Other	12 / 29 (41.4)	22.4 [11.5, NE]	13 / 21 (61.9)	12.6 [5.0, 18.9]	0.3946 [0.1770, 0.8800] 0.0231 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.8218
0	38 / 97 (39.2)	18.1 [13.1, 27.6]	45 / 88 (51.1)	17.6 [12.6, 20.6]	0.6785 [0.4396, 1.0471] 0.0798 0.0783	
≥ 1	86 / 149 (57.7)	13.9 [10.2, 16.0]	96 / 159 (60.4)	9.9 [7.7, 11.4]	0.7128 [0.5314, 0.9559] 0.0238 0.0232	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.0403
Gastric	83 / 153 (54.2)	11.9 [10.1, 14.8]	83 / 149 (55.7)	11.4 [9.6, 16.1]	0.8619 [0.6353, 1.1693] 0.3396 0.3386	
GEJ	41 / 93 (44.1)	18.0 [14.7, 22.5]	59 / 99 (59.6)	11.5 [9.2, 16.2]	0.4947 [0.3308, 0.7397] 0.0006 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.9078
Intestinal	35 / 69 (50.7)	16.6 [11.5, 20.5]	38 / 66 (57.6)	12.6 [9.9, 18.3]	0.7427 [0.4685, 1.1772] 0.2055 0.2046	
Diffuse	15 / 25 (60.0)	9.4 [7.9, 16.0]	11 / 19 (57.9)	8.7 [4.6, 16.1]	0.7436 [0.3381, 1.6352] 0.4612 0.4595	
Others	74 / 152 (48.7)	14.7 [11.9, 19.4]	93 / 163 (57.1)	11.1 [9.2, 16.1]	0.6606 [0.4858, 0.8982] 0.0082 0.0078	

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

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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.3187
<2	36 / 73 (49.3)	13.6 [10.1, 22.4]	44 / 75 (58.7)	15.5 [10.8, 17.6]	0.8530 [0.5474, 1.3290] 0.4821 0.4813	
≥ 2	88 / 173 (50.9)	14.7 [11.9, 17.7]	98 / 173 (56.6)	10.4 [8.7, 13.5]	0.6419 [0.4807, 0.8572] 0.0027 0.0025	

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

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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.3436
Yes	14 / 31 (45.2)	14.4 [8.7, 17.5]	15 / 30 (50.0)	16.6 [11.0, 21.5]	1.0844 [0.5074, 2.3174] 0.8344 0.8307	
No	110 / 215 (51.2)	14.7 [12.0, 17.7]	127 / 218 (58.3)	11.1 [9.6, 14.6]	0.6658 [0.5148, 0.8612] 0.0019 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.2160
Yes	9 / 20 (45.0)	16.6 [8.7, NE]	14 / 17 (82.4)	8.7 [5.8, 11.0]	0.3615 [0.1543, 0.8470] 0.0192 0.0159	
No	115 / 226 (50.9)	14.4 [12.0, 16.4]	128 / 231 (55.4)	13.4 [10.4, 16.1]	0.7287 [0.5657, 0.9386] 0.0143 0.0139	

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

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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.6416
Yes	18 / 39 (46.2)	16.3 [10.2, NE]	24 / 38 (63.2)	10.1 [7.4, 18.6]	0.5947 [0.3221, 1.0978] 0.0966 0.0937	
No	106 / 207 (51.2)	14.4 [11.9, 17.5]	118 / 210 (56.2)	12.6 [9.9, 16.1]	0.7148 [0.5491, 0.9305] 0.0126 0.0122	

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

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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.9819
Yes	73 / 147 (49.7)	14.2 [11.6, 16.6]	87 / 158 (55.1)	11.5 [9.7, 15.5]	0.6983 [0.5109, 0.9545] 0.0243 0.0235	
No	51 / 99 (51.5)	14.8 [11.5, 23.3]	55 / 90 (61.1)	11.1 [8.7, 18.6]	0.7073 [0.4824, 1.0370] 0.0761 0.0751	

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

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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.7713
Normal renal function	59 / 117 (50.4)	15.9 [13.6, 19.5]	72 / 120 (60.0)	9.9 [8.9, 13.4]	0.6600 [0.4660, 0.9346] 0.0192 0.0185	
Mild impairment	43 / 88 (48.9)	14.4 [11.6, 18.1]	46 / 88 (52.3)	16.0 [10.4, 18.6]	0.7902 [0.5206, 1.1993] 0.2686 0.2672	
Moderate impairment	22 / 41 (53.7)	11.5 [8.2, 27.6]	24 / 40 (60.0)	12.2 [6.3, 16.6]	0.6766 [0.3751, 1.2206] 0.1944 0.1916	

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

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Table 9.1.2 Overall survival (OS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.3914
Normal hepatic function	88 / 186 (47.3)	15.9 [13.9, 18.8]	94 / 185 (50.8)	14.6 [11.0, 17.6]	0.7384 [0.5515, 0.9886] 0.0417 0.0410	
Mild, Moderate or Severe dysfunction	36 / 60 (60.0)	10.5 [7.9, 13.1]	47 / 62 (75.8)	6.9 [4.6, 9.6]	0.6234 [0.4021, 0.9666] 0.0347 0.0332	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
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Anhang 4-G 2 Morbidität – FAS

Anhang 4-G 2.1 Progressionsfreies Überleben

Anhang 4-G 2.1.1 Progressionsfreies Überleben (PFS) – FAS

Daiichi Sankyo Europe GmbH
DS8201-A-U306 (DESTINY-GASTRIC04) - DCO 24-OCT-2024

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Statistical analyses for AMNOG (HTA Germany)

Table 9.2.1 Progression-Free Survival (PFS) - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
	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	166 (67.5)	6.7 [5.6, 7.1]	156 (62.9)	5.6 [4.9, 5.8]	0.7403 [0.5936, 0.9232] 0.0076	0.0074
Subjects with censoring event	80 (32.5)		92 (37.1)			
Ongoing	41 (16.7)		40 (16.1)			
Anti-cancer Therapy	21 (8.5)		17 (6.9)			
No Post-Baseline Tumor Assessment	12 (4.9)		27 (10.9)			
2 or more Missing Consecutive Tumor Assessments	5 (2.0)		6 (2.4)			
Withdrew Consent	1 (0.4)		1 (0.4)			
No Baseline Tumor Assessment	0		1 (0.4)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
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Anhang 4-G 2.1.2 Progressionsfreies Überleben (PFS) – Subgruppenanalyse – FAS

Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.3048
IHC 3+	139 / 207 (67.1)	6.7 [5.6, 7.1]	129 / 208 (62.0)	5.6 [5.1, 6.4]	0.7614 [0.5983, 0.9689] 0.0266 0.0263	
IHC 2+/ISH+	27 / 39 (69.2)	4.4 [3.0, 9.7]	27 / 40 (67.5)	3.6 [2.4, 5.4]	0.6389 [0.3678, 1.1098] 0.1118 0.1090	

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

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Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.8085
Asia [excluding mainland China]	39 / 57 (68.4)	6.9 [4.4, 10.9]	37 / 60 (61.7)	5.4 [4.0, 8.1]	0.7366 [0.4658, 1.1647] 0.1909 0.1888	
Western Europe	94 / 140 (67.1)	5.9 [5.6, 6.9]	83 / 139 (59.7)	5.6 [4.8, 5.9]	0.7730 [0.5744, 1.0402] 0.0892 0.0878	
Mainland China/Rest of World (ROW)	33 / 49 (67.3)	7.2 [4.2, 9.6]	36 / 49 (73.5)	5.6 [4.4, 7.0]	0.6213 [0.3842, 1.0046] 0.0522 0.0509	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
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Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.2.2_PFS_FAS_SUB.rtf

Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.9780
<6 Months	49 / 61 (80.3)	5.4 [4.0, 5.7]	41 / 61 (67.2)	4.2 [2.8, 5.0]	0.7760 [0.5091, 1.1828] 0.2383 0.2343	
≥ 6 Months	117 / 185 (63.2)	6.9 [5.9, 8.1]	115 / 187 (61.5)	5.6 [5.4, 6.6]	0.7159 [0.5525, 0.9276] 0.0115 0.0112	

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

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.9262
<65	96 / 140 (68.6)	6.8 [5.7, 7.5]	86 / 130 (66.2)	5.6 [4.2, 6.4]	0.7497 [0.5599, 1.0037] 0.0530 0.0521	
≥ 65	70 / 106 (66.0)	5.7 [5.3, 7.8]	70 / 118 (59.3)	5.6 [4.8, 6.5]	0.7228 [0.5157, 1.0130] 0.0595 0.0603	

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

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Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.6401
<75	153 / 222 (68.9)	6.7 [5.6, 7.1]	134 / 212 (63.2)	5.6 [4.8, 5.7]	0.7127 [0.5638, 0.9010] 0.0046 0.0044	
≥ 75	13 / 24 (54.2)	6.9 [5.6, 11.2]	22 / 36 (61.1)	6.5 [4.2, 9.9]	0.7780 [0.3901, 1.5514] 0.4759 0.4893	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.1016
Male	126 / 187 (67.4)	6.7 [5.6, 7.1]	130 / 205 (63.4)	5.5 [4.4, 5.8]	0.6655 [0.5183, 0.8544] 0.0014 0.0013	
Female	40 / 59 (67.8)	6.8 [4.3, 7.4]	26 / 43 (60.5)	5.6 [4.0, 8.0]	1.0126 [0.6126, 1.6739] 0.9609 0.9431	

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

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Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.5270
White	76 / 116 (65.5)	5.7 [4.4, 6.9]	76 / 130 (58.5)	5.5 [4.4, 5.8]	0.8282 [0.6020, 1.1393] 0.2467 0.2441	
Asian	68 / 101 (67.3)	7.2 [5.6, 8.7]	65 / 97 (67.0)	5.6 [4.3, 7.0]	0.6910 [0.4897, 0.9752] 0.0355 0.0349	
Other	22 / 29 (75.9)	6.9 [5.1, 8.7]	15 / 21 (71.4)	5.5 [2.9, 6.7]	0.4370 [0.2131, 0.8961] 0.0239 0.0205	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.8294
0	63 / 97 (64.9)	6.9 [5.6, 8.3]	43 / 88 (48.9)	6.0 [4.4, 7.9]	0.8041 [0.5433, 1.1900] 0.2756 0.2731	
≥ 1	103 / 149 (69.1)	6.3 [5.1, 7.0]	113 / 159 (71.1)	5.5 [4.4, 5.7]	0.7432 [0.5683, 0.9719] 0.0301 0.0306	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.2557
Gastric	102 / 153 (66.7)	5.9 [5.1, 7.4]	86 / 149 (57.7)	5.6 [4.4, 6.8]	0.8257 [0.6187, 1.1020] 0.1935 0.1942	
GEJ	64 / 93 (68.8)	6.9 [5.7, 8.0]	70 / 99 (70.7)	5.5 [4.4, 5.8]	0.6233 [0.4425, 0.8781] 0.0069 0.0064	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.3617
Intestinal	47 / 69 (68.1)	6.3 [5.1, 8.7]	36 / 66 (54.5)	4.9 [4.2, 5.6]	0.7457 [0.4799, 1.1586] 0.1918 0.1898	
Diffuse	13 / 25 (52.0)	6.9 [5.6, 14.0]	13 / 19 (68.4)	4.2 [2.6, 8.0]	0.4431 [0.1962, 1.0008] 0.0502 0.0408	
Others	106 / 152 (69.7)	6.7 [5.6, 7.2]	107 / 163 (65.6)	5.6 [5.3, 6.5]	0.7815 [0.5967, 1.0236] 0.0734 0.0734	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.8620
<2	43 / 73 (58.9)	6.8 [5.6, 8.6]	57 / 75 (76.0)	5.8 [4.8, 7.9]	0.7051 [0.4739, 1.0489] 0.0847 0.0848	
≥ 2	123 / 173 (71.1)	6.7 [5.6, 7.1]	99 / 173 (57.2)	5.4 [4.4, 5.6]	0.7419 [0.5678, 0.9694] 0.0287 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.7731
Yes	21 / 31 (67.7)	5.7 [4.1, 8.4]	17 / 30 (56.7)	5.4 [4.0, 8.1]	0.8281 [0.4325, 1.5857] 0.5693 0.5714	
No	145 / 215 (67.4)	6.8 [5.6, 7.2]	139 / 218 (63.8)	5.6 [4.8, 5.9]	0.7290 [0.5768, 0.9214] 0.0082 0.0080	

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

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Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.4055
Yes	14 / 20 (70.0)	8.0 [3.2, 9.6]	12 / 17 (70.6)	4.4 [2.6, 8.1]	0.4457 [0.1896, 1.0480] 0.0640 0.0563	
No	152 / 226 (67.3)	6.7 [5.6, 7.1]	144 / 231 (62.3)	5.6 [5.0, 5.9]	0.7574 [0.6022, 0.9527] 0.0176 0.0174	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.2.2_PFS_FAS_SUB.rtf

Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.9643
Yes	28 / 39 (71.8)	7.2 [4.4, 9.6]	27 / 38 (71.1)	5.4 [4.2, 8.1]	0.7404 [0.4316, 1.2704] 0.2753 0.2731	
No	138 / 207 (66.7)	6.4 [5.6, 7.0]	129 / 210 (61.4)	5.6 [4.8, 5.8]	0.7494 [0.5885, 0.9542] 0.0193 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.2.2_PFS_FAS_SUB.rtf

Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.8734
Yes	93 / 147 (63.3)	6.8 [5.6, 7.9]	97 / 158 (61.4)	5.6 [4.4, 6.0]	0.7259 [0.5452, 0.9664] 0.0282 0.0279	
No	73 / 99 (73.7)	6.6 [5.4, 7.2]	59 / 90 (65.6)	5.5 [4.8, 6.6]	0.7468 [0.5275, 1.0573] 0.0998 0.0975	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.2.2_PFS_FAS_SUB.rtf

Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.6646
Normal renal function	86 / 117 (73.5)	6.3 [4.4, 6.9]	83 / 120 (69.2)	5.5 [4.2, 5.9]	0.8052 [0.5948, 1.0901] 0.1610 0.1597	
Mild impairment	54 / 88 (61.4)	6.8 [5.6, 9.6]	49 / 88 (55.7)	5.6 [4.4, 7.1]	0.7085 [0.4799, 1.0460] 0.0829 0.0811	
Moderate impairment	26 / 41 (63.4)	7.2 [4.3, 8.4]	24 / 40 (60.0)	5.6 [4.0, 8.0]	0.6142 [0.3448, 1.0940] 0.0980 0.0952	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.2.2_PFS_FAS_SUB.rtf

Table 9.2.2 Progression-Free Survival (PFS) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.6056
Normal hepatic function	126 / 186 (67.7)	6.8 [5.7, 7.4]	112 / 185 (60.5)	5.6 [5.3, 6.8]	0.7624 [0.5897, 0.9857] 0.0385 0.0385	
Mild, Moderate or Severe dysfunction	40 / 60 (66.7)	5.4 [3.9, 7.8]	43 / 62 (69.4)	4.3 [3.1, 5.7]	0.6928 [0.4484, 1.0703] 0.0982 0.0960	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.2.2_PFS_FAS_SUB.rtf

Anhang 4-G 2.2Tumoransprechen

Anhang 4-G 2.2.1 Objektive Ansprechrate

Anhang 4-G 2.2.1.1 Objektive Ansprechrate (ORR) – Subgruppenanalyse – FAS

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT							0.4715
IHC 3+	92 / 207 (44.4) [37.6, 51.5]	63 / 208 (30.3) [24.1, 37.0]	1.84 [1.23, 2.76]	1.47 [1.14, 1.90]	14.16 [4.46, 23.85]	0.0029	
IHC 2+/ISH+	12 / 39 (30.8) [17.0, 47.6]	6 / 40 (15.0) [5.7, 29.8]	2.52 [0.84, 7.59]	2.05 [0.86, 4.92]	15.77 [-4.99, 36.53]	0.0969	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADRS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Geography stratification factor							0.6458
Asia [excluding mainland China]	22 / 57 (38.6) [26.0, 52.4]	12 / 60 (20.0) [10.8, 32.3]	2.51 [1.10, 5.75]	1.93 [1.06, 3.53]	18.60 [0.69, 36.50]	0.0275	
Western Europe	62 / 140 (44.3) [35.9, 52.9]	42 / 139 (30.2) [22.7, 38.6]	1.84 [1.12, 3.00]	1.47 [1.07, 2.01]	14.07 [2.13, 26.01]	0.0153	
Mainland China/Rest of World (ROW)	20 / 49 (40.8) [27.0, 55.8]	15 / 49 (30.6) [18.3, 45.4]	1.56 [0.68, 3.60]	1.33 [0.78, 2.29]	10.20 [-10.70, 31.11]	0.2943	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

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Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Time to progression on first-line therapy from IRT							0.9552
<6 Months	24 / 61 (39.3) [27.1, 52.7]	16 / 61 (26.2) [15.8, 39.1]	1.82 [0.85, 3.93]	1.50 [0.89, 2.53]	13.11 [-5.02, 31.25]	0.1244	
≥ 6 Months	80 / 185 (43.2) [36.0, 50.7]	53 / 187 (28.3) [22.0, 35.4]	1.93 [1.25, 2.96]	1.53 [1.15, 2.02]	14.90 [4.74, 25.07]	0.0028	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

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Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Age at randomization							0.5348
<65	60 / 140 (42.9) [34.5, 51.5]	34 / 130 (26.2) [18.8, 34.6]	2.12 [1.27, 3.54]	1.64 [1.16, 2.32]	16.70 [4.81, 28.59]	0.0041	
≥ 65	44 / 106 (41.5) [32.0, 51.5]	35 / 118 (29.7) [21.6, 38.8]	1.68 [0.97, 2.92]	1.40 [0.98, 2.00]	11.85 [-1.53, 25.23]	0.0645	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

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Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Age at randomization							0.7448
<75	95 / 222 (42.8) [36.2, 49.6]	59 / 212 (27.8) [21.9, 34.4]	1.94 [1.30, 2.90]	1.54 [1.18, 2.00]	14.96 [5.63, 24.30]	0.0011	
≥ 75	9 / 24 (37.5) [18.8, 59.4]	10 / 36 (27.8) [14.2, 45.2]	1.56 [0.52, 4.70]	1.35 [0.65, 2.82]	9.72 [-18.02, 37.47]	0.4316	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

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Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Sex							0.8806
Male	78 / 187 (41.7) [34.6, 49.1]	56 / 205 (27.3) [21.3, 34.0]	1.90 [1.25, 2.91]	1.53 [1.15, 2.02]	14.39 [4.55, 24.24]	0.0027	
Female	26 / 59 (44.1) [31.2, 57.6]	13 / 43 (30.2) [17.2, 46.1]	1.82 [0.79, 4.17]	1.46 [0.85, 2.49]	13.84 [-6.85, 34.52]	0.1577	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

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Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Race							0.6311
White	49 / 116 (42.2) [33.1, 51.8]	40 / 130 (30.8) [23.0, 39.5]	1.65 [0.97, 2.78]	1.37 [0.98, 1.92]	11.47 [-1.33, 24.28]	0.0621	
Asian	41 / 101 (40.6) [30.9, 50.8]	24 / 97 (24.7) [16.5, 34.5]	2.08 [1.13, 3.82]	1.64 [1.08, 2.50]	15.85 [1.98, 29.73]	0.0179	
Other	14 / 29 (48.3) [29.4, 67.5]	5 / 21 (23.8) [8.2, 47.2]	2.99 [0.86, 10.33]	2.03 [0.86, 4.76]	24.47 [-5.38, 54.31]	0.0816	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADRS
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Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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							0.7845
0	43 / 97 (44.3) [34.2, 54.8]	27 / 88 (30.7) [21.3, 41.4]	1.80 [0.98, 3.29]	1.44 [0.98, 2.12]	13.65 [-1.24, 28.54]	0.0566	
≥ 1	61 / 149 (40.9) [33.0, 49.3]	42 / 159 (26.4) [19.7, 34.0]	1.93 [1.19, 3.12]	1.55 [1.12, 2.14]	14.52 [3.42, 25.63]	0.0070	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADRS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Primary tumor location							0.3985
Gastric	62 / 153 (40.5) [32.7, 48.7]	36 / 149 (24.2) [17.5, 31.8]	2.14 [1.30, 3.51]	1.68 [1.19, 2.36]	16.36 [5.32, 27.40]	0.0024	
GEJ	42 / 93 (45.2) [34.8, 55.8]	33 / 99 (33.3) [24.2, 43.5]	1.65 [0.92, 2.95]	1.35 [0.95, 1.94]	11.83 [-2.95, 26.60]	0.0940	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

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Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Histological subtype							0.4422
Intestinal	30 / 69 (43.5) [31.6, 56.0]	16 / 66 (24.2) [14.5, 36.4]	2.40 [1.15, 5.02]	1.79 [1.08, 2.97]	19.24 [2.14, 36.33]	0.0189	
Diffuse	12 / 25 (48.0) [27.8, 68.7]	4 / 19 (21.1) [6.1, 45.6]	3.46 [0.89, 13.40]	2.28 [0.87, 5.96]	26.95 [-4.51, 58.40]	0.0688	
Others	62 / 152 (40.8) [32.9, 49.0]	49 / 163 (30.1) [23.1, 37.7]	1.60 [1.01, 2.55]	1.36 [1.00, 1.84]	10.73 [-0.42, 21.88]	0.0468	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADRS
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Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Number of metastatic sites							0.8001
<2	34 / 73 (46.6) [34.8, 58.6]	24 / 75 (32.0) [21.7, 43.8]	1.85 [0.95, 3.61]	1.46 [0.96, 2.20]	14.58 [-2.35, 31.50]	0.0703	
≥ 2	70 / 173 (40.5) [33.1, 48.2]	45 / 173 (26.0) [19.6, 33.2]	1.93 [1.23, 3.05]	1.56 [1.14, 2.12]	14.45 [4.06, 24.84]	0.0044	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADRS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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 adjuvant/neoadjuvant therapy							0.6270
Yes	12 / 31 (38.7) [21.8, 57.8]	9 / 30 (30.0) [14.7, 49.4]	1.47 [0.51, 4.27]	1.29 [0.64, 2.61]	8.71 [-18.30, 35.71]	0.4778	
No	92 / 215 (42.8) [36.1, 49.7]	60 / 218 (27.5) [21.7, 34.0]	1.97 [1.32, 2.94]	1.55 [1.19, 2.03]	15.27 [5.92, 24.61]	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] Two-sided exact 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADRS
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Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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 nivolumab or pembrolizumab treatment							0.8041
Yes	8 / 20 (40.0) [19.1, 63.9]	5 / 17 (29.4) [10.3, 56.0]	1.60 [0.40, 6.32]	1.36 [0.55, 3.38]	10.59 [-25.35, 46.53]	0.5072	
No	96 / 226 (42.5) [35.9, 49.2]	64 / 231 (27.7) [22.0, 34.0]	1.93 [1.30, 2.85]	1.53 [1.18, 1.98]	14.77 [5.68, 23.86]	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] Two-sided exact 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADRS
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Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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 treatment with immune-checkpoint inhibitor or other immuno-oncology therapy							0.9755
Yes	17 / 39 (43.6) [27.8, 60.4]	11 / 38 (28.9) [15.4, 45.9]	1.90 [0.74, 4.88]	1.51 [0.82, 2.78]	14.64 [-9.17, 38.46]	0.1846	
No	87 / 207 (42.0) [35.2, 49.1]	58 / 210 (27.6) [21.7, 34.2]	1.90 [1.26, 2.86]	1.52 [1.16, 2.00]	14.41 [4.89, 23.93]	0.0020	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

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Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Presence of liver metastasis at baseline							0.6199
Yes	67 / 147 (45.6) [37.4, 54.0]	45 / 158 (28.5) [21.6, 36.2]	2.10 [1.31, 3.38]	1.60 [1.18, 2.17]	17.10 [5.75, 28.45]	0.0020	
No	37 / 99 (37.4) [27.9, 47.7]	24 / 90 (26.7) [17.9, 37.0]	1.64 [0.88, 3.05]	1.40 [0.91, 2.15]	10.71 [-3.56, 24.97]	0.1168	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

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Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Renal function at baseline							0.6566
Normal renal function	47 / 117 (40.2) [31.2, 49.6]	35 / 120 (29.2) [21.2, 38.2]	1.63 [0.95, 2.80]	1.38 [0.96, 1.97]	11.00 [-1.88, 23.89]	0.0756	
Mild impairment	39 / 88 (44.3) [33.7, 55.3]	25 / 88 (28.4) [19.3, 39.0]	2.01 [1.07, 3.75]	1.56 [1.04, 2.34]	15.91 [0.75, 31.06]	0.0287	
Moderate impairment	18 / 41 (43.9) [28.5, 60.3]	9 / 40 (22.5) [10.8, 38.5]	2.70 [1.03, 7.08]	1.95 [1.00, 3.82]	21.40 [-1.02, 43.83]	0.0423	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

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Run date: 23JUN2025 11:02 (CET); Program name: t_binary_subgrp.sas; Output name: T.9.3.2_ORR_FAS_SUB.rtf

Table 9.3.2 Confirmed Objective Response Rate (ORR) - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX				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]
Hepatic function at baseline							0.9913
Normal hepatic function	82 / 186 (44.1) [36.8, 51.5]	54 / 185 (29.2) [22.8, 36.3]	1.91 [1.25, 2.94]	1.51 [1.15, 1.99]	14.90 [4.67, 25.12]	0.0029	
Mild, Moderate or Severe dysfunction	22 / 60 (36.7) [24.6, 50.1]	15 / 62 (24.2) [14.2, 36.7]	1.81 [0.83, 3.97]	1.52 [0.87, 2.63]	12.47 [-5.36, 30.31]	0.1356	

N: number of subjects in 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 95% 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
CI: confidence interval; OR: odds ratio; RD: risk difference; RR: relative risk

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Anhang 4-G 2.2.2 Dauer des Ansprechens

Anhang 4-G 2.2.2.1 Dauer des Ansprechens (DOR) – FAS

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Table 9.4.1 Duration of Response (DoR) - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
	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	62 / 104 (59.6)	7.4 [5.7, 10.1]	52 / 69 (75.4)	5.3 [4.1, 5.7]	0.5735 [0.3953, 0.8321] 0.0034	0.0033
Subjects with censoring event	42 / 104 (40.4)		17 / 69 (24.6)			
Ongoing	28 / 104 (26.9)		12 / 69 (17.4)			
Anti-cancer Therapy	10 / 104 (9.6)		4 / 69 (5.8)			
2 or more Missing Consecutive Tumor Assessments	3 / 104 (2.9)		1 / 69 (1.4)			
Withdrew Consent	1 / 104 (1.0)		0			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte.sas; Output name: T.9.4.1_DoR_FAS.rtf

Anhang 4-G 2.2.2.2 Dauer des Ansprechens (DOR) – Kaplan-Meier-Plot – FAS

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DS8201-A-U306 (DESTINY-GASTRIC04) - DCO 24-OCT-2024

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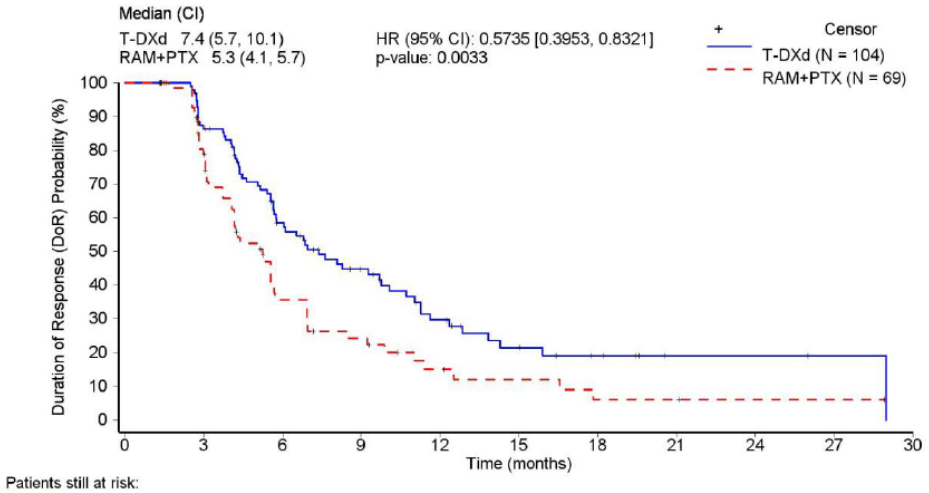
Figure 9.4.1 Duration of Response (DoR) - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:											
T-DXd	104	81	45	29	17	10	6	2	2	1	0
RAM+PTX	69	50	19	12	6	4	2	2	1	1	0
Patient with event:											
T-DXd	0	13	37	47	56	60	61	61	61	61	62
RAM+PTX	0	14	39	45	49	50	52	52	52	52	52
Patient censored:											
T-DXd	0	10	22	28	31	34	37	41	41	42	42
RAM+PTX	0	5	11	12	14	15	15	15	16	16	17

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; HR: Hazard Ratio; NE: not estimable

Data source:
DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
Program Location:
DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:18 (CET); Program name: f_km.sas; Output name: F.9.4.1_DoR_FAS.rtf

Anhang 4-G 2.2.3 Zeit bis zum Ansprechen

Anhang 4-G 2.2.3.1 Zeit bis zum Ansprechen (TTR) – FAS

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DS8201-A-U306 (DESTINY-GASTRIC04) - DCO 24-OCT-2024

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Table 9.6.1 Time to response (TTR) - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
	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	104 (42.3)	NE [4.2, NE]	69 (27.8)	NE [NE, NE]	1.5512 [1.1440, 2.1034] 0.0047	0.0042
Subjects with censoring event	142 (57.7)		179 (72.2)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte.sas; Output name: T.9.6.1_TTR_FAS.rtf

Anhang 4-G 2.2.3.2 Zeit bis zum Ansprechen (TTR) – Kaplan-Meier-Plot – FAS

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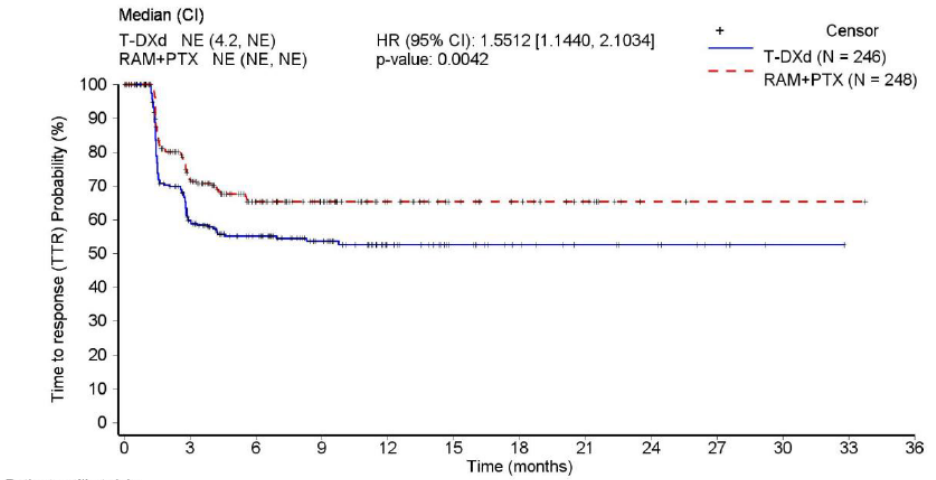
Figure 9.6.1 Time to response (TTR) - Kaplan-Meier plot - Full Analysis Set



Patients still at risk:													
T-DXd	246	128	93	58	35	21	14	10	8	4	1	0	0
RAM+PTX	248	136	82	55	34	22	15	9	2	1	1	1	0
Patient with event:													
T-DXd	0	92	101	103	104	104	104	104	104	104	104	104	104
RAM+PTX	0	59	69	69	69	69	69	69	69	69	69	69	69
Patient censored:													
T-DXd	0	26	52	85	107	121	128	132	134	138	141	142	142
RAM+PTX	0	53	97	124	145	157	164	170	177	178	178	178	179

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; HR: Hazard Ratio; NE: not estimable

Data source:
DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTE
Program Location:
DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:18 (CET); Program name: f_km.sas; Output name: F.9.6.1_TTR_FAS.rtf

Anhang 4-G 3 Patientenberichtete Fragebögen – FAS

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

Anhang 4-G 3.1.1 EQ-5D-5L VAS – Zeit bis zur ersten Verschlechterung um ≥15 % der Skalenspannweite – FAS

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DS8201-A-U306 (DESTINY-GASTRIC04) - DCO 24-OCT-2024

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Table 9.8.1 EQ-5D-5L VAS - Time to first deterioration - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
	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	79 (32.1)	11.8 [7.2, 18.0]	70 (28.2)	7.9 [5.1, 12.7]	0.8517 [0.6152, 1.1793] 0.3337	0.3441
Subjects with censoring event	167 (67.9)		178 (71.8)			
No Deterioration	127 (51.6)		106 (42.7)			
No Evaluable Visit	21 (8.5)		55 (22.2)			
No Baseline Data	19 (7.7)		17 (6.9)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte.sas; Output name: T.9.8.1_EQ5D_TTFDet_FAS.rtf

Anhang 4-G 3.1.2 EQ-5D-5L VAS – Zeit bis zur ersten Verschlechterung um ≥15 % der Skalenspannweite – Subgruppenanalyse – FAS

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.0891
IHC 3+	69 / 207 (33.3)	10.9 [6.2, 17.3]	57 / 208 (27.4)	9.0 [6.0, 12.7]	0.9619 [0.6760, 1.3686] 0.8290 0.8313	
IHC 2+/ISH+	10 / 39 (25.6)	18.0 [6.3, NE]	13 / 40 (32.5)	3.5 [2.1, NE]	0.4143 [0.1740, 0.9863] 0.0465 0.0455	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.8.2_EQ5D_TTFDet_FAS_SUB.rtf

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.1142
Asia [excluding mainland China]	28 / 57 (49.1)	6.3 [3.5, 10.9]	22 / 60 (36.7)	9.0 [3.4, NE]	1.0013 [0.5700, 1.7589] 0.9964 0.9902	
Western Europe	42 / 140 (30.0)	16.1 [5.6, 18.0]	30 / 139 (21.6)	12.4 [5.1, NE]	1.0073 [0.6276, 1.6168] 0.9759 0.9795	
Mainland China/Rest of World (ROW)	9 / 49 (18.4)	NE [NE, NE]	18 / 49 (36.7)	7.2 [3.5, NE]	0.4286 [0.1917, 0.9580] 0.0390 0.0332	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.8.2_EQ5D_TTFDet_FAS_SUB.rtf

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.0425
<6 Months	23 / 61 (37.7)	5.6 [3.5, NE]	11 / 61 (18.0)	12.4 [12.4, NE]	1.6539 [0.8044, 3.4009] 0.1713 0.1659	
≥ 6 Months	56 / 185 (30.3)	16.1 [8.6, NE]	59 / 187 (31.6)	7.6 [4.9, 12.7]	0.7160 [0.4945, 1.0368] 0.0769 0.0757	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.8.2_EQ5D_TTFDet_FAS_SUB.rtf

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.5527
<65	46 / 140 (32.9)	11.8 [7.2, 18.0]	37 / 130 (28.5)	9.0 [6.0, NE]	0.9110 [0.5886, 1.4100] 0.6757 0.6751	
≥ 65	33 / 106 (31.1)	17.3 [4.4, NE]	33 / 118 (28.0)	7.2 [3.5, NE]	0.8031 [0.4942, 1.3050] 0.3760 0.3770	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.8.2_EQ5D_TTFDet_FAS_SUB.rtf

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.4430
<75	72 / 222 (32.4)	11.8 [7.2, 18.0]	63 / 212 (29.7)	7.6 [5.1, 12.4]	0.8065 [0.5726, 1.1358] 0.2183 0.2168	
≥ 75	7 / 24 (29.2)	6.3 [2.1, NE]	7 / 36 (19.4)	NE [3.4, NE]	1.1805 [0.4128, 3.3763] 0.7569 0.7578	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.8.2_EQ5D_TTFDet_FAS_SUB.rtf

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.3983
Male	63 / 187 (33.7)	11.8 [6.3, 18.0]	55 / 205 (26.8)	9.0 [6.0, 12.7]	0.8978 [0.6220, 1.2959] 0.5649 0.5638	
Female	16 / 59 (27.1)	NE [3.7, NE]	15 / 43 (34.9)	4.9 [2.0, NE]	0.6422 [0.3173, 1.2998] 0.2183 0.2141	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.8.2_EQ5D_TTFDet_FAS_SUB.rtf

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.3681
White	36 / 116 (31.0)	9.7 [4.4, NE]	29 / 130 (22.3)	12.4 [4.9, NE]	1.0636 [0.6497, 1.7410] 0.8063 0.8090	
Asian	37 / 101 (36.6)	10.9 [6.3, NE]	35 / 97 (36.1)	7.2 [4.9, 12.7]	0.7810 [0.4905, 1.2435] 0.2976 0.2986	
Other	6 / 29 (20.7)	18.0 [4.2, NE]	6 / 21 (28.6)	6.0 [1.8, NE]	0.4339 [0.1266, 1.4879] 0.1842 0.1728	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.8.2_EQ5D_TTFDet_FAS_SUB.rtf

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.9601
0	37 / 97 (38.1)	9.7 [6.2, 17.3]	27 / 88 (30.7)	7.9 [4.8, NE]	0.8005 [0.4832, 1.3264] 0.3878 0.3864	
≥ 1	42 / 149 (28.2)	NE [6.3, NE]	43 / 159 (27.0)	10.2 [5.5, 12.7]	0.8800 [0.5744, 1.3484] 0.5572 0.5613	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.8.2_EQ5D_TTFDet_FAS_SUB.rtf

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.6857
Gastric	49 / 153 (32.0)	10.9 [6.2, NE]	46 / 149 (30.9)	7.2 [4.5, NE]	0.8086 [0.5394, 1.2123] 0.3039 0.3034	
GEJ	30 / 93 (32.3)	16.1 [6.3, 18.0]	24 / 99 (24.2)	10.2 [5.1, 12.7]	0.8757 [0.5030, 1.5245] 0.6388 0.6330	

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

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.1330
Intestinal	14 / 69 (20.3)	NE [6.3, NE]	17 / 66 (25.8)	9.0 [2.1, NE]	0.5314 [0.2593, 1.0892] 0.0843 0.0797	
Diffuse	11 / 25 (44.0)	7.2 [1.4, NE]	5 / 19 (26.3)	NE [2.1, NE]	1.7085 [0.5808, 5.0260] 0.3306 0.3256	
Others	54 / 152 (35.5)	10.9 [5.6, 18.0]	48 / 163 (29.4)	7.6 [5.1, 12.7]	0.9013 [0.6088, 1.3345] 0.6040 0.6031	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.8.2_EQ5D_TTFDet_FAS_SUB.rtf

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.8773
<2	24 / 73 (32.9)	17.3 [4.9, NE]	26 / 75 (34.7)	10.2 [3.6, NE]	0.9137 [0.5215, 1.6008] 0.7524 0.7528	
≥ 2	55 / 173 (31.8)	11.8 [6.2, NE]	44 / 173 (25.4)	7.2 [4.9, NE]	0.8312 [0.5570, 1.2403] 0.3653 0.3660	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.8.2_EQ5D_TTFDet_FAS_SUB.rtf

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.2959
Yes	14 / 31 (45.2)	6.2 [1.4, NE]	8 / 30 (26.7)	NE [1.5, NE]	1.3012 [0.5352, 3.1637] 0.5613 0.5741	
No	65 / 215 (30.2)	16.1 [8.2, NE]	62 / 218 (28.4)	7.9 [5.1, 12.4]	0.7929 [0.5587, 1.1254] 0.1940 0.1938	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.8.2_EQ5D_TTFDet_FAS_SUB.rtf

Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.2121
Yes	10 / 20 (50.0)	7.2 [2.1, NE]	4 / 17 (23.5)	7.6 [4.9, NE]	1.1941 [0.3529, 4.0409] 0.7754 0.7752	
No	69 / 226 (30.5)	16.1 [8.6, NE]	66 / 231 (28.6)	9.0 [4.9, 12.7]	0.8157 [0.5808, 1.1456] 0.2397 0.2394	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.2644
Yes	15 / 39 (38.5)	11.8 [4.9, NE]	9 / 38 (23.7)	7.6 [5.5, NE]	1.2105 [0.5248, 2.7919] 0.6542 0.6549	
No	64 / 207 (30.9)	16.1 [6.3, 18.0]	61 / 210 (29.0)	7.9 [4.9, 12.4]	0.8052 [0.5657, 1.1461] 0.2290 0.2290	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.6504
Yes	40 / 147 (27.2)	17.3 [8.2, NE]	35 / 158 (22.2)	10.2 [6.1, NE]	0.8960 [0.5672, 1.4152] 0.6377 0.6383	
No	39 / 99 (39.4)	7.2 [4.3, 18.0]	35 / 90 (38.9)	5.5 [3.1, 9.0]	0.8035 [0.5074, 1.2726] 0.3512 0.3523	

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

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Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.4699
Normal renal function	36 / 117 (30.8)	16.1 [5.6, NE]	31 / 120 (25.8)	7.9 [5.1, NE]	1.0060 [0.6202, 1.6316] 0.9808 0.9825	
Mild impairment	21 / 88 (23.9)	18.0 [8.2, NE]	21 / 88 (23.9)	9.0 [6.0, NE]	0.7160 [0.3885, 1.3197] 0.2843 0.2781	
Moderate impairment	22 / 41 (53.7)	4.4 [2.2, NE]	18 / 40 (45.0)	2.1 [1.4, 4.9]	0.6196 [0.3276, 1.1716] 0.1408 0.1374	

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

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Table 9.8.2 EQ-5D-5L VAS - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.5659
Normal hepatic function	61 / 186 (32.8)	11.8 [6.3, NE]	58 / 185 (31.4)	7.9 [4.9, 12.7]	0.8259 [0.5750, 1.1863] 0.3006 0.3007	
Mild, Moderate or Severe dysfunction	18 / 60 (30.0)	9.7 [4.2, NE]	12 / 62 (19.4)	6.1 [3.5, NE]	1.0156 [0.4838, 2.1322] 0.9673 0.9602	

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

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Anhang 4-G 3.1.3 EQ-5D-5L VAS – Tabellarische Darstellung der mittleren Veränderung über alle Zeitpunkte hinweg (MMRM) – FAS

Daiichi Sankyo Europe GmbH
DS8201-A-U306 (DESTINY-GASTRIC04) - DCO 24-OCT-2024

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Table 9.8.5 EQ-5D-5L VAS - Mixed Model for Repeated Measurement Overall - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Overall			
n	206	176	
LS Means [95 % CI]	-1.3456 [-3.6124; 0.9212]	-4.8330 [-7.4206; -2.2454]	
Standard error	1.1517	1.3150	
Difference of LS Means [95% CI]			3.4874 [0.5827; 6.3921]
Standard error for difference			1.4735
p-value			0.0189
Hedges' g [95% CI]			0.2052 [0.0035; 0.4070]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_adam/ADQS
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Anhang 4-G 3.1.4 EQ-5D-5L VAS – Tabellarische Darstellung der mittleren Veränderung im zeitlichen Verlauf (MMRM) – FAS

Table 9.8.4 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Day 22			
Change from baseline			
n	191	151	
LS Means [95 % CI]	0.1207 [-2.1087; 2.3502]	-2.2535 [-4.6872; 0.1801]	
Standard error	1.1339	1.2378	
Difference of LS Means [95% CI]			2.3743 [-0.4155; 5.1640]
Standard error for difference			1.4184
p-value			0.0950
Hedges' g [95% CI]			0.1531 [-0.0606; 0.3669]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.8.4 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Day 43			
Change from baseline			
n	186	130	
LS Means [95 % CI]	-0.4382 [-2.7840; 1.9076]	-1.8952 [-4.4944; 0.7041]	
Standard error	1.1932	1.3222	
Difference of LS Means [95% CI]			1.4570 [-1.5634; 4.4774]
Standard error for difference			1.5357
p-value			0.3434
Hedges' g [95% CI]			0.0920 [-0.1321; 0.3162]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Run date: 23JUN2025 11:04 (CET); Program name: t_mmrm.sas; Output name: T.9.8.4_EQ5D_MMRM_FAS.rtf

Table 9.8.4 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Day 64			
Change from baseline			
n	175	143	
LS Means [95 % CI]	-0.9592 [-3.4313; 1.5128]	-2.4096 [-5.0899; 0.2707]	
Standard error	1.2575	1.3635	
Difference of LS Means [95% CI]			1.4504 [-1.7169; 4.6176]
Standard error for difference			1.6100
p-value			0.3683
Hedges' g [95% CI]			0.0878 [-0.1333; 0.3088]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:04 (CET); Program name: t_mmrm.sas; Output name: T.9.8.4_EQ5D_MMRM_FAS.rtf

Table 9.8.4 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Day 106			
Change from baseline			
n	149	121	
LS Means [95 % CI]	-1.7660 [-4.4263; 0.8943]	-3.4168 [-6.3159; -0.5178]	
Standard error	1.3532	1.4746	
Difference of LS Means [95% CI]			1.6508 [-1.8335; 5.1351]
Standard error for difference			1.7706
p-value			0.3519
Hedges' g [95% CI]			0.1005 [-0.1395; 0.3405]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:04 (CET); Program name: t_mmrm.sas; Output name: T.9.8.4_EQ5D_MMRM_FAS.rtf

Table 9.8.4 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Day 148			
Change from baseline			
n	110	97	
LS Means [95 % CI]	-3.7091 [-6.7160; -0.7022]	-3.8647 [-7.0983; -0.6310]	
Standard error	1.5279	1.6430	
Difference of LS Means [95% CI]			0.1556 [-3.8567; 4.1678]
Standard error for difference			2.0360
p-value			0.9392
Hedges' g [95% CI]			0.0096 [-0.2634; 0.2826]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:04 (CET); Program name: t_mmrm.sas; Output name: T.9.8.4_EQ5D_MMRM_FAS.rtf

Table 9.8.4 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Day 190			
Change from baseline			
n	96	66	
LS Means [95 % CI]	-1.0297 [-3.8771; 1.8177]	-4.2128 [-7.4905; -0.9351]	
Standard error	1.4459	1.6648	
Difference of LS Means [95% CI]			3.1831 [-0.7386; 7.1048]
Standard error for difference			1.9881
p-value			0.1110
Hedges' g [95% CI]			0.2278 [-0.0866; 0.5421]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:04 (CET); Program name: t_mmrm.sas; Output name: T.9.8.4_EQ5D_MMRM_FAS.rtf

Table 9.8.4 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Day 232			
Change from baseline			
n	68	47	
LS Means [95 % CI]	-1.6659 [-4.9101; 1.5782]	-4.4862 [-8.2797; -0.6926]	
Standard error	1.6436	1.9224	
Difference of LS Means [95% CI]			2.8202 [-1.8020; 7.4425]
Standard error for difference			2.3370
p-value			0.2296
Hedges' g [95% CI]			0.2090 [-0.1637; 0.5818]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:04 (CET); Program name: t_mmrm.sas; Output name: T.9.8.4_EQ5D_MMRM_FAS.rtf

Table 9.8.4 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Day 274			
Change from baseline			
n	52	27	
LS Means [95 % CI]	-2.2601 [-6.5807; 2.0605]	-4.9288 [-10.7706; 0.9130]	
Standard error	2.1773	2.9420	
Difference of LS Means [95% CI]			2.6687 [-4.3601; 9.6975]
Standard error for difference			3.5335
p-value			0.4522
Hedges' g [95% CI]			0.1698 [-0.2959; 0.6355]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:04 (CET); Program name: t_mmrm.sas; Output name: T.9.8.4_EQ5D_MMRM_FAS.rtf

Table 9.8.4 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Day 316			
Change from baseline			
n	38	20	
LS Means [95 % CI]	-1.9615 [-5.2754; 1.3525]	-8.2933 [-12.5103; -4.0762]	
Standard error	1.6722	2.1208	
Difference of LS Means [95% CI]			6.3318 [1.2976; 11.3660]
Standard error for difference			2.5253
p-value			0.0144
Hedges' g [95% CI]			0.6224 [0.0692; 1.1756]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:04 (CET); Program name: t_mmrm.sas; Output name: T.9.8.4_EQ5D_MMRM_FAS.rtf

Table 9.8.4 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Day 358			
Change from baseline			
n	32	14	
LS Means [95 % CI]	-1.6647 [-5.5969; 2.2674]	-8.1581 [-13.4881; -2.8281]	
Standard error	1.9755	2.6709	
Difference of LS Means [95% CI]			6.4934 [0.1350; 12.8517]
Standard error for difference			3.1777
p-value			0.0455
Hedges' g [95% CI]			0.5888 [-0.0507; 1.2282]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:04 (CET); Program name: t_mmrm.sas; Output name: T.9.8.4_EQ5D_MMRM_FAS.rtf

Table 9.8.4 EQ-5D-5L VAS - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Day 400			
Change from baseline			
n	22	12	
LS Means [95 % CI]	0.5322 [-3.2873; 4.3517]	-9.2441 [-14.2208; -4.2674]	
Standard error	1.9181	2.4856	
Difference of LS Means [95% CI]			9.7762 [3.7612; 15.7912]
Standard error for difference			2.9940
p-value			0.0020
Hedges' g [95% CI]			1.0766 [0.3282; 1.8251]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:04 (CET); Program name: t_mmrm.sas; Output name: T.9.8.4_EQ5D_MMRM_FAS.rtf

Anhang 4-G 3.2 PGI-C

Anhang 4-G 3.2.1 PGI-C – Zeit bis zur ersten klinisch relevanten Verschlechterung– FAS

Daiichi Sankyo Europe GmbH
DS8201-A-U306 (DESTINY-GASTRIC04) - DCO 24-OCT-2024

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Table 9.11.1 PGI-C - Time to first deterioration - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
	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	67 (27.2)	22.1 [18.0, NE]	87 (35.1)	6.7 [5.0, 12.7]	0.5682 [0.4119, 0.7837] 0.0006	0.0005
Subjects with censoring event	179 (72.8)		161 (64.9)			
No Deterioration	159 (64.6)		114 (46.0)			
No Evaluable Visit	20 (8.1)		47 (19.0)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA2
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:18 (CET); Program name: t_tte.sas; Output name: T.9.11.1_PGIC_TTFDet_FAS.rtf

Anhang 4-G 3.2.2 PGI-C – Zeit bis zur ersten klinisch relevanten Verschlechterung – Subgruppenanalyse – FAS

Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.6640
IHC 3+	55 / 207 (26.6)	22.1 [13.1, NE]	72 / 208 (34.6)	8.1 [4.9, 12.7]	0.5884 [0.4136, 0.8372] 0.0032 0.0028	
IHC 2+/ISH+	12 / 39 (30.8)	18.0 [3.6, NE]	15 / 40 (37.5)	5.7 [1.5, NE]	0.4792 [0.2190, 1.0484] 0.0655 0.0577	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA2
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:18 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.11.2_PGIC_TTFDet_FAS_SUB.rtf

Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.9166
Asia [excluding mainland China]	18 / 57 (31.6)	NE [7.2, NE]	24 / 60 (40.0)	5.7 [4.5, NE]	0.6424 [0.3478, 1.1867] 0.1575 0.1526	
Western Europe	40 / 140 (28.6)	18.0 [10.4, NE]	49 / 139 (35.3)	6.2 [4.8, 12.4]	0.5397 [0.3542, 0.8224] 0.0041 0.0036	
Mainland China/Rest of World (ROW)	9 / 49 (18.4)	NE [NE, NE]	14 / 49 (28.6)	12.7 [3.7, NE]	0.5972 [0.2579, 1.3830] 0.2289 0.2233	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA2
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:18 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.11.2_PGIC_TTFDet_FAS_SUB.rtf

Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.3790
<6 Months	13 / 61 (21.3)	18.0 [18.0, NE]	20 / 61 (32.8)	5.0 [3.3, NE]	0.4291 [0.2121, 0.8683] 0.0186 0.0155	
≥ 6 Months	54 / 185 (29.2)	NE [13.1, NE]	67 / 187 (35.8)	8.1 [5.2, 13.0]	0.6245 [0.4358, 0.8951] 0.0104 0.0095	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA2
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:18 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.11.2_PGIC_TTFDet_FAS_SUB.rtf

Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.2433
<65	34 / 140 (24.3)	NE [18.0, NE]	46 / 130 (35.4)	6.7 [5.0, NE]	0.4903 [0.3139, 0.7658] 0.0017 0.0014	
≥ 65	33 / 106 (31.1)	22.1 [10.4, NE]	41 / 118 (34.7)	8.1 [4.5, 12.7]	0.6936 [0.4361, 1.1030] 0.1221 0.1190	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA2
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:18 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.11.2_PGIC_TTFDet_FAS_SUB.rtf

Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.2454
<75	58 / 222 (26.1)	22.1 [18.0, NE]	73 / 212 (34.4)	6.7 [4.9, 13.2]	0.5461 [0.3853, 0.7742] 0.0007 0.0006	
≥ 75	9 / 24 (37.5)	10.4 [2.1, NE]	14 / 36 (38.9)	8.1 [3.2, 13.0]	0.9355 [0.3989, 2.1944] 0.8783 0.8807	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA2
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:18 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.11.2_PGIC_TTFDet_FAS_SUB.rtf

Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.1462
Male	46 / 187 (24.6)	22.1 [18.0, NE]	72 / 205 (35.1)	8.1 [4.9, 12.7]	0.4835 [0.3321, 0.7040] 0.0001 0.0001	
Female	21 / 59 (35.6)	NE [3.0, NE]	15 / 43 (34.9)	6.5 [2.0, NE]	0.8463 [0.4342, 1.6495] 0.6241 0.6283	

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

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Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.3093
White	34 / 116 (29.3)	22.1 [6.7, NE]	47 / 130 (36.2)	5.2 [3.3, 12.4]	0.5604 [0.3597, 0.8733] 0.0105 0.0093	
Asian	27 / 101 (26.7)	NE [13.1, NE]	31 / 97 (32.0)	12.7 [5.7, NE]	0.7010 [0.4176, 1.1767] 0.1789 0.1756	
Other	6 / 29 (20.7)	18.0 [NE, NE]	9 / 21 (42.9)	5.6 [0.3, NE]	0.2380 [0.0765, 0.7405] 0.0132 0.0077	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.0373
0	21 / 97 (21.6)	22.1 [18.0, NE]	33 / 88 (37.5)	5.6 [4.5, NE]	0.3671 [0.2109, 0.6393] 0.0004 0.0002	
≥ 1	46 / 149 (30.9)	NE [10.5, NE]	54 / 159 (34.0)	8.3 [5.2, 12.7]	0.7435 [0.5009, 1.1036] 0.1413 0.1384	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.9323
Gastric	42 / 153 (27.5)	22.1 [22.1, NE]	54 / 149 (36.2)	6.2 [4.5, 13.0]	0.5920 [0.3948, 0.8877] 0.0112 0.0103	
GEJ	25 / 93 (26.9)	18.0 [10.5, NE]	33 / 99 (33.3)	12.4 [5.0, 13.2]	0.5354 [0.3154, 0.9089] 0.0207 0.0187	

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

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Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.1751
Intestinal	14 / 69 (20.3)	NE [10.5, NE]	25 / 66 (37.9)	5.7 [2.8, NE]	0.3483 [0.1796, 0.6756] 0.0018 0.0011	
Diffuse	9 / 25 (36.0)	NE [2.1, NE]	9 / 19 (47.4)	3.7 [2.0, NE]	0.6655 [0.2623, 1.6883] 0.3913 0.3913	
Others	44 / 152 (28.9)	22.1 [18.0, NE]	53 / 163 (32.5)	10.4 [5.6, 13.0]	0.6797 [0.4547, 1.0162] 0.0599 0.0574	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.7332
<2	20 / 73 (27.4)	18.0 [10.5, NE]	30 / 75 (40.0)	10.4 [4.9, 13.0]	0.5972 [0.3379, 1.0556] 0.0761 0.0725	
≥ 2	47 / 173 (27.2)	22.1 [13.1, NE]	57 / 173 (32.9)	6.5 [4.5, NE]	0.5669 [0.3843, 0.8363] 0.0042 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.3252
Yes	8 / 31 (25.8)	18.0 [6.2, NE]	13 / 30 (43.3)	5.6 [1.4, NE]	0.3670 [0.1452, 0.9279] 0.0342 0.0276	
No	59 / 215 (27.4)	22.1 [13.1, NE]	74 / 218 (33.9)	8.1 [5.0, 12.7]	0.6094 [0.4321, 0.8595] 0.0048 0.0043	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.8608
Yes	4 / 20 (20.0)	NE [7.2, NE]	4 / 17 (23.5)	NE [2.8, NE]	0.6484 [0.1587, 2.6487] 0.5462 0.5433	
No	63 / 226 (27.9)	22.1 [13.1, NE]	83 / 231 (35.9)	6.7 [4.9, 12.4]	0.5710 [0.4106, 0.7940] 0.0009 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.2064
Yes	9 / 39 (23.1)	NE [NE, NE]	7 / 38 (18.4)	NE [12.7, NE]	1.1007 [0.4080, 2.9692] 0.8497 0.8519	
No	58 / 207 (28.0)	22.1 [13.1, NE]	80 / 210 (38.1)	5.7 [4.8, 10.4]	0.5288 [0.3761, 0.7435] 0.0002 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.3535
Yes	31 / 147 (21.1)	NE [NE, NE]	52 / 158 (32.9)	8.3 [5.6, 13.0]	0.4879 [0.3123, 0.7624] 0.0016 0.0013	
No	36 / 99 (36.4)	18.0 [7.2, NE]	35 / 90 (38.9)	5.2 [3.7, NE]	0.6506 [0.4050, 1.0450] 0.0754 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.6183
Normal renal function	31 / 117 (26.5)	NE [10.5, NE]	46 / 120 (38.3)	6.5 [4.8, 13.2]	0.5668 [0.3592, 0.8943] 0.0147 0.0132	
Mild impairment	17 / 88 (19.3)	NE [18.0, NE]	23 / 88 (26.1)	12.7 [12.7, NE]	0.4911 [0.2608, 0.9247] 0.0276 0.0248	
Moderate impairment	19 / 41 (46.3)	6.2 [2.1, NE]	18 / 40 (45.0)	4.5 [3.3, NE]	0.7865 [0.4069, 1.5204] 0.4752 0.4761	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA2
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:18 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.11.2_PGIC_TTFDet_FAS_SUB.rtf

Table 9.11.2 PGI-C - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.8225
Normal hepatic function	53 / 186 (28.5)	22.1 [13.1, NE]	67 / 185 (36.2)	6.7 [4.9, NE]	0.5964 [0.4146, 0.8578] 0.0053 0.0048	
Mild, Moderate or Severe dysfunction	14 / 60 (23.3)	NE [6.2, NE]	19 / 62 (30.6)	8.3 [4.5, 13.0]	0.5277 [0.2638, 1.0556] 0.0708 0.0652	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA2
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:18 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.11.2_PGIC_TTFDet_FAS_SUB.rtf

Anhang 4-G 3.3 PGI-S

Anhang 4-G 3.3.1 PGI-S – Zeit bis zur ersten klinisch relevanten Verschlechterung – FAS

Daiichi Sankyo Europe GmbH
DS8201-A-U306 (DESTINY-GASTRIC04) - DCO 24-OCT-2024

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Table 9.10.1 PGI-S - Time to first deterioration - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
	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 (43.9)	3.5 [2.2, 5.6]	90 (36.3)	3.5 [2.1, 5.0]	0.9912 [0.7485, 1.3128] 0.9511	0.9304
Subjects with censoring event	138 (56.1)		158 (63.7)			
No Deterioration	89 (36.2)		74 (29.8)			
No Baseline Data	25 (10.2)		26 (10.5)			
No Evaluable Visit	23 (9.3)		57 (23.0)			
Baseline Score not Allowing for Deterioration	1 (0.4)		1 (0.4)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte.sas; Output name: T.9.10.1_PGIS_TTFDet_FAS.rtf

Anhang 4-G 3.3.2 PGI-S – Zeit bis zur ersten klinisch relevanten Verschlechterung – Subgruppenanalyse – FAS

Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.6344
IHC 3+	84 / 207 (40.6)	4.9 [2.5, 7.2]	75 / 208 (36.1)	4.5 [2.3, 5.1]	0.9619 [0.7042, 1.3138] 0.8069 0.7886	
IHC 2+/ISH+	24 / 39 (61.5)	1.4 [0.8, 3.5]	15 / 40 (37.5)	1.5 [0.8, NE]	1.1288 [0.5878, 2.1680] 0.7159 0.7191	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.10.2_PGIS_TTFDet_FAS_SUB.rtf

Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.7578
Asia [excluding mainland China]	36 / 57 (63.2)	2.1 [1.4, 3.5]	28 / 60 (46.7)	4.5 [1.4, 4.9]	1.1403 [0.6934, 1.8752] 0.6048 0.6058	
Western Europe	50 / 140 (35.7)	4.4 [2.5, NE]	43 / 139 (30.9)	3.5 [2.1, 5.0]	0.8961 [0.5958, 1.3477] 0.5983 0.5843	
Mainland China/Rest of World (ROW)	22 / 49 (44.9)	4.9 [1.4, NE]	19 / 49 (38.8)	3.3 [1.4, NE]	1.0479 [0.5669, 1.9372] 0.8813 0.8815	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.10.2_PGIS_TTFDet_FAS_SUB.rtf

Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.2576
<6 Months	25 / 61 (41.0)	4.9 [2.2, 6.3]	24 / 61 (39.3)	2.1 [1.0, 5.0]	0.7641 [0.4353, 1.3415] 0.3488 0.3476	
≥ 6 Months	83 / 185 (44.9)	3.5 [2.1, 6.7]	66 / 187 (35.3)	4.5 [2.3, 10.4]	1.1017 [0.7966, 1.5236] 0.5582 0.5806	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.6020
<65	59 / 140 (42.1)	4.9 [2.2, 7.2]	49 / 130 (37.7)	3.4 [1.9, NE]	0.9445 [0.6454, 1.3821] 0.7687 0.7591	
≥ 65	49 / 106 (46.2)	2.5 [1.4, 6.3]	41 / 118 (34.7)	3.5 [1.9, 4.9]	1.0903 [0.7196, 1.6522] 0.6833 0.7039	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.10.2_PGIS_TTFDet_FAS_SUB.rtf

Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.5321
<75	100 / 222 (45.0)	3.5 [2.1, 5.4]	78 / 212 (36.8)	3.5 [2.1, 4.9]	1.0399 [0.7728, 1.3994] 0.7960 0.8203	
≥ 75	8 / 24 (33.3)	14.7 [1.4, NE]	12 / 36 (33.3)	3.3 [0.9, NE]	0.7950 [0.3236, 1.9535] 0.6170 0.6246	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.9613
Male	84 / 187 (44.9)	3.5 [2.2, 6.2]	72 / 205 (35.1)	4.4 [2.2, 10.4]	1.0097 [0.7366, 1.3839] 0.9523 0.9708	
Female	24 / 59 (40.7)	2.2 [1.4, NE]	18 / 43 (41.9)	2.8 [1.5, 4.9]	1.0149 [0.5502, 1.8719] 0.9623 0.9471	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.3797
White	40 / 116 (34.5)	5.0 [2.3, NE]	40 / 130 (30.8)	3.5 [2.2, 10.4]	0.9286 [0.5990, 1.4395] 0.7404 0.7294	
Asian	58 / 101 (57.4)	2.8 [1.5, 4.9]	42 / 97 (43.3)	4.5 [1.4, NE]	1.1488 [0.7708, 1.7121] 0.4956 0.4851	
Other	10 / 29 (34.5)	4.2 [0.8, NE]	8 / 21 (38.1)	1.0 [1.0, NE]	0.6425 [0.2426, 1.7012] 0.3732 0.3778	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.10.2_PGIS_TTFDet_FAS_SUB.rtf

Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.2850
0	48 / 97 (49.5)	4.3 [2.1, 6.3]	40 / 88 (45.5)	2.3 [1.4, 4.5]	0.8340 [0.5469, 1.2717] 0.3990 0.3770	
≥ 1	60 / 149 (40.3)	2.9 [2.1, 7.6]	50 / 159 (31.4)	4.9 [2.1, 12.4]	1.1497 [0.7895, 1.6744] 0.4670 0.4648	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.10.2_PGIS_TTFDet_FAS_SUB.rtf

Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.8850
Gastric	70 / 153 (45.8)	3.4 [2.1, 6.2]	57 / 149 (38.3)	3.4 [1.5, 4.9]	0.9932 [0.6999, 1.4093] 0.9696 0.9530	
GEJ	38 / 93 (40.9)	4.2 [2.1, 14.7]	33 / 99 (33.3)	4.9 [2.2, 12.4]	1.0149 [0.6324, 1.6288] 0.9513 0.9604	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.8095
Intestinal	32 / 69 (46.4)	2.1 [1.4, 6.3]	20 / 66 (30.3)	2.0 [1.2, NE]	1.1380 [0.6481, 1.9983] 0.6526 0.6576	
Diffuse	13 / 25 (52.0)	1.5 [0.8, 7.2]	10 / 19 (52.6)	2.1 [0.8, NE]	1.1360 [0.4969, 2.5973] 0.7625 0.7700	
Others	63 / 152 (41.4)	4.9 [2.9, 7.6]	60 / 163 (36.8)	4.4 [2.8, 5.1]	0.9325 [0.6546, 1.3282] 0.6984 0.6877	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.2750
<2	26 / 73 (35.6)	7.2 [2.2, NE]	32 / 75 (42.7)	3.4 [1.5, 12.4]	0.7951 [0.4709, 1.3424] 0.3909 0.3742	
≥ 2	82 / 173 (47.4)	2.9 [2.1, 5.0]	58 / 173 (33.5)	3.5 [2.0, 5.0]	1.1013 [0.7866, 1.5419] 0.5740 0.5883	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.10.2_PGIS_TTFDet_FAS_SUB.rtf

Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.9672
Yes	13 / 31 (41.9)	6.2 [1.4, NE]	11 / 30 (36.7)	4.9 [1.4, NE]	0.9574 [0.4204, 2.1807] 0.9175 0.9034	
No	95 / 215 (44.2)	3.5 [2.1, 5.4]	79 / 218 (36.2)	3.5 [2.0, 4.9]	1.0089 [0.7484, 1.3602] 0.9536 0.9703	

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

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Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.2969
Yes	11 / 20 (55.0)	6.2 [0.8, NE]	5 / 17 (29.4)	NE [0.8, NE]	1.6480 [0.5713, 4.7539] 0.3554 0.3574	
No	97 / 226 (42.9)	3.5 [2.2, 5.4]	85 / 231 (36.8)	3.5 [2.0, 4.9]	0.9697 [0.7244, 1.2980] 0.8360 0.8181	

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

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Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.8292
Yes	21 / 39 (53.8)	3.5 [1.4, NE]	15 / 38 (39.5)	NE [0.8, NE]	1.0280 [0.5296, 1.9955] 0.9349 0.9306	
No	87 / 207 (42.0)	3.5 [2.2, 5.6]	75 / 210 (35.7)	3.5 [2.2, 4.9]	0.9958 [0.7307, 1.3571] 0.9789 0.9537	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.10.2_PGIS_TTFDet_FAS_SUB.rtf

Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.1934
Yes	66 / 147 (44.9)	2.9 [1.5, 5.0]	51 / 158 (32.3)	4.4 [1.9, 10.4]	1.1815 [0.8195, 1.7034] 0.3716 0.3896	
No	42 / 99 (42.4)	4.3 [2.2, NE]	39 / 90 (43.3)	3.1 [1.9, 4.9]	0.8237 [0.5311, 1.2774] 0.3863 0.3828	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.10.2_PGIS_TTFDet_FAS_SUB.rtf

Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.5666
Normal renal function	52 / 117 (44.4)	2.9 [2.1, 5.4]	47 / 120 (39.2)	3.5 [1.5, 10.4]	1.0704 [0.7204, 1.5906] 0.7363 0.7443	
Mild impairment	36 / 88 (40.9)	6.2 [1.5, NE]	26 / 88 (29.5)	4.9 [1.9, NE]	1.1782 [0.7108, 1.9527] 0.5247 0.5413	
Moderate impairment	20 / 41 (48.8)	3.5 [1.4, NE]	17 / 40 (42.5)	3.3 [1.4, 4.9]	0.7086 [0.3670, 1.3680] 0.3047 0.2933	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.10.2_PGIS_TTFDet_FAS_SUB.rtf

Table 9.10.2 PGI-S - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.2603
Normal hepatic function	81 / 186 (43.5)	3.5 [2.2, 6.3]	76 / 185 (41.1)	3.3 [1.9, 4.9]	0.9317 [0.6808, 1.2749] 0.6584 0.6433	
Mild, Moderate or Severe dysfunction	27 / 60 (45.0)	4.2 [1.5, 7.6]	14 / 62 (22.6)	5.1 [1.8, NE]	1.4144 [0.7393, 2.7060] 0.2949 0.2948	

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

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Anhang 4-G 3.4 FACT-Ga

Anhang 4-G 3.4.1 FACT-Ga – Zeit bis zur ersten Verschlechterung um ≥15 % der Skalenspannweite – FAS

Table 9.9.1 FACT-Ga - Time to first deterioration - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
Physical well-being (PWB)	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	92 (37.4)	6.2 [4.9, 16.1]	86 (34.7)	4.9 [3.8, 7.2]	0.8359 [0.6209, 1.1255] 0.2377	0.2353
Subjects with censoring event	154 (62.6)		162 (65.3)			
No Deterioration	112 (45.5)		87 (35.1)			
No Evaluable Visit	21 (8.5)		55 (22.2)			
No Baseline Data	18 (7.3)		19 (7.7)			
Baseline Score not Allowing for Deterioration	3 (1.2)		1 (0.4)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:01 (CET); Program name: t_tte.sas; Output name: T.9.9.1_FACT-Ga_TTFDet_FAS.rtf

Table 9.9.1 FACT-Ga - Time to first deterioration - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
Social/family well-being (SWB)	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	75 (30.5)	9.2 [6.2, NE]	75 (30.2)	5.0 [3.8, NE]	0.7938 [0.5758, 1.0944] 0.1588	0.1533
Subjects with censoring event	171 (69.5)		173 (69.8)			
No Deterioration	127 (51.6)		95 (38.3)			
No Evaluable Visit	21 (8.5)		55 (22.2)			
No Baseline Data	18 (7.3)		19 (7.7)			
Baseline Score not Allowing for Deterioration	5 (2.0)		4 (1.6)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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 9.9.1 FACT-Ga - Time to first deterioration - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
Functional well-being (FWB)	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	85 (34.6)	6.7 [5.1, 16.1]	80 (32.3)	4.9 [3.7, 6.3]	0.8167 [0.6007, 1.1104] 0.1964	0.1938
Subjects with censoring event	161 (65.4)		168 (67.7)			
No Deterioration	114 (46.3)		82 (33.1)			
No Evaluable Visit	21 (8.5)		55 (22.2)			
No Baseline Data	20 (8.1)		19 (7.7)			
Baseline Score not Allowing for Deterioration	6 (2.4)		12 (4.8)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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 9.9.1 FACT-Ga - Time to first deterioration - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
Emotional well-being (EWB)	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	71 (28.9)	12.2 [9.2, NE]	75 (30.2)	6.3 [5.0, NE]	0.7009 [0.5060, 0.9710] 0.0326	0.0316
Subjects with censoring event	175 (71.1)		173 (69.8)			
No Deterioration	135 (54.9)		98 (39.5)			
No Evaluable Visit	21 (8.5)		55 (22.2)			
No Baseline Data	19 (7.7)		20 (8.1)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte.sas; Output name: T.9.9.1_FACT-Ga_TTFDet_FAS.rtf

Table 9.9.1 FACT-Ga - Time to first deterioration - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
Gastric cancer subscale (GaCS)	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	77 (31.3)	9.7 [6.4, NE]	51 (20.6)	12.4 [7.2, NE]	1.2040 [0.8439, 1.7177] 0.3059	0.3066
Subjects with censoring event	169 (68.7)		197 (79.4)			
No Deterioration	128 (52.0)		121 (48.8)			
No Evaluable Visit	21 (8.5)		55 (22.2)			
No Baseline Data	17 (6.9)		20 (8.1)			
Baseline Score not Allowing for Deterioration	3 (1.2)		1 (0.4)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte.sas; Output name: T.9.9.1_FACT-Ga_TTFDet_FAS.rtf

Table 9.9.1 FACT-Ga - Time to first deterioration - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
Functional Assessment of Cancer Therapy-Gastric	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	56 (22.8)	16.1 [11.8, NE]	54 (21.8)	NE [7.2, NE]	0.7765 [0.5322, 1.1330] 0.1895	0.1896
Subjects with censoring event	190 (77.2)		194 (78.2)			
No Deterioration	149 (60.6)		119 (48.0)			
No Evaluable Visit	21 (8.5)		55 (22.2)			
No Baseline Data	20 (8.1)		20 (8.1)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte.sas; Output name: T.9.9.1_FACT-Ga_TTFDet_FAS.rtf

Table 9.9.1 FACT-Ga - Time to first deterioration - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	
The Functional Assessment of Cancer Therapy-General	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	63 (25.6)	13.1 [10.9, NE]	68 (27.4)	5.7 [4.9, NE]	0.6758 [0.4779, 0.9555] 0.0266	0.0255
Subjects with censoring event	183 (74.4)		180 (72.6)			
No Deterioration	142 (57.7)		105 (42.3)			
No Evaluable Visit	21 (8.5)		55 (22.2)			
No Baseline Data	20 (8.1)		20 (8.1)			

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:01 (CET); Program name: t_tte.sas; Output name: T.9.9.1_FACT-Ga_TTFDet_FAS.rtf

Anhang 4-G 3.4.2 FACT-Ga – Zeit bis zur ersten Verschlechterung um ≥15 % der Skalenspannweite – Subgruppenanalyse – FAS

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.4986
IHC 3+	74 / 207 (35.7)	7.6 [4.9, NE]	69 / 208 (33.2)	5.8 [3.9, 8.1]	0.8779 [0.6306, 1.2223] 0.4407 0.4384	
IHC 2+/ISH+	18 / 39 (46.2)	4.3 [2.1, NE]	17 / 40 (42.5)	3.3 [2.2, 4.9]	0.6806 [0.3461, 1.3386] 0.2649 0.2595	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.9421
Asia [excluding mainland China]	30 / 57 (52.6)	4.9 [2.1, 10.9]	27 / 60 (45.0)	3.5 [2.5, 7.7]	0.8794 [0.5174, 1.4949] 0.6351 0.6310	
Western Europe	47 / 140 (33.6)	5.0 [3.7, NE]	42 / 139 (30.2)	5.7 [3.7, 7.7]	0.8517 [0.5600, 1.2952] 0.4529 0.4485	
Mainland China/Rest of World (ROW)	15 / 49 (30.6)	NE [4.9, NE]	17 / 49 (34.7)	7.2 [3.4, NE]	0.7671 [0.3795, 1.5508] 0.4604 0.4561	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.7923
<6 Months	21 / 61 (34.4)	5.1 [2.3, NE]	19 / 61 (31.1)	4.9 [3.3, 6.6]	0.7841 [0.4174, 1.4729] 0.4496 0.4391	
≥ 6 Months	71 / 185 (38.4)	6.2 [4.2, 16.1]	67 / 187 (35.8)	4.9 [3.7, 8.1]	0.8726 [0.6231, 1.2218] 0.4274 0.4256	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.6386
<65	52 / 140 (37.1)	6.2 [4.9, NE]	49 / 130 (37.7)	4.8 [3.5, 7.7]	0.7790 [0.5250, 1.1558] 0.2147 0.2113	
≥ 65	40 / 106 (37.7)	4.9 [3.4, NE]	37 / 118 (31.4)	5.8 [3.3, 8.1]	0.9420 [0.5989, 1.4816] 0.7960 0.7942	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.6230
<75	84 / 222 (37.8)	6.2 [4.9, 16.1]	75 / 212 (35.4)	4.9 [3.5, 7.2]	0.8258 [0.6026, 1.1316] 0.2338 0.2299	
≥ 75	8 / 24 (33.3)	3.9 [1.4, NE]	11 / 36 (30.6)	6.5 [3.3, 8.1]	1.0389 [0.4170, 2.5885] 0.9347 0.9359	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.2820
Male	66 / 187 (35.3)	9.2 [4.9, NE]	70 / 205 (34.1)	4.9 [3.7, 7.7]	0.7598 [0.5396, 1.0698] 0.1156 0.1126	
Female	26 / 59 (44.1)	3.2 [2.1, NE]	16 / 43 (37.2)	3.8 [2.1, 9.0]	1.1063 [0.5924, 2.0660] 0.7513 0.7472	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.6721
White	37 / 116 (31.9)	9.2 [4.0, NE]	39 / 130 (30.0)	5.8 [3.7, 8.1]	0.7864 [0.4990, 1.2395] 0.3007 0.2976	
Asian	43 / 101 (42.6)	7.6 [3.5, NE]	40 / 97 (41.2)	4.9 [3.4, NE]	0.8251 [0.5338, 1.2753] 0.3868 0.3830	
Other	12 / 29 (41.4)	3.7 [1.5, NE]	7 / 21 (33.3)	5.6 [2.3, NE]	1.3491 [0.5277, 3.4489] 0.5319 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.0177
0	35 / 97 (36.1)	10.9 [5.0, NE]	37 / 88 (42.0)	4.8 [2.4, 6.6]	0.5331 [0.3315, 0.8574] 0.0095 0.0080	
≥ 1	57 / 149 (38.3)	4.9 [3.0, 9.2]	49 / 159 (30.8)	5.8 [3.5, 12.4]	1.1637 [0.7933, 1.7070] 0.4379 0.4378	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.3828
Gastric	63 / 153 (41.2)	5.0 [3.5, 9.2]	53 / 149 (35.6)	4.9 [3.5, 7.2]	0.9242 [0.6382, 1.3382] 0.6763 0.6704	
GEJ	29 / 93 (31.2)	16.1 [4.2, NE]	33 / 99 (33.3)	5.8 [3.8, 8.1]	0.7149 [0.4318, 1.1839] 0.1922 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.4384
Intestinal	24 / 69 (34.8)	9.2 [3.6, NE]	20 / 66 (30.3)	4.9 [2.1, NE]	0.8025 [0.4386, 1.4682] 0.4753 0.4700	
Diffuse	12 / 25 (48.0)	3.7 [1.3, NE]	7 / 19 (36.8)	5.8 [1.5, NE]	1.4903 [0.5858, 3.7916] 0.4024 0.4072	
Others	56 / 152 (36.8)	7.6 [4.9, NE]	59 / 163 (36.2)	4.9 [3.7, 7.7]	0.7858 [0.5430, 1.1373] 0.2013 0.1984	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.5386
<2	28 / 73 (38.4)	5.1 [2.1, NE]	33 / 75 (44.0)	4.9 [3.5, 9.0]	1.0006 [0.6025, 1.6618] 0.9981 0.9846	
≥ 2	64 / 173 (37.0)	7.7 [4.3, 20.1]	53 / 173 (30.6)	4.9 [3.5, 7.7]	0.7921 [0.5477, 1.1454] 0.2155 0.2142	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.9262
Yes	13 / 31 (41.9)	5.1 [2.1, NE]	11 / 30 (36.7)	3.9 [3.3, NE]	0.9207 [0.4103, 2.0663] 0.8413 0.8333	
No	79 / 215 (36.7)	7.6 [4.3, 20.1]	75 / 218 (34.4)	4.9 [3.7, 7.7]	0.8340 [0.6058, 1.1480] 0.2655 0.2625	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.1929
Yes	9 / 20 (45.0)	6.2 [3.0, NE]	3 / 17 (17.6)	NE [1.9, NE]	1.7143 [0.4529, 6.4885] 0.4273 0.4193	
No	83 / 226 (36.7)	6.2 [4.0, 20.1]	83 / 231 (35.9)	4.9 [3.5, 6.6]	0.8180 [0.6014, 1.1124] 0.2002 0.1957	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.8077
Yes	16 / 39 (41.0)	7.7 [4.9, NE]	12 / 38 (31.6)	NE [3.4, NE]	0.9125 [0.4288, 1.9416] 0.8121 0.8063	
No	76 / 207 (36.7)	5.1 [3.7, 20.1]	74 / 210 (35.2)	4.9 [3.7, 6.6]	0.8440 [0.6105, 1.1668] 0.3046 0.2986	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.2052
Yes	50 / 147 (34.0)	7.6 [4.0, NE]	46 / 158 (29.1)	7.2 [5.6, 9.0]	0.9731 [0.6502, 1.4565] 0.8946 0.8945	
No	42 / 99 (42.4)	5.1 [3.5, 16.1]	40 / 90 (44.4)	3.5 [2.3, 4.9]	0.6782 [0.4352, 1.0570] 0.0863 0.0827	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.9387
Normal renal function	40 / 117 (34.2)	9.2 [4.2, NE]	42 / 120 (35.0)	5.6 [3.5, 12.4]	0.8305 [0.5365, 1.2858] 0.4050 0.3998	
Mild impairment	31 / 88 (35.2)	6.2 [4.0, NE]	27 / 88 (30.7)	6.5 [3.9, 9.0]	0.8743 [0.5203, 1.4690] 0.6119 0.6034	
Moderate impairment	21 / 41 (51.2)	2.4 [1.4, NE]	17 / 40 (42.5)	3.5 [1.5, 5.8]	0.8632 [0.4510, 1.6520] 0.6568 0.6618	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Physical well-being (PWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.3923
Normal hepatic function	70 / 186 (37.6)	6.2 [4.3, NE]	72 / 185 (38.9)	4.9 [3.5, 7.7]	0.8115 [0.5823, 1.1309] 0.2175 0.2142	
Mild, Moderate or Severe dysfunction	22 / 60 (36.7)	7.6 [3.5, NE]	14 / 62 (22.6)	4.9 [3.5, NE]	1.0571 [0.5359, 2.0851] 0.8728 0.8720	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.9214
IHC 3+	62 / 207 (30.0)	9.2 [6.1, NE]	62 / 208 (29.8)	4.9 [3.7, NE]	0.8036 [0.5646, 1.1437] 0.2247 0.2232	
IHC 2+/ISH+	13 / 39 (33.3)	7.7 [2.5, NE]	13 / 40 (32.5)	5.4 [2.1, NE]	0.7483 [0.3450, 1.6229] 0.4629 0.4393	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.8880
Asia [excluding mainland China]	25 / 57 (43.9)	6.2 [2.1, 7.7]	26 / 60 (43.3)	2.5 [2.1, 4.9]	0.7023 [0.4022, 1.2264] 0.2141 0.2095	
Western Europe	31 / 140 (22.1)	NE [8.2, NE]	29 / 139 (20.9)	14.5 [5.4, NE]	0.8420 [0.5069, 1.3986] 0.5066 0.5027	
Mainland China/Rest of World (ROW)	19 / 49 (38.8)	7.7 [2.2, NE]	20 / 49 (40.8)	3.8 [2.1, NE]	0.8409 [0.4480, 1.5785] 0.5896 0.5791	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.9740
<6 Months	21 / 61 (34.4)	7.7 [2.4, NE]	19 / 61 (31.1)	3.8 [2.3, NE]	0.7688 [0.4105, 1.4399] 0.4115 0.3999	
≥ 6 Months	54 / 185 (29.2)	13.1 [6.1, NE]	56 / 187 (29.9)	6.3 [4.2, NE]	0.7957 [0.5473, 1.1570] 0.2316 0.2290	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.2467
<65	46 / 140 (32.9)	8.2 [5.4, NE]	40 / 130 (30.8)	6.3 [3.8, NE]	0.9217 [0.6030, 1.4089] 0.7066 0.7110	
≥ 65	29 / 106 (27.4)	NE [5.1, NE]	35 / 118 (29.7)	4.9 [2.9, NE]	0.6388 [0.3889, 1.0493] 0.0767 0.0721	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.7239
<75	68 / 222 (30.6)	13.1 [6.2, NE]	65 / 212 (30.7)	5.4 [3.7, NE]	0.7821 [0.5561, 1.0999] 0.1578 0.1548	
≥ 75	7 / 24 (29.2)	7.7 [1.6, NE]	10 / 36 (27.8)	4.9 [2.9, NE]	1.0030 [0.3685, 2.7299] 0.9953 0.9964	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.7538
Male	60 / 187 (32.1)	7.7 [5.8, NE]	61 / 205 (29.8)	5.6 [3.7, NE]	0.8058 [0.5630, 1.1533] 0.2379 0.2351	
Female	15 / 59 (25.4)	9.2 [3.6, NE]	14 / 43 (32.6)	4.9 [2.1, NE]	0.6762 [0.3258, 1.4036] 0.2937 0.2894	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.2104
White	21 / 116 (18.1)	NE [8.2, NE]	30 / 130 (23.1)	14.5 [4.2, NE]	0.5991 [0.3429, 1.0467] 0.0719 0.0684	
Asian	44 / 101 (43.6)	6.3 [3.6, 9.2]	41 / 97 (42.3)	3.5 [2.2, 4.9]	0.7968 [0.5193, 1.2225] 0.2982 0.2970	
Other	10 / 29 (34.5)	4.2 [1.5, NE]	4 / 21 (19.0)	NE [2.9, NE]	1.9879 [0.6165, 6.4098] 0.2501 0.2413	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.8565
0	31 / 97 (32.0)	NE [4.9, NE]	28 / 88 (31.8)	5.6 [3.5, NE]	0.7710 [0.4617, 1.2875] 0.3202 0.3119	
≥ 1	44 / 149 (29.5)	9.2 [5.4, NE]	47 / 159 (29.6)	4.9 [3.7, NE]	0.8120 [0.5378, 1.2261] 0.3220 0.3251	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.5290
Gastric	46 / 153 (30.1)	NE [5.4, NE]	50 / 149 (33.6)	4.9 [2.9, NE]	0.7493 [0.5016, 1.1194] 0.1588 0.1521	
GEJ	29 / 93 (31.2)	8.2 [5.8, NE]	25 / 99 (25.3)	6.3 [4.7, NE]	0.8848 [0.5171, 1.5141] 0.6552 0.6578	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.6101
Intestinal	16 / 69 (23.2)	13.1 [7.7, NE]	17 / 66 (25.8)	4.7 [2.9, NE]	0.5855 [0.2939, 1.1662] 0.1278 0.1217	
Diffuse	8 / 25 (32.0)	5.8 [0.8, NE]	8 / 19 (42.1)	2.8 [1.4, NE]	0.7732 [0.2870, 2.0834] 0.6110 0.5979	
Others	51 / 152 (33.6)	8.2 [4.9, NE]	50 / 163 (30.7)	5.6 [4.2, NE]	0.8869 [0.6000, 1.3109] 0.5470 0.5436	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.4512
<2	24 / 73 (32.9)	8.2 [4.9, NE]	28 / 75 (37.3)	4.9 [3.5, NE]	0.9616 [0.5563, 1.6619] 0.8883 0.8885	
≥ 2	51 / 173 (29.5)	13.1 [6.1, NE]	47 / 173 (27.2)	5.4 [3.8, NE]	0.7361 [0.4946, 1.0956] 0.1310 0.1277	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.8316
Yes	12 / 31 (38.7)	6.1 [2.2, NE]	10 / 30 (33.3)	4.9 [2.3, NE]	0.8132 [0.3470, 1.9055] 0.6341 0.6336	
No	63 / 215 (29.3)	13.1 [6.3, NE]	65 / 218 (29.8)	5.4 [3.7, NE]	0.7844 [0.5544, 1.1099] 0.1704 0.1663	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.9685
Yes	6 / 20 (30.0)	NE [4.9, NE]	5 / 17 (29.4)	NE [1.4, NE]	0.7656 [0.2330, 2.5150] 0.6598 0.6693	
No	69 / 226 (30.5)	9.2 [6.2, NE]	70 / 231 (30.3)	5.0 [3.7, NE]	0.7968 [0.5709, 1.1120] 0.1816 0.1787	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.8010
Yes	15 / 39 (38.5)	7.7 [3.6, NE]	13 / 38 (34.2)	5.0 [3.5, NE]	0.8616 [0.4089, 1.8156] 0.6952 0.6974	
No	60 / 207 (29.0)	9.2 [6.2, NE]	62 / 210 (29.5)	5.4 [3.7, NE]	0.7781 [0.5451, 1.1106] 0.1669 0.1633	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.6384
Yes	40 / 147 (27.2)	13.1 [5.4, NE]	42 / 158 (26.6)	5.6 [3.8, NE]	0.8414 [0.5454, 1.2981] 0.4350 0.4336	
No	35 / 99 (35.4)	8.2 [5.1, NE]	33 / 90 (36.7)	4.7 [2.4, NE]	0.7261 [0.4500, 1.1717] 0.1899 0.1881	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.0777
Normal renal function	37 / 117 (31.6)	9.2 [5.1, NE]	32 / 120 (26.7)	NE [5.0, NE]	1.1026 [0.6864, 1.7712] 0.6862 0.6863	
Mild impairment	25 / 88 (28.4)	8.2 [5.8, NE]	28 / 88 (31.8)	4.9 [3.5, NE]	0.6251 [0.3632, 1.0760] 0.0900 0.0858	
Moderate impairment	13 / 41 (31.7)	7.7 [3.8, NE]	15 / 40 (37.5)	2.1 [1.5, NE]	0.3863 [0.1762, 0.8466] 0.0175 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Social/family well-being (SWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.2713
Normal hepatic function	57 / 186 (30.6)	8.2 [6.2, NE]	64 / 185 (34.6)	4.9 [3.5, 14.5]	0.7224 [0.5046, 1.0340] 0.0756 0.0728	
Mild, Moderate or Severe dysfunction	18 / 60 (30.0)	NE [3.7, NE]	11 / 62 (17.7)	NE [3.7, NE]	1.1843 [0.5589, 2.5093] 0.6589 0.6620	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.7895
IHC 3+	67 / 207 (32.4)	9.2 [6.2, NE]	65 / 208 (31.3)	5.1 [3.7, 13.2]	0.8344 [0.5926, 1.1747] 0.2996 0.3018	
IHC 2+/ISH+	18 / 39 (46.2)	3.5 [1.4, NE]	15 / 40 (37.5)	3.5 [0.9, 7.2]	0.7472 [0.3726, 1.4985] 0.4117 0.3952	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.1467
Asia [excluding mainland China]	21 / 57 (36.8)	15.6 [6.2, NE]	24 / 60 (40.0)	3.5 [1.5, 6.3]	0.6453 [0.3577, 1.1643] 0.1458 0.1427	
Western Europe	45 / 140 (32.1)	6.4 [3.7, NE]	32 / 139 (23.0)	6.3 [4.9, NE]	1.1320 [0.7180, 1.7847] 0.5935 0.5986	
Mainland China/Rest of World (ROW)	19 / 49 (38.8)	NE [2.0, NE]	24 / 49 (49.0)	2.5 [1.0, 6.2]	0.6446 [0.3529, 1.1776] 0.1533 0.1476	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.3432
<6 Months	15 / 61 (24.6)	18.7 [5.0, NE]	14 / 61 (23.0)	4.2 [2.1, NE]	0.6136 [0.2953, 1.2750] 0.1906 0.1929	
≥ 6 Months	70 / 185 (37.8)	6.7 [3.5, 16.1]	66 / 187 (35.3)	5.1 [3.7, 6.3]	0.8987 [0.6415, 1.2590] 0.5348 0.5268	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.7245
<65	45 / 140 (32.1)	8.4 [6.4, NE]	45 / 130 (34.6)	6.0 [3.7, 7.2]	0.7753 [0.5123, 1.1732] 0.2285 0.2275	
≥ 65	40 / 106 (37.7)	3.5 [2.1, NE]	35 / 118 (29.7)	3.7 [2.1, NE]	0.9239 [0.5863, 1.4557] 0.7328 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.0805
<75	73 / 222 (32.9)	9.2 [6.4, 18.7]	70 / 212 (33.0)	5.1 [3.7, 6.3]	0.7595 [0.5463, 1.0561] 0.1019 0.0993	
≥ 75	12 / 24 (50.0)	2.1 [0.9, 5.1]	10 / 36 (27.8)	3.7 [1.5, NE]	1.4793 [0.6382, 3.4288] 0.3612 0.3411	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.2371
Male	71 / 187 (38.0)	6.4 [3.5, 16.1]	65 / 205 (31.7)	5.1 [3.5, 7.2]	0.9279 [0.6614, 1.3017] 0.6647 0.6576	
Female	14 / 59 (23.7)	NE [5.1, NE]	15 / 43 (34.9)	4.9 [2.1, 13.2]	0.5833 [0.2774, 1.2267] 0.1552 0.1490	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.1344
White	35 / 116 (30.2)	6.7 [3.7, NE]	30 / 130 (23.1)	7.2 [4.5, NE]	1.1360 [0.6963, 1.8534] 0.6097 0.6117	
Asian	39 / 101 (38.6)	15.6 [3.5, NE]	43 / 97 (44.3)	2.4 [1.5, 6.2]	0.6070 [0.3930, 0.9377] 0.0245 0.0237	
Other	11 / 29 (37.9)	5.1 [1.5, NE]	7 / 21 (33.3)	4.2 [1.1, NE]	0.7970 [0.2896, 2.1937] 0.6605 0.6625	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.9993
0	38 / 97 (39.2)	6.4 [5.0, 18.7]	31 / 88 (35.2)	4.8 [3.7, 7.2]	0.7945 [0.4923, 1.2822] 0.3461 0.3348	
≥ 1	47 / 149 (31.5)	9.2 [3.5, NE]	49 / 159 (30.8)	4.9 [2.5, NE]	0.8298 [0.5558, 1.2391] 0.3618 0.3579	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.0483
Gastric	52 / 153 (34.0)	9.2 [5.1, 18.7]	57 / 149 (38.3)	3.7 [2.1, 6.0]	0.6656 [0.4562, 0.9711] 0.0347 0.0326	
GEJ	33 / 93 (35.5)	6.4 [3.5, NE]	23 / 99 (23.2)	7.7 [4.9, NE]	1.2692 [0.7421, 2.1707] 0.3839 0.3835	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.4186
Intestinal	19 / 69 (27.5)	18.7 [3.7, NE]	20 / 66 (30.3)	3.7 [2.1, NE]	0.6105 [0.3253, 1.1459] 0.1245 0.1210	
Diffuse	7 / 25 (28.0)	NE [0.8, NE]	5 / 19 (26.3)	NE [0.8, NE]	1.0420 [0.3280, 3.3108] 0.9443 0.9331	
Others	59 / 152 (38.8)	6.4 [3.5, 15.6]	55 / 163 (33.7)	6.0 [3.5, 7.7]	0.9231 [0.6386, 1.3343] 0.6703 0.6706	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.8590
<2	23 / 73 (31.5)	9.2 [2.2, NE]	29 / 75 (38.7)	6.2 [3.7, 13.2]	0.8586 [0.4957, 1.4870] 0.5864 0.5870	
≥ 2	62 / 173 (35.8)	6.7 [5.0, 16.1]	51 / 173 (29.5)	4.5 [3.3, 6.3]	0.8174 [0.5634, 1.1858] 0.2881 0.2842	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.4790
Yes	16 / 31 (51.6)	2.2 [0.8, 6.4]	11 / 30 (36.7)	3.3 [1.4, 4.4]	0.9615 [0.4295, 2.1523] 0.9238 0.8978	
No	69 / 215 (32.1)	9.2 [6.4, 18.7]	69 / 218 (31.7)	6.0 [3.7, 7.2]	0.7896 [0.5652, 1.1032] 0.1662 0.1634	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.5028
Yes	7 / 20 (35.0)	NE [1.4, NE]	7 / 17 (41.2)	3.7 [0.8, NE]	0.5901 [0.2057, 1.6933] 0.3267 0.3057	
No	78 / 226 (34.5)	6.7 [5.0, 16.1]	73 / 231 (31.6)	4.9 [3.5, 6.3]	0.8604 [0.6248, 1.1848] 0.3570 0.3536	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.5840
Yes	18 / 39 (46.2)	6.2 [1.4, NE]	17 / 38 (44.7)	3.5 [0.8, NE]	0.7248 [0.3723, 1.4112] 0.3438 0.3395	
No	67 / 207 (32.4)	8.4 [5.1, 16.1]	63 / 210 (30.0)	6.0 [3.7, 7.2]	0.8577 [0.6075, 1.2109] 0.3830 0.3784	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.4115
Yes	47 / 147 (32.0)	15.6 [3.7, NE]	46 / 158 (29.1)	6.3 [3.7, 13.2]	0.9334 [0.6213, 1.4022] 0.7398 0.7305	
No	38 / 99 (38.4)	6.7 [5.1, NE]	34 / 90 (37.8)	3.8 [2.1, 6.2]	0.6977 [0.4369, 1.1141] 0.1317 0.1268	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.0651
Normal renal function	34 / 117 (29.1)	16.1 [5.0, NE]	42 / 120 (35.0)	4.9 [3.7, 6.3]	0.7136 [0.4530, 1.1242] 0.1457 0.1417	
Mild impairment	34 / 88 (38.6)	6.2 [2.1, NE]	22 / 88 (25.0)	13.2 [2.5, NE]	1.2684 [0.7417, 2.1692] 0.3851 0.3906	
Moderate impairment	17 / 41 (41.5)	6.7 [2.1, 18.7]	16 / 40 (40.0)	2.1 [1.4, 6.2]	0.4335 [0.2102, 0.8940] 0.0236 0.0200	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional well-being (FWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.8830
Normal hepatic function	68 / 186 (36.6)	6.7 [3.7, 18.7]	67 / 185 (36.2)	4.9 [3.3, 7.2]	0.8332 [0.5940, 1.1686] 0.2904 0.2885	
Mild, Moderate or Severe dysfunction	17 / 60 (28.3)	16.1 [3.7, NE]	13 / 62 (21.0)	6.3 [3.5, NE]	0.8735 [0.4194, 1.8190] 0.7178 0.7079	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.4230
IHC 3+	54 / 207 (26.1)	12.2 [10.4, NE]	63 / 208 (30.3)	6.3 [5.0, NE]	0.6600 [0.4584, 0.9502] 0.0254 0.0243	
IHC 2+/ISH+	17 / 39 (43.6)	4.3 [2.4, 17.3]	12 / 40 (30.0)	5.6 [1.8, NE]	0.8980 [0.4266, 1.8903] 0.7769 0.7757	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.7613
Asia [excluding mainland China]	23 / 57 (40.4)	10.6 [4.4, NE]	21 / 60 (35.0)	5.0 [3.5, NE]	0.8627 [0.4755, 1.5653] 0.6271 0.6260	
Western Europe	31 / 140 (22.1)	15.2 [10.4, NE]	31 / 139 (22.3)	7.2 [5.7, NE]	0.6988 [0.4240, 1.1517] 0.1598 0.1589	
Mainland China/Rest of World (ROW)	17 / 49 (34.7)	9.2 [2.8, NE]	23 / 49 (46.9)	3.3 [1.4, NE]	0.6283 [0.3354, 1.1771] 0.1468 0.1384	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.0991
<6 Months	16 / 61 (26.2)	15.2 [4.6, NE]	21 / 61 (34.4)	5.0 [2.1, 6.5]	0.3834 [0.1928, 0.7627] 0.0063 0.0047	
≥ 6 Months	55 / 185 (29.7)	11.8 [9.2, NE]	54 / 187 (28.9)	9.0 [5.5, NE]	0.8211 [0.5637, 1.1960] 0.3043 0.3017	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.7771
<65	36 / 140 (25.7)	NE [15.2, NE]	37 / 130 (28.5)	9.0 [5.7, NE]	0.7453 [0.4709, 1.1798] 0.2097 0.2062	
≥ 65	35 / 106 (33.0)	9.2 [5.0, 12.2]	38 / 118 (32.2)	5.0 [3.5, 6.5]	0.6346 [0.3959, 1.0172] 0.0589 0.0556	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.8619
<75	64 / 222 (28.8)	15.2 [9.0, NE]	64 / 212 (30.2)	6.3 [5.0, NE]	0.7144 [0.5048, 1.0111] 0.0577 0.0563	
≥ 75	7 / 24 (29.2)	10.4 [1.6, NE]	11 / 36 (30.6)	5.0 [2.1, NE]	0.7186 [0.2749, 1.8786] 0.5003 0.4907	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.4622
Male	56 / 187 (29.9)	12.2 [9.2, NE]	64 / 205 (31.2)	6.3 [5.0, 12.4]	0.6588 [0.4574, 0.9489] 0.0250 0.0238	
Female	15 / 59 (25.4)	NE [4.4, NE]	11 / 43 (25.6)	NE [3.5, NE]	0.8495 [0.3892, 1.8543] 0.6821 0.6829	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.2693
White	25 / 116 (21.6)	NE [9.2, NE]	31 / 130 (23.8)	7.2 [5.0, NE]	0.6690 [0.3945, 1.1343] 0.1356 0.1321	
Asian	39 / 101 (38.6)	10.6 [4.9, NE]	35 / 97 (36.1)	6.3 [3.5, NE]	0.8566 [0.5423, 1.3531] 0.5071 0.5027	
Other	7 / 29 (24.1)	12.2 [8.8, NE]	9 / 21 (42.9)	5.6 [1.1, NE]	0.1236 [0.0314, 0.4867] 0.0028 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.2946
0	30 / 97 (30.9)	11.8 [8.8, NE]	31 / 88 (35.2)	6.0 [3.7, 9.0]	0.5491 [0.3303, 0.9128] 0.0208 0.0192	
≥ 1	41 / 149 (27.5)	12.2 [5.6, NE]	44 / 159 (27.7)	6.3 [5.0, NE]	0.8285 [0.5413, 1.2681] 0.3864 0.3821	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.3645
Gastric	50 / 153 (32.7)	12.2 [4.9, NE]	48 / 149 (32.2)	6.0 [4.4, NE]	0.8079 [0.5431, 1.2019] 0.2925 0.2888	
GEJ	21 / 93 (22.6)	11.8 [9.0, NE]	27 / 99 (27.3)	12.4 [5.0, NE]	0.5659 [0.3195, 1.0022] 0.0509 0.0480	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.7322
Intestinal	20 / 69 (29.0)	10.6 [3.8, NE]	22 / 66 (33.3)	3.7 [2.1, NE]	0.5761 [0.3132, 1.0596] 0.0761 0.0720	
Diffuse	5 / 25 (20.0)	NE [1.4, NE]	5 / 19 (26.3)	NE [1.5, NE]	0.7829 [0.2258, 2.7150] 0.6997 0.6982	
Others	46 / 152 (30.3)	11.8 [8.8, NE]	48 / 163 (29.4)	6.5 [5.0, NE]	0.7680 [0.5120, 1.1518] 0.2018 0.1982	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.3678
<2	18 / 73 (24.7)	12.2 [11.8, NE]	23 / 75 (30.7)	12.4 [5.0, NE]	0.8625 [0.4645, 1.6014] 0.6394 0.6319	
≥ 2	53 / 173 (30.6)	10.6 [8.8, NE]	52 / 173 (30.1)	5.6 [3.5, 9.0]	0.6131 [0.4169, 0.9017] 0.0129 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.9328
Yes	10 / 31 (32.3)	15.2 [2.2, NE]	9 / 30 (30.0)	5.6 [2.0, NE]	0.7472 [0.2946, 1.8948] 0.5393 0.5335	
No	61 / 215 (28.4)	11.8 [9.2, NE]	66 / 218 (30.3)	6.3 [5.0, NE]	0.7060 [0.4981, 1.0006] 0.0504 0.0491	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.7636
Yes	6 / 20 (30.0)	9.2 [4.6, NE]	6 / 17 (35.3)	NE [0.9, NE]	0.5743 [0.1751, 1.8834] 0.3601 0.3528	
No	65 / 226 (28.8)	12.2 [9.0, NE]	69 / 231 (29.9)	6.0 [5.0, NE]	0.7225 [0.5145, 1.0147] 0.0607 0.0588	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.7433
Yes	14 / 39 (35.9)	9.2 [3.5, NE]	14 / 38 (36.8)	6.3 [2.1, NE]	0.7672 [0.3656, 1.6101] 0.4835 0.4842	
No	57 / 207 (27.5)	12.2 [10.4, NE]	61 / 210 (29.0)	6.0 [4.8, NE]	0.6909 [0.4808, 0.9929] 0.0457 0.0443	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.7082
Yes	41 / 147 (27.9)	11.8 [6.2, NE]	44 / 158 (27.8)	6.3 [4.5, NE]	0.7485 [0.4887, 1.1465] 0.1830 0.1803	
No	30 / 99 (30.3)	12.2 [9.0, NE]	31 / 90 (34.4)	6.0 [3.8, NE]	0.6459 [0.3888, 1.0731] 0.0915 0.0896	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.3907
Normal renal function	26 / 117 (22.2)	NE [NE, NE]	38 / 120 (31.7)	6.3 [4.8, NE]	0.5706 [0.3463, 0.9400] 0.0276 0.0254	
Mild impairment	27 / 88 (30.7)	10.4 [5.0, NE]	21 / 88 (23.9)	9.0 [6.0, NE]	0.9555 [0.5368, 1.7007] 0.8769 0.8744	
Moderate impairment	18 / 41 (43.9)	10.6 [3.9, 12.2]	16 / 40 (40.0)	3.7 [2.1, 6.0]	0.4842 [0.2316, 1.0122] 0.0539 0.0490	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Emotional well-being (EWB)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.6989
Normal hepatic function	56 / 186 (30.1)	12.2 [10.4, NE]	62 / 185 (33.5)	6.0 [4.4, NE]	0.7037 [0.4895, 1.0115] 0.0577 0.0559	
Mild, Moderate or Severe dysfunction	15 / 60 (25.0)	NE [6.2, NE]	12 / 62 (19.4)	12.4 [4.5, NE]	0.7980 [0.3726, 1.7088] 0.5613 0.5599	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.4000
IHC 3+	58 / 207 (28.0)	12.0 [7.8, NE]	42 / 208 (20.2)	12.4 [7.5, NE]	1.1108 [0.7453, 1.6554] 0.6058 0.6061	
IHC 2+/ISH+	19 / 39 (48.7)	5.1 [2.2, 11.8]	9 / 40 (22.5)	7.2 [3.5, NE]	1.6307 [0.7362, 3.6123] 0.2282 0.2240	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.4561
Asia [excluding mainland China]	25 / 57 (43.9)	6.7 [3.5, NE]	15 / 60 (25.0)	6.3 [5.0, NE]	1.3616 [0.7154, 2.5916] 0.3472 0.3429	
Western Europe	37 / 140 (26.4)	12.0 [6.4, NE]	21 / 139 (15.1)	12.4 [7.5, NE]	1.3857 [0.8103, 2.3697] 0.2335 0.2316	
Mainland China/Rest of World (ROW)	15 / 49 (30.6)	11.8 [5.7, NE]	15 / 49 (30.6)	NE [3.5, NE]	0.8655 [0.4201, 1.7831] 0.6954 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.4528
<6 Months	21 / 61 (34.4)	6.3 [4.5, NE]	15 / 61 (24.6)	7.5 [3.5, NE]	0.9361 [0.4808, 1.8225] 0.8460 0.8489	
≥ 6 Months	56 / 185 (30.3)	12.0 [7.6, NE]	36 / 187 (19.3)	NE [7.4, NE]	1.2904 [0.8469, 1.9661] 0.2354 0.2337	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.0750
<65	41 / 140 (29.3)	12.0 [7.6, NE]	33 / 130 (25.4)	12.4 [6.3, NE]	0.9168 [0.5784, 1.4534] 0.7119 0.7123	
≥ 65	36 / 106 (34.0)	7.8 [4.5, NE]	18 / 118 (15.3)	NE [6.3, NE]	1.7968 [1.0194, 3.1672] 0.0427 0.0396	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.6277
<75	72 / 222 (32.4)	9.7 [6.4, NE]	43 / 212 (20.3)	12.4 [7.4, NE]	1.2407 [0.8488, 1.8135] 0.2656 0.2653	
≥ 75	5 / 24 (20.8)	NE [2.1, NE]	8 / 36 (22.2)	7.7 [5.0, NE]	0.9207 [0.3000, 2.8258] 0.8852 0.8841	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.6895
Male	59 / 187 (31.6)	11.8 [6.4, NE]	43 / 205 (21.0)	12.4 [7.2, NE]	1.1468 [0.7716, 1.7044] 0.4982 0.4980	
Female	18 / 59 (30.5)	8.4 [3.5, NE]	8 / 43 (18.6)	NE [6.2, NE]	1.3259 [0.5759, 3.0526] 0.5073 0.5006	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.6952
White	30 / 116 (25.9)	9.7 [5.7, NE]	20 / 130 (15.4)	12.4 [7.5, NE]	1.3407 [0.7605, 2.3636] 0.3109 0.3103	
Asian	40 / 101 (39.6)	7.6 [4.9, NE]	26 / 97 (26.8)	NE [5.0, NE]	1.1847 [0.7209, 1.9470] 0.5036 0.4989	
Other	7 / 29 (24.1)	NE [4.2, NE]	5 / 21 (23.8)	5.6 [5.1, NE]	0.6253 [0.1843, 2.1218] 0.4513 0.4476	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.3216
0	31 / 97 (32.0)	9.7 [6.4, NE]	21 / 88 (23.9)	7.5 [5.6, NE]	0.9442 [0.5402, 1.6504] 0.8403 0.8363	
≥ 1	46 / 149 (30.9)	11.8 [4.9, NE]	30 / 159 (18.9)	12.4 [7.4, NE]	1.4003 [0.8828, 2.2211] 0.1526 0.1489	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.7306
Gastric	53 / 153 (34.6)	7.8 [4.9, NE]	35 / 149 (23.5)	7.4 [5.1, NE]	1.1572 [0.7533, 1.7776] 0.5050 0.5044	
GEJ	24 / 93 (25.8)	16.1 [6.4, NE]	16 / 99 (16.2)	12.4 [7.7, NE]	1.2642 [0.6694, 2.3873] 0.4698 0.4684	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.7087
Intestinal	18 / 69 (26.1)	9.7 [5.7, NE]	12 / 66 (18.2)	7.7 [7.4, NE]	0.9217 [0.4390, 1.9352] 0.8294 0.8299	
Diffuse	11 / 25 (44.0)	5.7 [1.4, NE]	5 / 19 (26.3)	6.3 [3.5, NE]	1.6363 [0.5661, 4.7294] 0.3632 0.3559	
Others	48 / 152 (31.6)	11.8 [6.4, NE]	34 / 163 (20.9)	12.4 [6.5, NE]	1.2349 [0.7949, 1.9185] 0.3480 0.3472	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.1491
<2	24 / 73 (32.9)	NE [3.5, NE]	17 / 75 (22.7)	12.4 [7.5, NE]	1.7748 [0.9523, 3.3077] 0.0709 0.0671	
≥ 2	53 / 173 (30.6)	9.7 [6.7, NE]	34 / 173 (19.7)	7.4 [6.3, NE]	0.9689 [0.6274, 1.4963] 0.8867 0.8873	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.9899
Yes	10 / 31 (32.3)	NE [3.5, NE]	5 / 30 (16.7)	NE [3.5, NE]	1.2875 [0.4364, 3.7984] 0.6471 0.6516	
No	67 / 215 (31.2)	9.7 [6.4, NE]	46 / 218 (21.1)	12.4 [7.2, NE]	1.2084 [0.8294, 1.7608] 0.3243 0.3237	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.6912
Yes	7 / 20 (35.0)	NE [3.0, NE]	3 / 17 (17.6)	NE [6.3, NE]	1.5877 [0.4084, 6.1725] 0.5046 0.5008	
No	70 / 226 (31.0)	9.7 [6.4, NE]	48 / 231 (20.8)	12.4 [7.2, NE]	1.1870 [0.8212, 1.7159] 0.3618 0.3618	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.8162
Yes	17 / 39 (43.6)	7.6 [3.0, NE]	10 / 38 (26.3)	NE [3.5, NE]	1.3059 [0.5948, 2.8673] 0.5060 0.4969	
No	60 / 207 (29.0)	12.0 [6.7, NE]	41 / 210 (19.5)	12.4 [7.4, NE]	1.1833 [0.7944, 1.7625] 0.4077 0.4085	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.3690
Yes	40 / 147 (27.2)	11.8 [7.9, NE]	26 / 158 (16.5)	NE [7.5, NE]	1.3688 [0.8351, 2.2437] 0.2131 0.2118	
No	37 / 99 (37.4)	7.6 [5.7, NE]	25 / 90 (27.8)	6.3 [5.0, NE]	1.0056 [0.6019, 1.6800] 0.9831 0.9784	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.1498
Normal renal function	34 / 117 (29.1)	11.8 [7.6, NE]	32 / 120 (26.7)	7.5 [6.3, NE]	0.8442 [0.5191, 1.3729] 0.4949 0.4950	
Mild impairment	23 / 88 (26.1)	NE [5.7, NE]	10 / 88 (11.4)	NE [NE, NE]	1.9852 [0.9446, 4.1721] 0.0703 0.0647	
Moderate impairment	20 / 41 (48.8)	6.3 [2.9, 8.4]	9 / 40 (22.5)	6.3 [4.3, NE]	1.4894 [0.6739, 3.2917] 0.3248 0.3215	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Gastric cancer subscale (GaCS)	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.2514
Normal hepatic function	61 / 186 (32.8)	8.4 [6.3, NE]	38 / 185 (20.5)	NE [7.5, NE]	1.3630 [0.9077, 2.0467] 0.1354 0.1341	
Mild, Moderate or Severe dysfunction	16 / 60 (26.7)	16.1 [4.5, NE]	13 / 62 (21.0)	7.4 [4.3, NE]	0.8267 [0.3969, 1.7218] 0.6111 0.6125	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.5515
IHC 3+	43 / 207 (20.8)	16.1 [13.1, NE]	44 / 208 (21.2)	NE [7.4, NE]	0.7341 [0.4800, 1.1227] 0.1539 0.1539	
IHC 2+/ISH+	13 / 39 (33.3)	11.8 [2.4, NE]	10 / 40 (25.0)	7.2 [3.3, NE]	0.9618 [0.4182, 2.2123] 0.9270 0.9255	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.3678
Asia [excluding mainland China]	14 / 57 (24.6)	14.6 [9.0, NE]	16 / 60 (26.7)	NE [3.5, NE]	0.5949 [0.2840, 1.2463] 0.1687 0.1676	
Western Europe	28 / 140 (20.0)	16.1 [9.7, NE]	20 / 139 (14.4)	NE [7.4, NE]	1.0532 [0.5916, 1.8750] 0.8602 0.8590	
Mainland China/Rest of World (ROW)	14 / 49 (28.6)	NE [4.9, NE]	18 / 49 (36.7)	6.3 [3.5, NE]	0.6860 [0.3390, 1.3882] 0.2946 0.2921	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.5691
<6 Months	12 / 61 (19.7)	NE [9.0, NE]	13 / 61 (21.3)	7.5 [3.7, NE]	0.6567 [0.2977, 1.4489] 0.2976 0.2940	
≥ 6 Months	44 / 185 (23.8)	16.1 [11.8, NE]	41 / 187 (21.9)	NE [7.2, NE]	0.8145 [0.5300, 1.2517] 0.3494 0.3512	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.6225
<65	33 / 140 (23.6)	14.6 [9.7, NE]	34 / 130 (26.2)	7.5 [5.7, NE]	0.7098 [0.4381, 1.1502] 0.1640 0.1630	
≥ 65	23 / 106 (21.7)	NE [9.0, NE]	20 / 118 (16.9)	NE [NE, NE]	0.9170 [0.5017, 1.6761] 0.7783 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.6745
<75	53 / 222 (23.9)	16.1 [11.8, NE]	48 / 212 (22.6)	NE [6.3, NE]	0.7782 [0.5242, 1.1553] 0.2136 0.2135	
≥ 75	3 / 24 (12.5)	NE [5.0, NE]	6 / 36 (16.7)	NE [3.6, NE]	0.5426 [0.1349, 2.1825] 0.3893 0.3843	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.0797
Male	39 / 187 (20.9)	NE [13.1, NE]	46 / 205 (22.4)	NE [6.3, NE]	0.6297 [0.4071, 0.9740] 0.0377 0.0362	
Female	17 / 59 (28.8)	8.4 [3.0, NE]	8 / 43 (18.6)	NE [4.5, NE]	1.3595 [0.5844, 3.1627] 0.4759 0.4768	

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

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.4945
White	21 / 116 (18.1)	NE [9.7, NE]	19 / 130 (14.6)	NE [7.5, NE]	0.9768 [0.5240, 1.8210] 0.9411 0.9421	
Asian	29 / 101 (28.7)	14.6 [9.0, NE]	29 / 97 (29.9)	NE [3.6, NE]	0.6836 [0.4037, 1.1575] 0.1569 0.1576	
Other	6 / 29 (20.7)	NE [4.2, NE]	6 / 21 (28.6)	5.6 [1.8, NE]	0.3705 [0.1074, 1.2785] 0.1161 0.1038	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.0197
0	19 / 97 (19.6)	NE [14.6, NE]	24 / 88 (27.3)	7.2 [4.9, NE]	0.4405 [0.2386, 0.8130] 0.0087 0.0070	
≥ 1	37 / 149 (24.8)	13.1 [7.9, NE]	30 / 159 (18.9)	NE [7.4, NE]	1.1293 [0.6958, 1.8327] 0.6227 0.6193	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.7505
Gastric	39 / 153 (25.5)	14.6 [8.4, NE]	38 / 149 (25.5)	7.2 [4.9, NE]	0.7263 [0.4621, 1.1415] 0.1657 0.1652	
GEJ	17 / 93 (18.3)	NE [13.1, NE]	16 / 99 (16.2)	NE [7.5, NE]	0.8243 [0.4130, 1.6455] 0.5838 0.5840	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.1876
Intestinal	13 / 69 (18.8)	13.1 [9.0, NE]	17 / 66 (25.8)	7.4 [2.1, NE]	0.4182 [0.1987, 0.8801] 0.0216 0.0182	
Diffuse	7 / 25 (28.0)	NE [1.6, NE]	4 / 19 (21.1)	NE [3.5, NE]	1.4120 [0.4126, 4.8322] 0.5826 0.5807	
Others	36 / 152 (23.7)	16.1 [11.8, NE]	33 / 163 (20.2)	NE [7.2, NE]	0.8918 [0.5541, 1.4355] 0.6374 0.6374	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.0671
<2	16 / 73 (21.9)	NE [NE, NE]	14 / 75 (18.7)	NE [7.5, NE]	1.4103 [0.6877, 2.8919] 0.3481 0.3485	
≥ 2	40 / 173 (23.1)	14.6 [9.7, NE]	40 / 173 (23.1)	7.4 [4.9, NE]	0.5722 [0.3663, 0.8939] 0.0142 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.9262
Yes	8 / 31 (25.8)	NE [3.4, NE]	6 / 30 (20.0)	NE [3.9, NE]	0.9857 [0.3410, 2.8497] 0.9788 0.9800	
No	48 / 215 (22.3)	16.1 [11.8, NE]	48 / 218 (22.0)	NE [7.2, NE]	0.7633 [0.5102, 1.1420] 0.1888 0.1894	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.3953
Yes	3 / 20 (15.0)	NE [4.9, NE]	4 / 17 (23.5)	NE [0.8, NE]	0.4657 [0.1035, 2.0954] 0.3193 0.3078	
No	53 / 226 (23.5)	16.1 [11.8, NE]	50 / 231 (21.6)	NE [7.2, NE]	0.8166 [0.5532, 1.2054] 0.3079 0.3082	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.8009
Yes	13 / 39 (33.3)	11.8 [3.5, NE]	11 / 38 (28.9)	6.3 [3.5, NE]	0.8675 [0.3860, 1.9497] 0.7309 0.7312	
No	43 / 207 (20.8)	16.1 [13.1, NE]	43 / 210 (20.5)	NE [7.4, NE]	0.7553 [0.4933, 1.1564] 0.1966 0.1964	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.1147
Yes	31 / 147 (21.1)	NE [9.7, NE]	27 / 158 (17.1)	NE [7.5, NE]	0.9964 [0.5941, 1.6712] 0.9891 0.9885	
No	25 / 99 (25.3)	16.1 [14.6, NE]	27 / 90 (30.0)	5.5 [3.6, NE]	0.5619 [0.3207, 0.9844] 0.0439 0.0416	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.2391
Normal renal function	24 / 117 (20.5)	13.1 [11.8, NE]	31 / 120 (25.8)	7.4 [5.6, NE]	0.6149 [0.3588, 1.0539] 0.0769 0.0745	
Mild impairment	21 / 88 (23.9)	NE [14.6, NE]	13 / 88 (14.8)	NE [NE, NE]	1.2987 [0.6483, 2.6015] 0.4610 0.4607	
Moderate impairment	11 / 41 (26.8)	NE [6.7, NE]	10 / 40 (25.0)	NE [3.3, NE]	0.5332 [0.2186, 1.3004] 0.1668 0.1628	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
Functional Assessment of Cancer Therapy-Gastric	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.5165
Normal hepatic function	43 / 186 (23.1)	NE [11.8, NE]	45 / 185 (24.3)	NE [6.3, NE]	0.7410 [0.4856, 1.1307] 0.1644 0.1643	
Mild, Moderate or Severe dysfunction	13 / 60 (21.7)	16.1 [9.7, NE]	9 / 62 (14.5)	NE [4.5, NE]	0.9894 [0.4221, 2.3189] 0.9804 0.9793	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.7638
IHC 3+	50 / 207 (24.2)	13.1 [10.4, NE]	54 / 208 (26.0)	13.2 [4.9, NE]	0.6955 [0.4724, 1.0239] 0.0657 0.0646	
IHC 2+/ISH+	13 / 39 (33.3)	11.8 [2.4, NE]	14 / 40 (35.0)	5.4 [2.1, 7.2]	0.6017 [0.2761, 1.3116] 0.2014 0.1929	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.8302
Asia [excluding mainland China]	18 / 57 (31.6)	10.9 [6.2, NE]	20 / 60 (33.3)	4.9 [3.5, NE]	0.6231 [0.3243, 1.1973] 0.1557 0.1535	
Western Europe	28 / 140 (20.0)	16.1 [11.7, NE]	26 / 139 (18.7)	13.2 [5.4, NE]	0.7750 [0.4532, 1.3253] 0.3518 0.3505	
Mainland China/Rest of World (ROW)	17 / 49 (34.7)	11.8 [3.6, NE]	22 / 49 (44.9)	3.4 [2.1, NE]	0.6332 [0.3357, 1.1942] 0.1580 0.1545	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.9596
<6 Months	14 / 61 (23.0)	20.1 [20.1, NE]	14 / 61 (23.0)	6.3 [3.3, NE]	0.7778 [0.3696, 1.6369] 0.5080 0.5089	
≥ 6 Months	49 / 185 (26.5)	11.8 [10.4, NE]	54 / 187 (28.9)	5.7 [4.9, NE]	0.6769 [0.4590, 0.9981] 0.0489 0.0476	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.9771
<65	37 / 140 (26.4)	13.1 [8.4, NE]	40 / 130 (30.8)	6.3 [4.9, NE]	0.6737 [0.4301, 1.0553] 0.0845 0.0833	
≥ 65	26 / 106 (24.5)	20.1 [10.4, NE]	28 / 118 (23.7)	NE [3.7, NE]	0.7332 [0.4284, 1.2551] 0.2579 0.2539	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.9888
<75	60 / 222 (27.0)	13.1 [10.4, NE]	62 / 212 (29.2)	5.6 [4.9, NE]	0.6561 [0.4581, 0.9397] 0.0215 0.0206	
≥ 75	3 / 24 (12.5)	NE [NE, NE]	6 / 36 (16.7)	NE [3.6, NE]	0.5938 [0.1482, 2.3784] 0.4616 0.4595	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.5282
Male	49 / 187 (26.2)	13.1 [10.9, NE]	56 / 205 (27.3)	5.6 [4.9, NE]	0.6391 [0.4327, 0.9441] 0.0245 0.0234	
Female	14 / 59 (23.7)	8.4 [3.6, NE]	12 / 43 (27.9)	13.2 [2.4, NE]	0.8388 [0.3790, 1.8565] 0.6645 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.6129
White	21 / 116 (18.1)	16.1 [10.4, NE]	26 / 130 (20.0)	13.2 [4.9, NE]	0.6690 [0.3758, 1.1910] 0.1719 0.1694	
Asian	37 / 101 (36.6)	10.9 [5.4, NE]	36 / 97 (37.1)	4.9 [3.5, NE]	0.7233 [0.4548, 1.1503] 0.1712 0.1721	
Other	5 / 29 (17.2)	NE [4.2, NE]	6 / 21 (28.6)	5.6 [1.8, NE]	0.3705 [0.1074, 1.2785] 0.1161 0.1038	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.0371
0	23 / 97 (23.7)	16.1 [10.9, NE]	29 / 88 (33.0)	5.1 [4.5, 13.2]	0.4176 [0.2391, 0.7292] 0.0021 0.0016	
≥ 1	40 / 149 (26.8)	13.1 [5.4, NE]	39 / 159 (24.5)	NE [4.9, NE]	0.9393 [0.6038, 1.4612] 0.7811 0.7808	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.4190
Gastric	43 / 153 (28.1)	11.8 [6.7, NE]	49 / 149 (32.9)	4.9 [3.5, 7.2]	0.6105 [0.4041, 0.9223] 0.0191 0.0178	
GEJ	20 / 93 (21.5)	16.1 [11.7, NE]	19 / 99 (19.2)	NE [5.5, NE]	0.8343 [0.4435, 1.5698] 0.5744 0.5737	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.3574
Intestinal	14 / 69 (20.3)	20.1 [13.1, NE]	18 / 66 (27.3)	4.9 [3.3, NE]	0.4425 [0.2155, 0.9086] 0.0264 0.0227	
Diffuse	6 / 25 (24.0)	NE [2.1, NE]	4 / 19 (21.1)	NE [2.1, NE]	1.1568 [0.3256, 4.1104] 0.8219 0.8217	
Others	43 / 152 (28.3)	11.7 [8.4, NE]	46 / 163 (28.2)	5.7 [4.9, NE]	0.7498 [0.4937, 1.1387] 0.1768 0.1739	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.2755
<2	17 / 73 (23.3)	NE [10.4, NE]	21 / 75 (28.0)	13.2 [4.9, NE]	0.8953 [0.4718, 1.6991] 0.7351 0.7321	
≥ 2	46 / 173 (26.6)	13.1 [8.4, NE]	47 / 173 (27.2)	5.1 [4.5, NE]	0.5747 [0.3804, 0.8682] 0.0085 0.0078	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.4622
Yes	10 / 31 (32.3)	NE [3.0, NE]	7 / 30 (23.3)	NE [3.3, NE]	1.0633 [0.4026, 2.8084] 0.9014 0.8998	
No	53 / 215 (24.7)	13.1 [10.9, NE]	61 / 218 (28.0)	5.7 [4.9, NE]	0.6488 [0.4484, 0.9388] 0.0217 0.0209	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.7297
Yes	4 / 20 (20.0)	NE [4.9, NE]	4 / 17 (23.5)	NE [0.8, NE]	0.5495 [0.1357, 2.2249] 0.4014 0.3947	
No	59 / 226 (26.1)	13.1 [10.9, NE]	64 / 231 (27.7)	5.6 [4.9, NE]	0.7036 [0.4930, 1.0042] 0.0527 0.0515	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.4179
Yes	15 / 39 (38.5)	11.8 [3.6, NE]	12 / 38 (31.6)	6.3 [3.4, NE]	0.9016 [0.4210, 1.9307] 0.7897 0.7964	
No	48 / 207 (23.2)	16.1 [10.9, NE]	56 / 210 (26.7)	5.7 [4.9, NE]	0.6381 [0.4330, 0.9404] 0.0232 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTEQSA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.0795
Yes	37 / 147 (25.2)	13.1 [10.4, NE]	35 / 158 (22.2)	13.2 [5.6, NE]	0.8981 [0.5654, 1.4265] 0.6489 0.6493	
No	26 / 99 (26.3)	16.1 [10.9, NE]	33 / 90 (36.7)	4.9 [3.5, 7.2]	0.4794 [0.2838, 0.8099] 0.0060 0.0050	

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

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Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.1603
Normal renal function	24 / 117 (20.5)	16.1 [11.8, NE]	34 / 120 (28.3)	5.7 [4.9, NE]	0.5768 [0.3412, 0.9752] 0.0400 0.0381	
Mild impairment	25 / 88 (28.4)	11.7 [4.9, NE]	19 / 88 (21.6)	13.2 [4.9, NE]	1.0309 [0.5671, 1.8741] 0.9204 0.9240	
Moderate impairment	14 / 41 (34.1)	10.4 [6.2, NE]	15 / 40 (37.5)	3.5 [1.5, NE]	0.3878 [0.1773, 0.8484] 0.0177 0.0144	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Table 9.9.2 FACT-Ga - Time to first deterioration - Subgroup Analysis - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246		Ram + PTX N = 248		T-DXd vs. Ram + PTX	Interaction
The Functional Assessment of Cancer Therapy-General	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.2928
Normal hepatic function	50 / 186 (26.9)	11.8 [10.4, NE]	59 / 185 (31.9)	5.5 [4.9, NE]	0.6294 [0.4303, 0.9206] 0.0170 0.0162	
Mild, Moderate or Severe dysfunction	13 / 60 (21.7)	16.1 [16.1, NE]	9 / 62 (14.5)	NE [4.5, NE]	1.0104 [0.4310, 2.3687] 0.9810 0.9842	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.9.2_FACT-Ga_TTFDet_FAS_SUB.rtf

Anhang 4-G 3.4.3 FACT-Ga – Grafische Darstellung der mittleren Veränderung im zeitlichen Verlauf (MMRM) – FAS

Daiichi Sankyo Europe GmbH
DS8201-A-U306 (DESTINY-GASTRIC04) - DCO 24-OCT-2024

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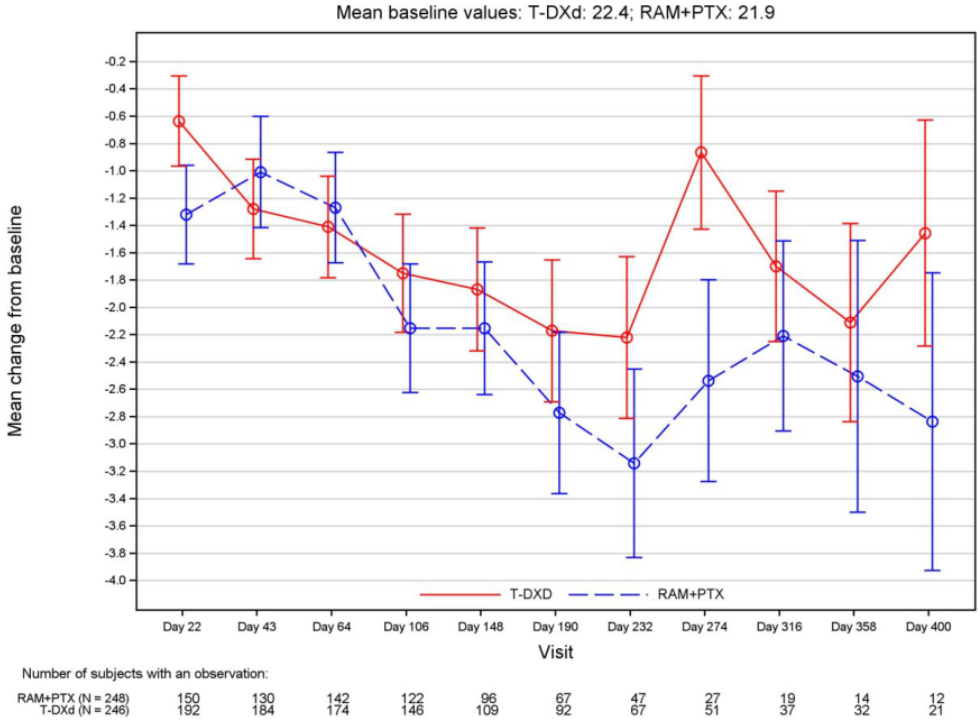
Final
Statistical analyses for AMNOG (HTA Germany)

Figure 9.9.3 FACT-Ga - Mean change from baseline plot - Full Analysis Set

Physical well-being (PWB)



Mean changes from baseline are estimated LS means (error bars: Standard Error) from MMRM model.
LS: least square; MMRM: mixed model for repeated measurements

Data source:
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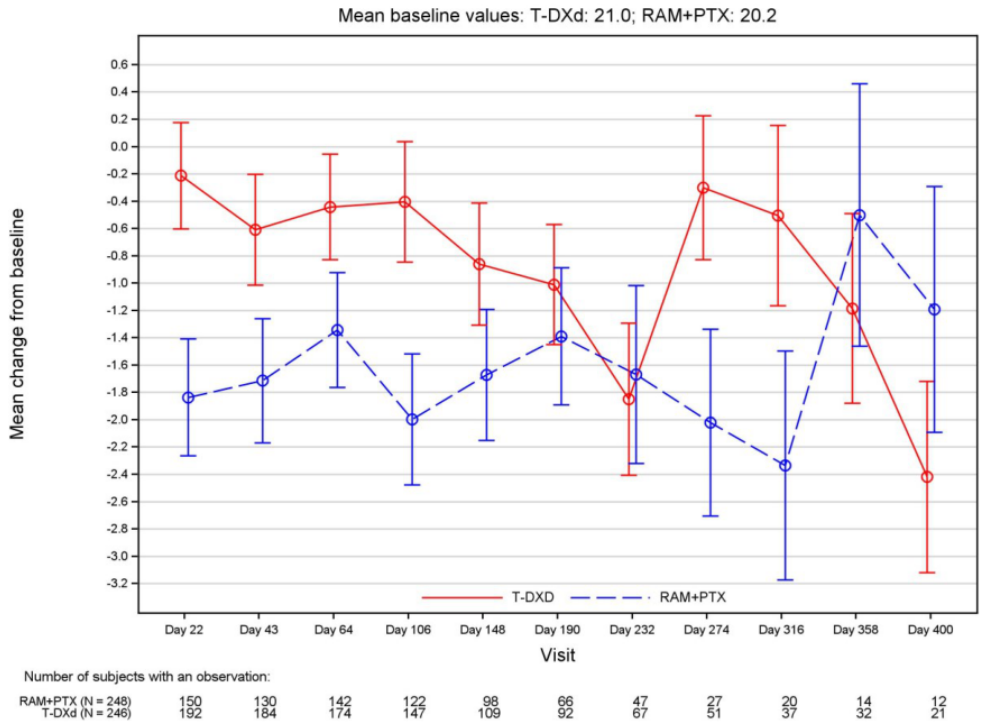
Figure 9.9.3 FACT-Ga - Mean change from baseline plot - Full Analysis Set

Social/family well-being (SWB)



Mean changes from baseline are estimated LS means (error bars: Standard Error) from MMRM model.
LS: least square; MMRM: mixed model for repeated measurements

Data source:
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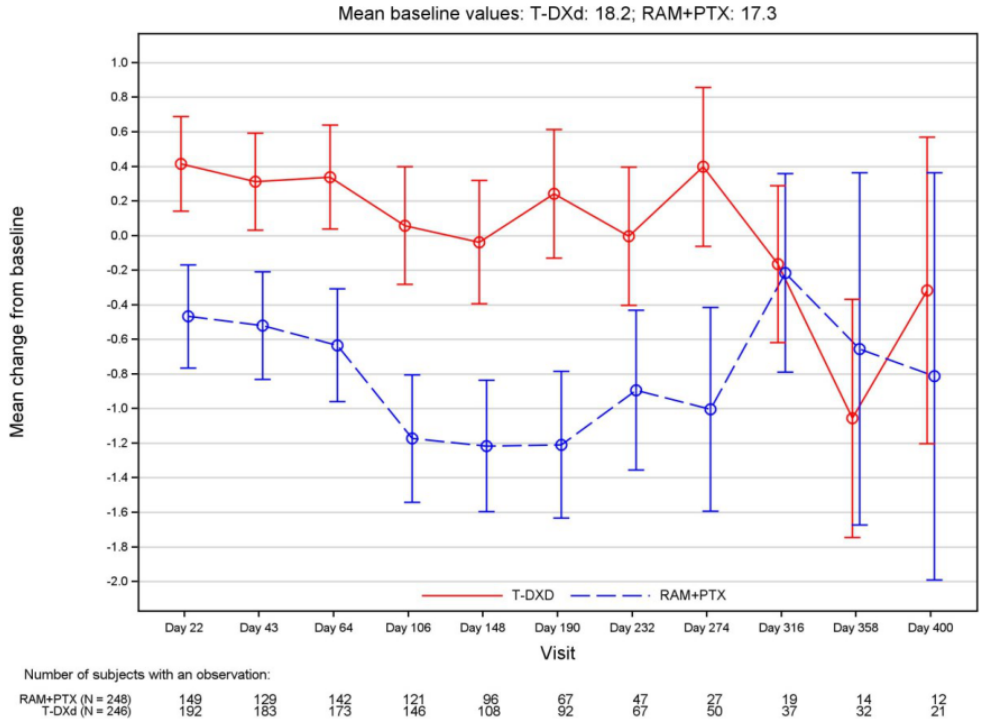
Figure 9.9.3 FACT-Ga - Mean change from baseline plot - Full Analysis Set

Emotional well-being (EWB)



Mean changes from baseline are estimated LS means (error bars: Standard Error) from MMRM model.
LS: least square; MMRM: mixed model for repeated measurements

Data source:
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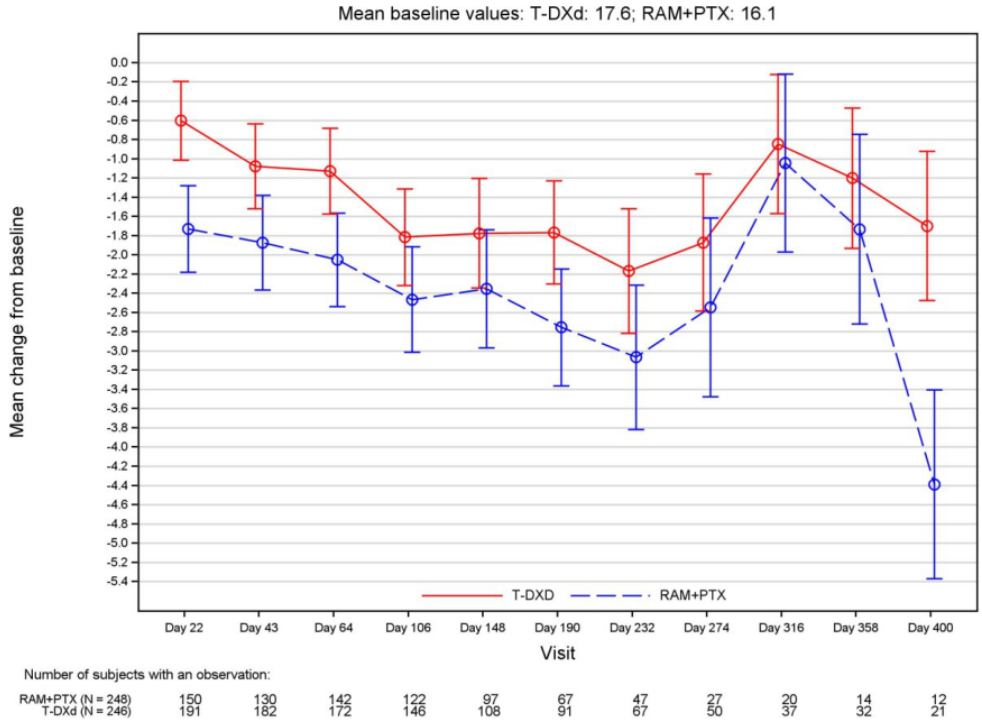
Figure 9.9.3 FACT-Ga - Mean change from baseline plot - Full Analysis Set

Functional well-being (FWB)



Mean changes from baseline are estimated LS means (error bars: Standard Error) from MMRM model.
LS: least square; MMRM: mixed model for repeated measurements

Data source:
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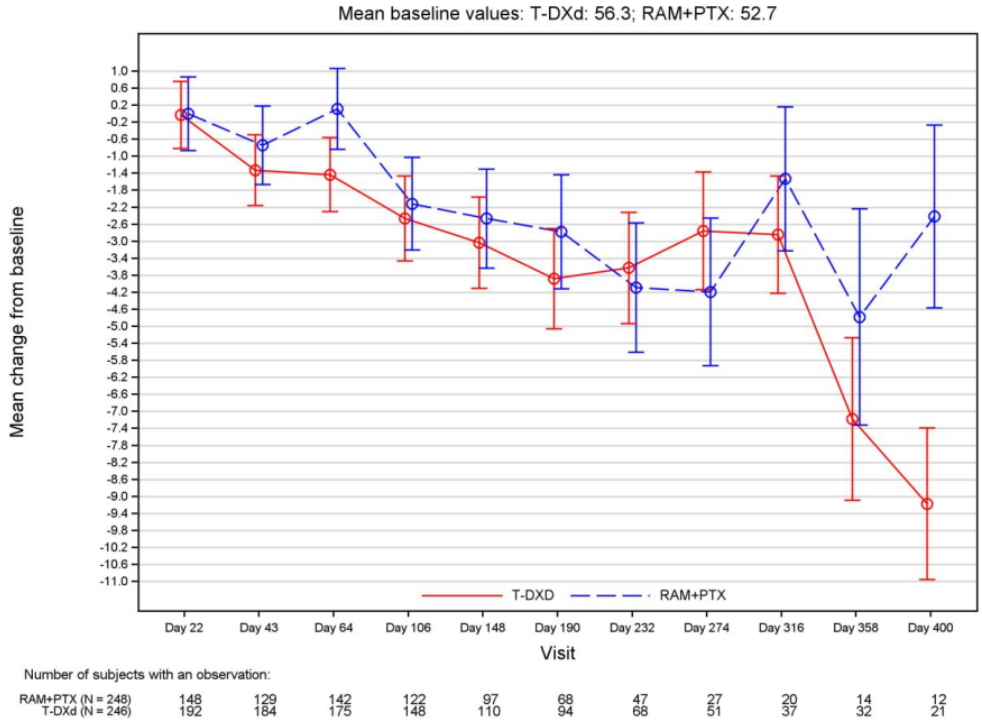
Figure 9.9.3 FACT-Ga - Mean change from baseline plot - Full Analysis Set

Gastric cancer subscale (GaCS)



Mean changes from baseline are estimated LS means (error bars: Standard Error) from MMRM model.
LS: least square; MMRM: mixed model for repeated measurements

Data source:
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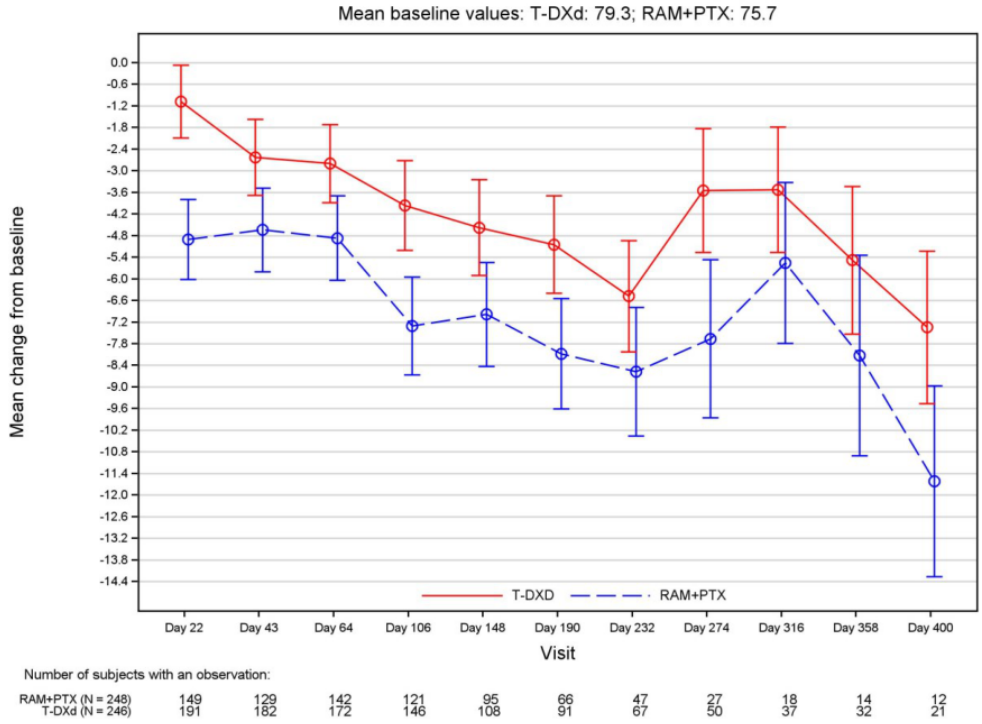
Figure 9.9.3 FACT-Ga - Mean change from baseline plot - Full Analysis Set

The Functional Assessment of Cancer Therapy-General



Mean changes from baseline are estimated LS means (error bars: Standard Error) from MMRM model.
LS: least square; MMRM: mixed model for repeated measurements

Data source:
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Program Location:
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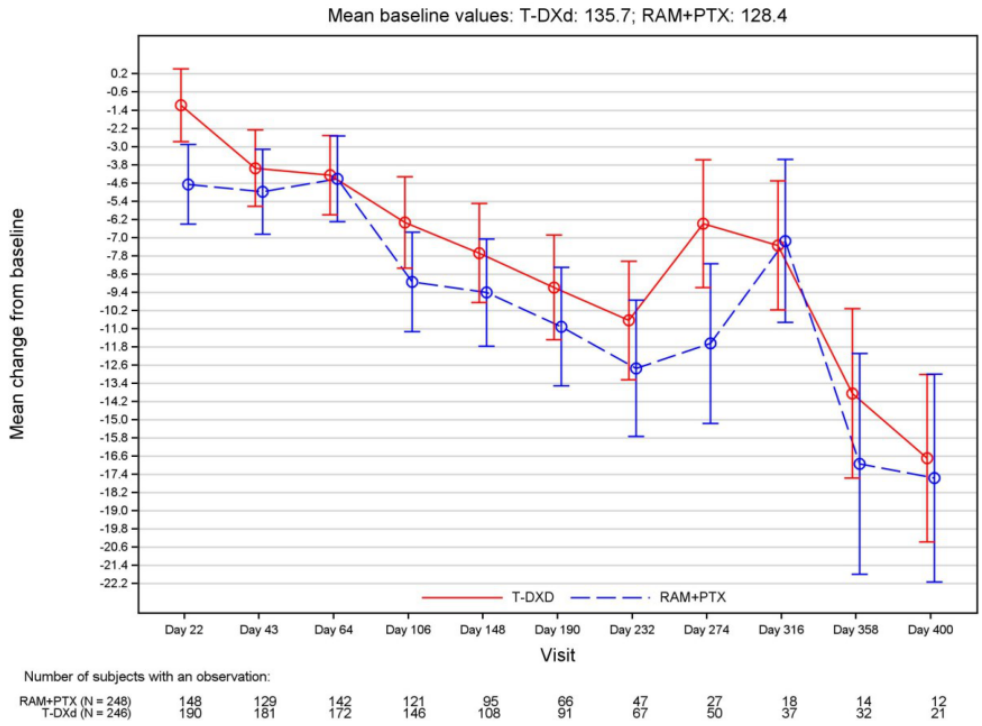
Run date: 23JUN2025 11:05 (CET); Program name: f_mmrm_chg.sas; Output name: F.9.9.3_FACT-Ga_CHG_FAS.rtf

Figure 9.9.3 FACT-Ga - Mean change from baseline plot - Full Analysis Set

Functional Assessment of Cancer Therapy-Gastric



Mean changes from baseline are estimated LS means (error bars: Standard Error) from MMRM model.
LS: least square; MMRM: mixed model for repeated measurements

Data source:
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Anhang 4-G 3.4.4 FACT-Ga – Tabellarische Darstellung der mittleren Veränderung über alle Zeitpunkte hinweg (MMRM) – FAS

Table 9.9.5 FACT-Ga - Mixed Model for Repeated Measurement Overall - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Overall			
n	207	174	
LS Means [95 % CI]	-1.5868 [-2.3435; -0.8301]	-2.1722 [-3.0509; -1.2935]	
Standard error	0.3841	0.4462	
Difference of LS Means [95% CI]			0.5854 [-0.4359; 1.6066]
Standard error for difference			0.5173
p-value			0.2594
Hedges' g [95% CI]			0.1026 [-0.0991; 0.3043]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_programs/tlf
Run date: 16JUL2025 15:20 (CET); Program name: t_mmrm.sas; Output name: T.9.9.5_FACT-Ga_MMRM_FAS.rtf

Table 9.9.5 FACT-Ga - Mixed Model for Repeated Measurement Overall - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Overall			
n	207	174	
LS Means [95 % CI]	-0.8906 [-1.5882; -0.1931]	-1.6060 [-2.3992; -0.8129]	
Standard error	0.3547	0.4034	
Difference of LS Means [95% CI]			0.7154 [-0.1717; 1.6025]
Standard error for difference			0.4505
p-value			0.1135
Hedges' g [95% CI]			0.1372 [-0.0646; 0.3390]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_programs/tlf
Run date: 16JUL2025 15:20 (CET); Program name: t_mmrm.sas; Output name: T.9.9.5_FACT-Ga_MMRM_FAS.rtf

Table 9.9.5 FACT-Ga - Mixed Model for Repeated Measurement Overall - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Overall			
n	206	173	
LS Means [95 % CI]	0.0170 [-0.5584; 0.5924]	-0.7995 [-1.4784; -0.1207]	
Standard error	0.2921	0.3446	
Difference of LS Means [95% CI]			0.8165 [0.0396; 1.5935]
Standard error for difference			0.3936
p-value			0.0395
Hedges' g [95% CI]			0.1873 [-0.0153; 0.3898]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_programs/tlf
Run date: 16JUL2025 15:20 (CET); Program name: t_mmrm.sas; Output name: T.9.9.5_FACT-Ga_MMRM_FAS.rtf

Table 9.9.5 FACT-Ga - Mixed Model for Repeated Measurement Overall - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Overall			
n	205	174	
LS Means [95 % CI]	-1.4500 [-2.3153; -0.5847]	-2.3641 [-3.3548; -1.3733]	
Standard error	0.4400	0.5039	
Difference of LS Means [95% CI]			0.9141 [-0.2144; 2.0426]
Standard error for difference			0.5731
p-value			0.1119
Hedges' g [95% CI]			0.1412 [-0.0611; 0.3435]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_programs/tlf
Run date: 16JUL2025 15:20 (CET); Program name: t_mmrm.sas; Output name: T.9.9.5_FACT-Ga_MMRM_FAS.rtf

Table 9.9.5 FACT-Ga - Mixed Model for Repeated Measurement Overall - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Overall			
n	208	173	
LS Means [95 % CI]	-3.4295 [-5.2908; -1.5681]	-2.2707 [-4.3867; -0.1547]	
Standard error	0.9460	1.0757	
Difference of LS Means [95% CI]			-1.1588 [-3.6685; 1.3509]
Standard error for difference			1.2740
p-value			0.3640
Hedges' g [95% CI]			-0.0833 [-0.2851; 0.1184]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_programs/tlf
Run date: 16JUL2025 15:20 (CET); Program name: t_mmrm.sas; Output name: T.9.9.5_FACT-Ga_MMRM_FAS.rtf

Table 9.9.5 FACT-Ga - Mixed Model for Repeated Measurement Overall - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Overall			
n	205	173	
LS Means [95 % CI]	-4.2241 [-6.3979; -2.0502]	-7.1188 [-9.5973; -4.6403]	
Standard error	1.1050	1.2603	
Difference of LS Means [95% CI]			2.8948 [0.0409; 5.7487]
Standard error for difference			1.4489
p-value			0.0468
Hedges' g [95% CI]			0.1786 [-0.0241; 0.3814]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_adam/ADQS
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Run date: 16JUL2025 15:20 (CET); Program name: t_mmrm.sas; Output name: T.9.9.5_FACT-Ga_MMRM_FAS.rtf

Table 9.9.5 FACT-Ga - Mixed Model for Repeated Measurement Overall - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Overall			
n	205	173	
LS Means [95 % CI]	-7.9500 [-11.7050; -4.1951]	-9.9386 [-14.2044; -5.6728]	
Standard error	1.9083	2.1684	
Difference of LS Means [95% CI]			1.9886 [-3.0436; 7.0207]
Standard error for difference			2.5539
p-value			0.4370
Hedges' g [95% CI]			0.0712 [-0.1312; 0.2736]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250708_AMNOG_Addendum_1_ID012/rstrct_adam/ADQS
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Anhang 4-G 3.4.5 FACT-Ga – Tabellarische Darstellung der mittleren Veränderung im zeitlichen Verlauf (MMRM) – FAS

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Day 22			
Change from baseline			
n	192	150	
LS Means [95 % CI]	-0.6351 [-1.2846; 0.0143]	-1.3193 [-2.0274; -0.6111]	
Standard error	0.3303	0.3602	
Difference of LS Means [95% CI]			0.6841 [-0.1189; 1.4872]
Standard error for difference			0.4083
p-value			0.0947
Hedges' g [95% CI]			0.1515 [-0.0624; 0.3654]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Day 43			
Change from baseline			
n	184	130	
LS Means [95 % CI]	-1.2780 [-1.9954; -0.5607]	-1.0073 [-1.8075; -0.2071]	
Standard error	0.3649	0.4071	
Difference of LS Means [95% CI]			-0.2707 [-1.2068; 0.6654]
Standard error for difference			0.4759
p-value			0.5698
Hedges' g [95% CI]			-0.0560 [-0.2806; 0.1686]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Day 64			
Change from baseline			
n	174	142	
LS Means [95 % CI]	-1.4088 [-2.1389; -0.6787]	-1.2680 [-2.0624; -0.4735]	
Standard error	0.3714	0.4042	
Difference of LS Means [95% CI]			-0.1409 [-1.0721; 0.7904]
Standard error for difference			0.4734
p-value			0.7662
Hedges' g [95% CI]			-0.0289 [-0.2506; 0.1928]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Day 106			
Change from baseline			
n	146	122	
LS Means [95 % CI]	-1.7498 [-2.5993; -0.9003]	-2.1527 [-3.0776; -1.2278]	
Standard error	0.4321	0.4704	
Difference of LS Means [95% CI]			0.4029 [-0.7272; 1.5330]
Standard error for difference			0.5742
p-value			0.4835
Hedges' g [95% CI]			0.0771 [-0.1634; 0.3176]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Day 148			
Change from baseline			
n	109	96	
LS Means [95 % CI]	-1.8665 [-2.7532; -0.9799]	-2.1518 [-3.1086; -1.1949]	
Standard error	0.4506	0.4862	
Difference of LS Means [95% CI]			0.2852 [-0.8989; 1.4694]
Standard error for difference			0.6010
p-value			0.6355
Hedges' g [95% CI]			0.0600 [-0.2143; 0.3344]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Day 190			
Change from baseline			
n	92	67	
LS Means [95 % CI]	-2.1708 [-3.1949; -1.1466]	-2.7711 [-3.9351; -1.6071]	
Standard error	0.5199	0.5910	
Difference of LS Means [95% CI]			0.6004 [-0.8499; 2.0506]
Standard error for difference			0.7352
p-value			0.4152
Hedges' g [95% CI]			0.1213 [-0.1937; 0.4364]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Day 232			
Change from baseline			
n	67	47	
LS Means [95 % CI]	-2.2201 [-3.3905; -1.0497]	-3.1407 [-4.5023; -1.7792]	
Standard error	0.5930	0.6900	
Difference of LS Means [95% CI]			0.9206 [-0.7888; 2.6300]
Standard error for difference			0.8650
p-value			0.2889
Hedges' g [95% CI]			0.1904 [-0.1834; 0.5641]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Day 274			
Change from baseline			
n	51	27	
LS Means [95 % CI]	-0.8637 [-1.9747; 0.2474]	-2.5356 [-3.9964; -1.0748]	
Standard error	0.5613	0.7380	
Difference of LS Means [95% CI]			1.6720 [-0.0752; 3.4191]
Standard error for difference			0.8808
p-value			0.0605
Hedges' g [95% CI]			0.4191 [-0.0520; 0.8902]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Day 316			
Change from baseline			
n	37	19	
LS Means [95 % CI]	-1.6983 [-2.7862; -0.6104]	-2.2066 [-3.5844; -0.8288]	
Standard error	0.5497	0.6960	
Difference of LS Means [95% CI]			0.5083 [-1.1585; 2.1751]
Standard error for difference			0.8402
p-value			0.5466
Hedges' g [95% CI]			0.1545 [-0.3994; 0.7084]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Day 358			
Change from baseline			
n	32	14	
LS Means [95 % CI]	-2.1094 [-3.5570; -0.6618]	-2.5052 [-4.4896; -0.5207]	
Standard error	0.7259	0.9948	
Difference of LS Means [95% CI]			0.3958 [-1.9979; 2.7895]
Standard error for difference			1.1978
p-value			0.7422
Hedges' g [95% CI]			0.0973 [-0.5310; 0.7257]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Physical well-being (PWB)			
Day 400			
Change from baseline			
n	21	12	
LS Means [95 % CI]	-1.4546 [-3.1122; 0.2031]	-2.8359 [-5.0188; -0.6530]	
Standard error	0.8289	1.0902	
Difference of LS Means [95% CI]			1.3814 [-1.3021; 4.0648]
Standard error for difference			1.3378
p-value			0.3065
Hedges' g [95% CI]			0.3555 [-0.3589; 1.0699]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Day 22			
Change from baseline			
n	192	150	
LS Means [95 % CI]	-0.2122 [-0.9765; 0.5521]	-1.8362 [-2.6793; -0.9931]	
Standard error	0.3888	0.4289	
Difference of LS Means [95% CI]			1.6240 [0.6243; 2.6238]
Standard error for difference			0.5083
p-value			0.0015
Hedges' g [95% CI]			0.3041 [0.0893; 0.5189]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Day 43			
Change from baseline			
n	184	130	
LS Means [95 % CI]	-0.6092 [-1.4061; 0.1876]	-1.7141 [-2.6082; -0.8201]	
Standard error	0.4054	0.4549	
Difference of LS Means [95% CI]			1.1049 [0.0398; 2.1700]
Standard error for difference			0.5416
p-value			0.0421
Hedges' g [95% CI]			0.2052 [-0.0200; 0.4303]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Day 64			
Change from baseline			
n	174	142	
LS Means [95 % CI]	-0.4415 [-1.2020; 0.3189]	-1.3430 [-2.1698; -0.5162]	
Standard error	0.3869	0.4206	
Difference of LS Means [95% CI]			0.9015 [-0.0727; 1.8757]
Standard error for difference			0.4952
p-value			0.0696
Hedges' g [95% CI]			0.1776 [-0.0444; 0.3997]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Day 106			
Change from baseline			
n	147	122	
LS Means [95 % CI]	-0.4042 [-1.2711; 0.4627]	-1.9973 [-2.9425; -1.0521]	
Standard error	0.4410	0.4808	
Difference of LS Means [95% CI]			1.5931 [0.4512; 2.7350]
Standard error for difference			0.5802
p-value			0.0064
Hedges' g [95% CI]			0.2980 [0.0567; 0.5394]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Day 148			
Change from baseline			
n	109	98	
LS Means [95 % CI]	-0.8603 [-1.7393; 0.0187]	-1.6716 [-2.6152; -0.7281]	
Standard error	0.4469	0.4796	
Difference of LS Means [95% CI]			0.8113 [-0.3379; 1.9606]
Standard error for difference			0.5835
p-value			0.1656
Hedges' g [95% CI]			0.1718 [-0.1015; 0.4452]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Day 190			
Change from baseline			
n	92	66	
LS Means [95 % CI]	-1.0098 [-1.8758; -0.1439]	-1.3889 [-2.3789; -0.3988]	
Standard error	0.4401	0.5031	
Difference of LS Means [95% CI]			0.3790 [-0.8016; 1.5597]
Standard error for difference			0.5990
p-value			0.5275
Hedges' g [95% CI]			0.0906 [-0.2258; 0.4069]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Day 232			
Change from baseline			
n	67	47	
LS Means [95 % CI]	-1.8495 [-2.9495; -0.7495]	-1.6672 [-2.9527; -0.3817]	
Standard error	0.5577	0.6516	
Difference of LS Means [95% CI]			-0.1823 [-1.7726; 1.4080]
Standard error for difference			0.8048
p-value			0.8211
Hedges' g [95% CI]			-0.0400 [-0.4130; 0.3329]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Day 274			
Change from baseline			
n	51	27	
LS Means [95 % CI]	-0.3000 [-1.3432; 0.7433]	-2.0208 [-3.3747; -0.6669]	
Standard error	0.5281	0.6849	
Difference of LS Means [95% CI]			1.7208 [0.1118; 3.3299]
Standard error for difference			0.8124
p-value			0.0363
Hedges' g [95% CI]			0.4605 [-0.0116; 0.9325]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Day 316			
Change from baseline			
n	37	20	
LS Means [95 % CI]	-0.5056 [-1.8127; 0.8014]	-2.3345 [-3.9965; -0.6726]	
Standard error	0.6600	0.8379	
Difference of LS Means [95% CI]			1.8289 [-0.2095; 3.8674]
Standard error for difference			1.0264
p-value			0.0781
Hedges' g [95% CI]			0.4597 [-0.0908; 1.0101]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Day 358			
Change from baseline			
n	32	14	
LS Means [95 % CI]	-1.1853 [-2.5635; 0.1929]	-0.5003 [-2.4092; 1.4086]	
Standard error	0.6945	0.9605	
Difference of LS Means [95% CI]			-0.6850 [-2.9675; 1.5975]
Standard error for difference			1.1469
p-value			0.5520
Hedges' g [95% CI]			-0.1756 [-0.8047; 0.4534]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Social/family well-being (SWB)			
Day 400			
Change from baseline			
n	21	12	
LS Means [95 % CI]	-2.4192 [-3.8149; -1.0236]	-1.1923 [-2.9865; 0.6020]	
Standard error	0.7015	0.9006	
Difference of LS Means [95% CI]			-1.2270 [-3.4262; 0.9723]
Standard error for difference			1.1014
p-value			0.2693
Hedges' g [95% CI]			-0.3763 [-1.0913; 0.3388]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Day 22			
Change from baseline			
n	192	149	
LS Means [95 % CI]	0.4152 [-0.1215; 0.9520]	-0.4670 [-1.0521; 0.1180]	
Standard error	0.2730	0.2976	
Difference of LS Means [95% CI]			0.8823 [0.2084; 1.5562]
Standard error for difference			0.3427
p-value			0.0104
Hedges' g [95% CI]			0.2368 [0.0220; 0.4515]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Day 43			
Change from baseline			
n	183	129	
LS Means [95 % CI]	0.3130 [-0.2399; 0.8659]	-0.5191 [-1.1298; 0.0916]	
Standard error	0.2813	0.3106	
Difference of LS Means [95% CI]			0.8321 [0.1246; 1.5396]
Standard error for difference			0.3597
p-value			0.0213
Hedges' g [95% CI]			0.2248 [-0.0012; 0.4508]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Day 64			
Change from baseline			
n	173	142	
LS Means [95 % CI]	0.3388 [-0.2526; 0.9302]	-0.6333 [-1.2732; 0.0065]	
Standard error	0.3009	0.3255	
Difference of LS Means [95% CI]			0.9721 [0.2150; 1.7293]
Standard error for difference			0.3849
p-value			0.0120
Hedges' g [95% CI]			0.2473 [0.0245; 0.4700]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Day 106			
Change from baseline			
n	146	121	
LS Means [95 % CI]	0.0579 [-0.6111; 0.7268]	-1.1728 [-1.8980; -0.4476]	
Standard error	0.3403	0.3689	
Difference of LS Means [95% CI]			1.2306 [0.3448; 2.1165]
Standard error for difference			0.4502
p-value			0.0066
Hedges' g [95% CI]			0.3002 [0.0579; 0.5425]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Day 148			
Change from baseline			
n	108	96	
LS Means [95 % CI]	-0.0372 [-0.7383; 0.6638]	-1.2154 [-1.9634; -0.4675]	
Standard error	0.3563	0.3801	
Difference of LS Means [95% CI]			1.1782 [0.2520; 2.1044]
Standard error for difference			0.4701
p-value			0.0129
Hedges' g [95% CI]			0.3161 [0.0395; 0.5928]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Day 190			
Change from baseline			
n	92	67	
LS Means [95 % CI]	0.2425 [-0.4884; 0.9733]	-1.2085 [-2.0438; -0.3732]	
Standard error	0.3711	0.4242	
Difference of LS Means [95% CI]			1.4510 [0.4323; 2.4697]
Standard error for difference			0.5164
p-value			0.0055
Hedges' g [95% CI]			0.4099 [0.0919; 0.7279]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Day 232			
Change from baseline			
n	67	47	
LS Means [95 % CI]	-0.0034 [-0.7923; 0.7856]	-0.8932 [-1.8043; 0.0179]	
Standard error	0.4002	0.4622	
Difference of LS Means [95% CI]			0.8898 [-0.2337; 2.0133]
Standard error for difference			0.5690
p-value			0.1198
Hedges' g [95% CI]			0.2734 [-0.1012; 0.6480]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Day 274			
Change from baseline			
n	50	27	
LS Means [95 % CI]	0.3984 [-0.5089; 1.3057]	-1.0028 [-2.1688; 0.1631]	
Standard error	0.4591	0.5894	
Difference of LS Means [95% CI]			1.4012 [-0.0112; 2.8137]
Standard error for difference			0.7130
p-value			0.0518
Hedges' g [95% CI]			0.4357 [-0.0374; 0.9088]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Day 316			
Change from baseline			
n	37	19	
LS Means [95 % CI]	-0.1645 [-1.0624; 0.7333]	-0.2149 [-1.3537; 0.9239]	
Standard error	0.4534	0.5747	
Difference of LS Means [95% CI]			0.0504 [-1.3326; 1.4333]
Standard error for difference			0.6965
p-value			0.9425
Hedges' g [95% CI]			0.0186 [-0.5346; 0.5717]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Day 358			
Change from baseline			
n	32	14	
LS Means [95 % CI]	-1.0561 [-2.4314; 0.3191]	-0.6544 [-2.6890; 1.3802]	
Standard error	0.6890	1.0184	
Difference of LS Means [95% CI]			-0.4017 [-2.8209; 2.0174]
Standard error for difference			1.2094
p-value			0.7409
Hedges' g [95% CI]			-0.1020 [-0.7304; 0.5264]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Emotional well-being (EWB)			
Day 400			
Change from baseline			
n	21	12	
LS Means [95 % CI]	-0.3171 [-2.1035; 1.4694]	-0.8131 [-3.1903; 1.5642]	
Standard error	0.8863	1.1775	
Difference of LS Means [95% CI]			0.4960 [-2.4501; 3.4422]
Standard error for difference			1.4570
p-value			0.7353
Hedges' g [95% CI]			0.1190 [-0.5909; 0.8288]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Day 22			
Change from baseline			
n	191	150	
LS Means [95 % CI]	-0.6027 [-1.4100; 0.2047]	-1.7284 [-2.6136; -0.8431]	
Standard error	0.4107	0.4503	
Difference of LS Means [95% CI]			1.1257 [0.1186; 2.1328]
Standard error for difference			0.5121
p-value			0.0286
Hedges' g [95% CI]			0.2004 [-0.0140; 0.4147]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Day 43			
Change from baseline			
n	182	130	
LS Means [95 % CI]	-1.0770 [-1.9464; -0.2076]	-1.8741 [-2.8433; -0.9049]	
Standard error	0.4423	0.4930	
Difference of LS Means [95% CI]			0.7971 [-0.3306; 1.9248]
Standard error for difference			0.5734
p-value			0.1654
Hedges' g [95% CI]			0.1365 [-0.0888; 0.3618]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Day 64			
Change from baseline			
n	172	142	
LS Means [95 % CI]	-1.1277 [-2.0025; -0.2529]	-2.0515 [-3.0033; -1.0996]	
Standard error	0.4450	0.4842	
Difference of LS Means [95% CI]			0.9237 [-0.1855; 2.0330]
Standard error for difference			0.5639
p-value			0.1023
Hedges' g [95% CI]			0.1587 [-0.0639; 0.3813]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Day 106			
Change from baseline			
n	146	122	
LS Means [95 % CI]	-1.8157 [-2.8060; -0.8254]	-2.4658 [-3.5451; -1.3865]	
Standard error	0.5038	0.5490	
Difference of LS Means [95% CI]			0.6501 [-0.6492; 1.9494]
Standard error for difference			0.6603
p-value			0.3256
Hedges' g [95% CI]			0.1067 [-0.1339; 0.3473]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Day 148			
Change from baseline			
n	108	97	
LS Means [95 % CI]	-1.7751 [-2.8975; -0.6527]	-2.3526 [-3.5587; -1.1465]	
Standard error	0.5706	0.6131	
Difference of LS Means [95% CI]			0.5775 [-0.9238; 2.0789]
Standard error for difference			0.7624
p-value			0.4494
Hedges' g [95% CI]			0.0962 [-0.1781; 0.3705]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Day 190			
Change from baseline			
n	91	67	
LS Means [95 % CI]	-1.7664 [-2.8205; -0.7124]	-2.7537 [-3.9491; -1.5582]	
Standard error	0.5357	0.6076	
Difference of LS Means [95% CI]			0.9872 [-0.4497; 2.4242]
Standard error for difference			0.7292
p-value			0.1772
Hedges' g [95% CI]			0.1944 [-0.1218; 0.5107]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Day 232			
Change from baseline			
n	67	47	
LS Means [95 % CI]	-2.1656 [-3.4429; -0.8883]	-3.0657 [-4.5455; -1.5859]	
Standard error	0.6480	0.7507	
Difference of LS Means [95% CI]			0.9001 [-0.9327; 2.7329]
Standard error for difference			0.9283
p-value			0.3336
Hedges' g [95% CI]			0.1706 [-0.2029; 0.5442]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Day 274			
Change from baseline			
n	50	27	
LS Means [95 % CI]	-1.8713 [-3.2809; -0.4616]	-2.5466 [-4.3888; -0.7044]	
Standard error	0.7131	0.9311	
Difference of LS Means [95% CI]			0.6753 [-1.5401; 2.8908]
Standard error for difference			1.1181
p-value			0.5471
Hedges' g [95% CI]			0.1344 [-0.3341; 0.6030]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Day 316			
Change from baseline			
n	37	20	
LS Means [95 % CI]	-0.8477 [-2.2807; 0.5853]	-1.0438 [-2.8754; 0.7879]	
Standard error	0.7241	0.9240	
Difference of LS Means [95% CI]			0.1961 [-2.0305; 2.4226]
Standard error for difference			1.1215
p-value			0.8616
Hedges' g [95% CI]			0.0448 [-0.4992; 0.5889]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Day 358			
Change from baseline			
n	32	14	
LS Means [95 % CI]	-1.2011 [-2.6466; 0.2444]	-1.7337 [-3.6905; 0.2231]	
Standard error	0.7302	0.9868	
Difference of LS Means [95% CI]			0.5326 [-1.8080; 2.8732]
Standard error for difference			1.1788
p-value			0.6524
Hedges' g [95% CI]			0.1307 [-0.4979; 0.7593]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional well-being (FWB)			
Day 400			
Change from baseline			
n	21	12	
LS Means [95 % CI]	-1.6993 [-3.2416; -0.1570]	-4.3889 [-6.3434; -2.4345]	
Standard error	0.7766	0.9824	
Difference of LS Means [95% CI]			2.6896 [0.2954; 5.0839]
Standard error for difference			1.2006
p-value			0.0282
Hedges' g [95% CI]			0.7488 [0.0169; 1.4807]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Day 22			
Change from baseline			
n	192	148	
LS Means [95 % CI]	-0.0250 [-1.5720; 1.5219]	0.0025 [-1.7008; 1.7058]	
Standard error	0.7868	0.8663	
Difference of LS Means [95% CI]			-0.0275 [-1.9584; 1.9033]
Standard error for difference			0.9818
p-value			0.9776
Hedges' g [95% CI]			-0.0026 [-0.2169; 0.2118]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Day 43			
Change from baseline			
n	184	129	
LS Means [95 % CI]	-1.3265 [-2.9569; 0.3040]	-0.7397 [-2.5512; 1.0719]	
Standard error	0.8293	0.9214	
Difference of LS Means [95% CI]			-0.5868 [-2.6757; 1.5021]
Standard error for difference			1.0620
p-value			0.5809
Hedges' g [95% CI]			-0.0535 [-0.2787; 0.1716]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Day 64			
Change from baseline			
n	175	142	
LS Means [95 % CI]	-1.4310 [-3.1388; 0.2768]	0.1151 [-1.7476; 1.9777]	
Standard error	0.8688	0.9476	
Difference of LS Means [95% CI]			-1.5460 [-3.7226; 0.6306]
Standard error for difference			1.1065
p-value			0.1633
Hedges' g [95% CI]			-0.1353 [-0.3569; 0.0864]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Day 106			
Change from baseline			
n	148	122	
LS Means [95 % CI]	-2.4623 [-4.4202; -0.5043]	-2.1174 [-4.2587; 0.0239]	
Standard error	0.9961	1.0893	
Difference of LS Means [95% CI]			-0.3449 [-2.9460; 2.2562]
Standard error for difference			1.3221
p-value			0.7944
Hedges' g [95% CI]			-0.0285 [-0.2682; 0.2112]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Day 148			
Change from baseline			
n	110	97	
LS Means [95 % CI]	-3.0320 [-5.1408; -0.9231]	-2.4652 [-4.7508; -0.1795]	
Standard error	1.0720	1.1618	
Difference of LS Means [95% CI]			-0.5668 [-3.3920; 2.2584]
Standard error for difference			1.4344
p-value			0.6931
Hedges' g [95% CI]			-0.0498 [-0.3228; 0.2232]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Day 190			
Change from baseline			
n	94	68	
LS Means [95 % CI]	-3.8814 [-6.2022; -1.5606]	-2.7780 [-5.4165; -0.1394]	
Standard error	1.1789	1.3405	
Difference of LS Means [95% CI]			-1.1034 [-4.3707; 2.1638]
Standard error for difference			1.6577
p-value			0.5063
Hedges' g [95% CI]			-0.0974 [-0.4096; 0.2148]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Day 232			
Change from baseline			
n	68	47	
LS Means [95 % CI]	-3.6253 [-6.2055; -1.0451]	-4.0843 [-7.0811; -1.0876]	
Standard error	1.3085	1.5200	
Difference of LS Means [95% CI]			0.4590 [-3.2783; 4.1964]
Standard error for difference			1.8929
p-value			0.8087
Hedges' g [95% CI]			0.0428 [-0.3290; 0.4147]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Day 274			
Change from baseline			
n	51	27	
LS Means [95 % CI]	-2.7513 [-5.4869; -0.0157]	-4.1882 [-7.6143; -0.7620]	
Standard error	1.3837	1.7329	
Difference of LS Means [95% CI]			1.4369 [-2.7692; 5.6429]
Standard error for difference			2.1239
p-value			0.5000
Hedges' g [95% CI]			0.1483 [-0.3187; 0.6154]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Day 316			
Change from baseline			
n	37	20	
LS Means [95 % CI]	-2.8388 [-5.5663; -0.1113]	-1.5312 [-4.8814; 1.8190]	
Standard error	1.3782	1.6914	
Difference of LS Means [95% CI]			-1.3076 [-5.4392; 2.8240]
Standard error for difference			2.0823
p-value			0.5315
Hedges' g [95% CI]			-0.1590 [-0.7038; 0.3857]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Day 358			
Change from baseline			
n	32	14	
LS Means [95 % CI]	-7.1796 [-10.9770; -3.3822]	-4.7772 [-9.8297; 0.2752]	
Standard error	1.9103	2.5404	
Difference of LS Means [95% CI]			-2.4024 [-8.5882; 3.7834]
Standard error for difference			3.1067
p-value			0.4417
Hedges' g [95% CI]			-0.2262 [-0.8559; 0.4035]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Gastric cancer subscale (GaCS)			
Day 400			
Change from baseline			
n	21	12	
LS Means [95 % CI]	-9.1708 [-12.6961; -5.6456]	-2.4140 [-6.6652; 1.8371]	
Standard error	1.7809	2.1469	
Difference of LS Means [95% CI]			-6.7568 [-12.1261; -1.3876]
Standard error for difference			2.7083
p-value			0.0141
Hedges' g [95% CI]			-0.8332 [-1.5704; -0.0960]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Day 22			
Change from baseline			
n	191	149	
LS Means [95 % CI]	-1.0806 [-3.0683; 0.9072]	-4.9047 [-7.0806; -2.7287]	
Standard error	1.0111	1.1068	
Difference of LS Means [95% CI]			3.8241 [1.3410; 6.3071]
Standard error for difference			1.2626
p-value			0.0026
Hedges' g [95% CI]			0.2770 [0.0618; 0.4923]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Day 43			
Change from baseline			
n	182	129	
LS Means [95 % CI]	-2.6259 [-4.6910; -0.5608]	-4.6399 [-6.9267; -2.3530]	
Standard error	1.0504	1.1632	
Difference of LS Means [95% CI]			2.0140 [-0.6250; 4.6529]
Standard error for difference			1.3417
p-value			0.1343
Hedges' g [95% CI]			0.1458 [-0.0801; 0.3716]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Day 64			
Change from baseline			
n	172	142	
LS Means [95 % CI]	-2.7992 [-4.9247; -0.6737]	-4.8704 [-7.1761; -2.5647]	
Standard error	1.0812	1.1729	
Difference of LS Means [95% CI]			2.0712 [-0.6136; 4.7560]
Standard error for difference			1.3648
p-value			0.1301
Hedges' g [95% CI]			0.1467 [-0.0759; 0.3692]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Day 106			
Change from baseline			
n	146	121	
LS Means [95 % CI]	-3.9637 [-6.4134; -1.5140]	-7.3068 [-9.9788; -4.6349]	
Standard error	1.2462	1.3592	
Difference of LS Means [95% CI]			3.3431 [0.1142; 6.5720]
Standard error for difference			1.6409
p-value			0.0425
Hedges' g [95% CI]			0.2221 [-0.0196; 0.4638]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Day 148			
Change from baseline			
n	108	95	
LS Means [95 % CI]	-4.5746 [-7.1880; -1.9612]	-6.9845 [-9.8146; -4.1544]	
Standard error	1.3286	1.4386	
Difference of LS Means [95% CI]			2.4099 [-1.0668; 5.8865]
Standard error for difference			1.7651
p-value			0.1734
Hedges' g [95% CI]			0.1726 [-0.1036; 0.4488]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Day 190			
Change from baseline			
n	91	66	
LS Means [95 % CI]	-5.0474 [-7.7058; -2.3889]	-8.0757 [-11.0870; -5.0644]	
Standard error	1.3507	1.5302	
Difference of LS Means [95% CI]			3.0283 [-0.6249; 6.6815]
Standard error for difference			1.8534
p-value			0.1037
Hedges' g [95% CI]			0.2374 [-0.0806; 0.5553]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Day 232			
Change from baseline			
n	67	47	
LS Means [95 % CI]	-6.4767 [-9.5171; -3.4363]	-8.5772 [-12.0949; -5.0594]	
Standard error	1.5431	1.7853	
Difference of LS Means [95% CI]			2.1005 [-2.2442; 6.4451]
Standard error for difference			2.2017
p-value			0.3414
Hedges' g [95% CI]			0.1673 [-0.2063; 0.5408]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Day 274			
Change from baseline			
n	50	27	
LS Means [95 % CI]	-3.5451 [-6.9348; -0.1554]	-7.6602 [-12.0003; -3.3200]	
Standard error	1.7147	2.1938	
Difference of LS Means [95% CI]			4.1151 [-1.1338; 9.3639]
Standard error for difference			2.6488
p-value			0.1231
Hedges' g [95% CI]			0.3430 [-0.1283; 0.8142]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Day 316			
Change from baseline			
n	37	18	
LS Means [95 % CI]	-3.5288 [-6.9664; -0.0913]	-5.5524 [-9.9736; -1.1311]	
Standard error	1.7390	2.2337	
Difference of LS Means [95% CI]			2.0235 [-3.3309; 7.3780]
Standard error for difference			2.7016
p-value			0.4555
Hedges' g [95% CI]			0.1948 [-0.3696; 0.7593]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Day 358			
Change from baseline			
n	32	14	
LS Means [95 % CI]	-5.4808 [-9.5369; -1.4248]	-8.1239 [-13.6500; -2.5979]	
Standard error	2.0461	2.7850	
Difference of LS Means [95% CI]			2.6431 [-4.0062; 9.2924]
Standard error for difference			3.3467
p-value			0.4317
Hedges' g [95% CI]			0.2310 [-0.3988; 0.8608]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
The Functional Assessment of Cancer Therapy-General			
Day 400			
Change from baseline			
n	21	12	
LS Means [95 % CI]	-7.3418 [-11.5509; -3.1327]	-11.6114 [-16.8870; -6.3358]	
Standard error	2.1168	2.6481	
Difference of LS Means [95% CI]			4.2695 [-2.2737; 10.8128]
Standard error for difference			3.2781
p-value			0.1972
Hedges' g [95% CI]			0.4377 [-0.2794; 1.1548]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Day 22			
Change from baseline			
n	190	148	
LS Means [95 % CI]	-1.1716 [-4.3201; 1.9769]	-4.6532 [-8.0997; -1.2066]	
Standard error	1.6013	1.7530	
Difference of LS Means [95% CI]			3.4815 [-0.4160; 7.3790]
Standard error for difference			1.9818
p-value			0.0798
Hedges' g [95% CI]			0.1597 [-0.0555; 0.3749]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Day 43			
Change from baseline			
n	181	129	
LS Means [95 % CI]	-3.9408 [-7.2593; -0.6223]	-4.9785 [-8.6390; -1.3181]	
Standard error	1.6878	1.8618	
Difference of LS Means [95% CI]			1.0377 [-3.1766; 5.2521]
Standard error for difference			2.1426
p-value			0.6285
Hedges' g [95% CI]			0.0469 [-0.1790; 0.2728]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
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Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Day 64			
Change from baseline			
n	172	142	
LS Means [95 % CI]	-4.2537 [-7.6743; -0.8331]	-4.4085 [-8.1188; -0.6982]	
Standard error	1.7401	1.8875	
Difference of LS Means [95% CI]			0.1548 [-4.1569; 4.4665]
Standard error for difference			2.1920
p-value			0.9437
Hedges' g [95% CI]			0.0068 [-0.2154; 0.2290]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Day 106			
Change from baseline			
n	146	121	
LS Means [95 % CI]	-6.3287 [-10.2804; -2.3770]	-8.9386 [-13.2439; -4.6332]	
Standard error	2.0103	2.1902	
Difference of LS Means [95% CI]			2.6099 [-2.6041; 7.8239]
Standard error for difference			2.6500
p-value			0.3254
Hedges' g [95% CI]			0.1075 [-0.1336; 0.3487]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Day 148			
Change from baseline			
n	108	95	
LS Means [95 % CI]	-7.6774 [-11.9551; -3.3997]	-9.4082 [-14.0410; -4.7755]	
Standard error	2.1747	2.3550	
Difference of LS Means [95% CI]			1.7308 [-3.9882; 7.4497]
Standard error for difference			2.9037
p-value			0.5517
Hedges' g [95% CI]			0.0757 [-0.2000; 0.3515]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Day 190			
Change from baseline			
n	91	66	
LS Means [95 % CI]	-9.1848 [-13.7121; -4.6575]	-10.9059 [-16.0210; -5.7908]	
Standard error	2.2999	2.5988	
Difference of LS Means [95% CI]			1.7211 [-4.5687; 8.0109]
Standard error for difference			3.1910
p-value			0.5902
Hedges' g [95% CI]			0.0793 [-0.2377; 0.3963]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Day 232			
Change from baseline			
n	67	47	
LS Means [95 % CI]	-10.6347 [-15.7622; -5.5071]	-12.7379 [-18.6407; -6.8350]	
Standard error	2.6021	2.9958	
Difference of LS Means [95% CI]			2.1032 [-5.2535; 9.4599]
Standard error for difference			3.7284
p-value			0.5734
Hedges' g [95% CI]			0.0995 [-0.2736; 0.4727]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Day 274			
Change from baseline			
n	50	27	
LS Means [95 % CI]	-6.3911 [-11.9411; -0.8410]	-11.6520 [-18.6016; -4.7025]	
Standard error	2.8074	3.5148	
Difference of LS Means [95% CI]			5.2610 [-3.2460; 13.7679]
Standard error for difference			4.2949
p-value			0.2231
Hedges' g [95% CI]			0.2696 [-0.2004; 0.7397]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Day 316			
Change from baseline			
n	37	18	
LS Means [95 % CI]	-7.3359 [-12.9364; -1.7355]	-7.1409 [-14.2379; -0.0439]	
Standard error	2.8312	3.5844	
Difference of LS Means [95% CI]			-0.1950 [-8.8472; 8.4572]
Standard error for difference			4.3630
p-value			0.9644
Hedges' g [95% CI]			-0.0116 [-0.5748; 0.5517]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Day 358			
Change from baseline			
n	32	14	
LS Means [95 % CI]	-13.8391 [-21.2293; -6.4489]	-16.9346 [-26.5831; -7.2861]	
Standard error	3.7196	4.8560	
Difference of LS Means [95% CI]			3.0956 [-8.7583; 14.9494]
Standard error for difference			5.9577
p-value			0.6048
Hedges' g [95% CI]			0.1504 [-0.4784; 0.7791]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Table 9.9.4 FACT-Ga - Mixed Model for Repeated Measurement - Full Analysis Set

DESTINY Gastric-04	T-DXd N = 246	Ram + PTX N = 248	T-DXd vs. Ram + PTX
Functional Assessment of Cancer Therapy-Gastric			
Day 400			
Change from baseline			
n	21	12	
LS Means [95 % CI]	-16.6924 [-24.0162; -9.3686]	-17.5659 [-26.6616; -8.4701]	
Standard error	3.6838	4.5672	
Difference of LS Means [95% CI]			0.8735 [-10.4999; 12.2469]
Standard error for difference			5.7025
p-value			0.8787
Hedges' g [95% CI]			0.0516 [-0.6578; 0.7610]

N: number of patients in analysis set; n: number of observations
LS Means estimate and its 95% CI are calculated using a REML (restricted maximum likelihood) based mixed model repeated measure including terms for treatment, stratification factors, time of visit, treatment-by-visit interaction and baseline score.
Hedges' g is derived based on the LS Means.
The analysis only includes assessments up to the time point where there are at least 10 patients on each of the treatments.
CI: confidence interval; LS: least square; MMRM: mixed model for repeated measurements

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADQS
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_mmrm.sas; Output name: T.9.9.4_FACT-Ga_MMRM_FAS.rtf

Sicherheit – SAF

Anhang 4-G 4.1 Gesamtraten Unerwünschter Ereignisse

Anhang 4-G 4.1.1 Unerwünschte Ereignisse – SAF

Daiichi Sankyo Europe GmbH
DS8201-A-U306 (DESTINY-GASTRIC04) - DCO 24-OCT-2024

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Table 9.13.1 Treatment-Emergent Adverse Events (TEAEs) - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
TEAE	244 (100)	0.1 [0.1, 0.2]	228 (97.9)	0.2 [0.2, 0.2]	1.1721 [0.9762, 1.4074] 0.0888	0.0966
Serious TEAE	100 (41.0)	13.7 [6.6, NE]	101 (43.3)	8.0 [6.2, 11.2]	0.8707 [0.6586, 1.1512] 0.3313	0.3299
Severe (CTCAE grade ≥3) TEAE	166 (68.0)	2.3 [1.6, 3.5]	172 (73.8)	1.6 [1.0, 2.2]	0.7942 [0.6405, 0.9847] 0.0357	0.0342
TEAEs associated with discontinuation of study medication	35 (14.3)	22.1 [17.1, NE]	40 (17.2)	NE [NE, NE]	0.6135 [0.3855, 0.9762] 0.0393	0.0376

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_tte_wo_cens.sas; Output name: T.9.13.1_TEAE_SAF.rtf

Anhang 4-G 4.1.2 Unerwünschte Ereignisse – Subgruppenanalyse – SAF

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.1799
IHC 3+	205 / 205 (100)	0.1 [0.1, 0.2]	191 / 196 (97.4)	0.2 [0.2, 0.2]	1.0980 [0.9009, 1.3381] 0.3544 0.3670	
IHC 2+/ISH+	39 / 39 (100)	0.1 [0.1, 0.2]	37 / 37 (100)	0.2 [0.1, 0.4]	1.7010 [1.0607, 2.7278] 0.0275 0.0303	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.0760
Asia [excluding mainland China]	57 / 57 (100)	0.2 [0.1, 0.2]	59 / 59 (100)	0.2 [0.2, 0.3]	0.9976 [0.6853, 1.4524] 0.9902 0.9219	
Western Europe	138 / 138 (100)	0.1 [0.1, 0.2]	124 / 129 (96.1)	0.2 [0.1, 0.2]	1.0643 [0.8348, 1.3570] 0.6151 0.6081	
Mainland China/Rest of World (ROW)	49 / 49 (100)	0.1 [0.1, 0.1]	45 / 45 (100)	0.2 [0.2, 0.3]	1.7814 [1.1721, 2.7073] 0.0069 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.7275
<6 Months	61 / 61 (100)	0.1 [0.1, 0.2]	57 / 57 (100)	0.2 [0.1, 0.3]	1.2504 [0.8677, 1.8019] 0.2306 0.2629	
≥ 6 Months	183 / 183 (100)	0.1 [0.1, 0.2]	171 / 176 (97.2)	0.2 [0.2, 0.3]	1.1319 [0.9175, 1.3965] 0.2475 0.2486	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.9615
<65	139 / 139 (100)	0.1 [0.1, 0.2]	121 / 123 (98.4)	0.2 [0.2, 0.3]	1.1543 [0.9032, 1.4751] 0.2515 0.2604	
≥ 65	105 / 105 (100)	0.1 [0.1, 0.2]	107 / 110 (97.3)	0.2 [0.2, 0.2]	1.1511 [0.8779, 1.5094] 0.3088 0.3276	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.1956
<75	220 / 220 (100)	0.1 [0.1, 0.2]	194 / 198 (98.0)	0.2 [0.2, 0.2]	1.1999 [0.9881, 1.4570] 0.0659 0.0733	
≥ 75	24 / 24 (100)	0.2 [0.1, 0.4]	34 / 35 (97.1)	0.2 [0.1, 0.3]	0.8833 [0.5157, 1.5128] 0.6512 0.6545	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.8423
Male	186 / 186 (100)	0.1 [0.1, 0.2]	190 / 194 (97.9)	0.2 [0.2, 0.2]	1.1501 [0.9386, 1.4093] 0.1774 0.2052	
Female	58 / 58 (100)	0.1 [0.1, 0.2]	38 / 39 (97.4)	0.2 [0.1, 0.3]	1.1691 [0.7723, 1.7698] 0.4601 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.0962
White	115 / 115 (100)	0.1 [0.1, 0.2]	115 / 120 (95.8)	0.2 [0.2, 0.3]	1.2757 [0.9827, 1.6562] 0.0675 0.0584	
Asian	101 / 101 (100)	0.1 [0.1, 0.2]	93 / 93 (100)	0.2 [0.2, 0.3]	1.1608 [0.8714, 1.5462] 0.3082 0.3695	
Other	28 / 28 (100)	0.1 [0.1, 0.3]	20 / 20 (100)	0.1 [0.0, 0.3]	0.6409 [0.3512, 1.1694] 0.1470 0.1223	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.7988
0	96 / 96 (100)	0.2 [0.1, 0.3]	79 / 81 (97.5)	0.2 [0.1, 0.3]	1.1240 [0.8330, 1.5168] 0.4444 0.4910	
≥ 1	148 / 148 (100)	0.1 [0.1, 0.2]	149 / 152 (98.0)	0.2 [0.2, 0.2]	1.2018 [0.9562, 1.5105] 0.1150 0.1238	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.1531
Gastric	152 / 152 (100)	0.1 [0.1, 0.2]	138 / 139 (99.3)	0.2 [0.2, 0.2]	1.0271 [0.8145, 1.2954] 0.8211 0.8445	
GEJ	92 / 92 (100)	0.1 [0.1, 0.2]	90 / 94 (95.7)	0.2 [0.2, 0.3]	1.3478 [1.0057, 1.8063] 0.0457 0.0483	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.1157
Intestinal	68 / 68 (100)	0.1 [0.1, 0.2]	60 / 63 (95.2)	0.2 [0.1, 0.3]	1.4646 [1.0299, 2.0828] 0.0337 0.0338	
Diffuse	25 / 25 (100)	0.2 [0.1, 0.3]	18 / 18 (100)	0.1 [0.0, 0.3]	0.7689 [0.4124, 1.4335] 0.4083 0.4022	
Others	151 / 151 (100)	0.1 [0.1, 0.2]	150 / 152 (98.7)	0.2 [0.2, 0.2]	1.0666 [0.8494, 1.3393] 0.5789 0.6250	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.8919
<2	72 / 72 (100)	0.1 [0.1, 0.2]	72 / 72 (100)	0.2 [0.2, 0.3]	1.0932 [0.7860, 1.5206] 0.5964 0.6298	
≥ 2	172 / 172 (100)	0.1 [0.1, 0.2]	156 / 161 (96.9)	0.2 [0.2, 0.2]	1.1542 [0.9283, 1.4351] 0.1969 0.2042	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.9106
Yes	31 / 31 (100)	0.2 [0.1, 0.3]	27 / 28 (96.4)	0.3 [0.1, 0.4]	1.0776 [0.6352, 1.8280] 0.7818 0.8111	
No	213 / 213 (100)	0.1 [0.1, 0.2]	201 / 205 (98.0)	0.2 [0.2, 0.2]	1.1545 [0.9514, 1.4009] 0.1457 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 Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.0852
Yes	20 / 20 (100)	0.1 [0.1, 0.3]	16 / 16 (100)	0.3 [0.1, 0.4]	2.4046 [1.1578, 4.9940] 0.0186 0.0242	
No	224 / 224 (100)	0.1 [0.1, 0.2]	212 / 217 (97.7)	0.2 [0.2, 0.2]	1.0945 [0.9064, 1.3217] 0.3478 0.3626	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.2551
Yes	39 / 39 (100)	0.1 [0.1, 0.3]	36 / 36 (100)	0.2 [0.2, 0.4]	1.5964 [1.0049, 2.5360] 0.0476 0.0513	
No	205 / 205 (100)	0.1 [0.1, 0.2]	192 / 197 (97.5)	0.2 [0.2, 0.2]	1.0930 [0.8971, 1.3318] 0.3776 0.3880	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.3953
Yes	145 / 145 (100)	0.2 [0.1, 0.2]	146 / 149 (98.0)	0.2 [0.2, 0.2]	1.0848 [0.8608, 1.3670] 0.4904 0.4910	
No	99 / 99 (100)	0.1 [0.1, 0.1]	82 / 84 (97.6)	0.2 [0.2, 0.3]	1.2811 [0.9530, 1.7221] 0.1008 0.1148	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.0371
Normal renal function	116 / 116 (100)	0.1 [0.1, 0.2]	111 / 114 (97.4)	0.2 [0.2, 0.3]	1.3499 [1.0382, 1.7552] 0.0251 0.0237	
Mild impairment	87 / 87 (100)	0.1 [0.1, 0.2]	79 / 81 (97.5)	0.2 [0.2, 0.3]	1.1736 [0.8634, 1.5952] 0.3069 0.3321	
Moderate impairment	41 / 41 (100)	0.2 [0.1, 0.3]	38 / 38 (100)	0.1 [0.1, 0.2]	0.7233 [0.4577, 1.1430] 0.1653 0.1423	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.0346
Normal hepatic function	185 / 185 (100)	0.1 [0.1, 0.2]	172 / 177 (97.2)	0.2 [0.2, 0.3]	1.2817 [1.0399, 1.5798] 0.0200 0.0233	
Mild, Moderate or Severe dysfunction	59 / 59 (100)	0.2 [0.1, 0.2]	55 / 55 (100)	0.2 [0.1, 0.2]	0.8447 [0.5810, 1.2280] 0.3766 0.3947	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

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Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.0001
IHC 3+	90 / 205 (43.9)	7.9 [5.9, 18.9]	77 / 196 (39.3)	10.7 [7.6, 13.8]	1.0864 [0.7998, 1.4757] 0.5960 0.5976	
IHC 2+/ISH+	10 / 39 (25.6)	NE [NE, NE]	24 / 37 (64.9)	2.8 [1.4, 7.1]	0.2690 [0.1263, 0.5730] 0.0007 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.3551
Asia [excluding mainland China]	15 / 57 (26.3)	NE [13.7, NE]	23 / 59 (39.0)	13.8 [4.5, NE]	0.6066 [0.3158, 1.1653] 0.1335 0.1295	
Western Europe	59 / 138 (42.8)	7.9 [5.8, NE]	54 / 129 (41.9)	8.5 [5.9, 12.3]	0.9357 [0.6460, 1.3553] 0.7252 0.7245	
Mainland China/Rest of World (ROW)	26 / 49 (53.1)	5.0 [2.7, NE]	24 / 45 (53.3)	6.2 [3.1, 10.7]	1.0189 [0.5835, 1.7794] 0.9474 0.9476	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.2303
<6 Months	25 / 61 (41.0)	NE [3.5, NE]	30 / 57 (52.6)	4.6 [2.2, 12.3]	0.6540 [0.3842, 1.1134] 0.1178 0.1156	
≥ 6 Months	75 / 183 (41.0)	13.7 [6.7, NE]	71 / 176 (40.3)	9.2 [6.3, 13.8]	0.9401 [0.6782, 1.3031] 0.7109 0.7115	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.1534
<65	51 / 139 (36.7)	15.3 [7.9, NE]	55 / 123 (44.7)	7.6 [5.9, 12.3]	0.7081 [0.4828, 1.0385] 0.0773 0.0763	
≥ 65	49 / 105 (46.7)	6.5 [4.2, NE]	46 / 110 (41.8)	8.0 [5.7, NE]	1.1120 [0.7426, 1.6651] 0.6064 0.6089	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.4119
<75	90 / 220 (40.9)	15.3 [6.6, NE]	87 / 198 (43.9)	7.7 [6.0, 10.7]	0.8254 [0.6135, 1.1105] 0.2050 0.2042	
≥ 75	10 / 24 (41.7)	13.7 [1.1, NE]	14 / 35 (40.0)	11.2 [4.5, NE]	1.2016 [0.5262, 2.7436] 0.6629 0.6665	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.2414
Male	78 / 186 (41.9)	13.7 [5.8, NE]	89 / 194 (45.9)	7.7 [5.7, 10.7]	0.8034 [0.5911, 1.0920] 0.1622 0.1608	
Female	22 / 58 (37.9)	NE [6.5, NE]	12 / 39 (30.8)	NE [6.3, NE]	1.2068 [0.5966, 2.4411] 0.6011 0.6002	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.4791
White	51 / 115 (44.3)	7.7 [5.1, 18.9]	50 / 120 (41.7)	8.5 [6.2, 12.3]	1.0127 [0.6848, 1.4975] 0.9497 0.9510	
Asian	36 / 101 (35.6)	NE [6.6, NE]	41 / 93 (44.1)	8.0 [5.7, NE]	0.7461 [0.4761, 1.1694] 0.2014 0.1986	
Other	13 / 28 (46.4)	6.5 [2.5, NE]	10 / 20 (50.0)	4.5 [2.1, NE]	0.8356 [0.3638, 1.9196] 0.6722 0.6721	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.1066
0	25 / 96 (26.0)	18.9 [13.7, NE]	27 / 81 (33.3)	9.2 [7.1, NE]	0.6003 [0.3466, 1.0398] 0.0686 0.0658	
≥ 1	75 / 148 (50.7)	5.1 [3.8, 7.9]	74 / 152 (48.7)	6.3 [4.6, 10.7]	1.0678 [0.7742, 1.4728] 0.6893 0.6900	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.6943
Gastric	58 / 152 (38.2)	NE [6.5, NE]	60 / 139 (43.2)	7.6 [5.8, 13.8]	0.8379 [0.5835, 1.2030] 0.3378 0.3371	
GEJ	42 / 92 (45.7)	13.0 [5.1, 18.9]	41 / 94 (43.6)	9.2 [6.0, 12.3]	0.8689 [0.5610, 1.3458] 0.5291 0.5270	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.2529
Intestinal	32 / 68 (47.1)	6.7 [4.2, NE]	23 / 63 (36.5)	13.8 [4.5, NE]	1.1756 [0.6861, 2.0144] 0.5560 0.5569	
Diffuse	8 / 25 (32.0)	NE [1.6, NE]	4 / 18 (22.2)	NE [NE, NE]	1.5383 [0.4625, 5.1169] 0.4824 0.4790	
Others	60 / 151 (39.7)	15.3 [6.6, NE]	74 / 152 (48.7)	7.4 [5.9, 9.2]	0.7402 [0.5251, 1.0434] 0.0859 0.0847	

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

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.7759
<2	27 / 72 (37.5)	NE [5.5, NE]	31 / 72 (43.1)	10.7 [7.1, NE]	0.9201 [0.5485, 1.5434] 0.7523 0.7495	
≥ 2	73 / 172 (42.4)	13.0 [5.9, NE]	70 / 161 (43.5)	6.3 [5.8, 13.8]	0.8349 [0.6006, 1.1606] 0.2830 0.2813	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.1444
Yes	15 / 31 (48.4)	6.6 [2.1, NE]	8 / 28 (28.6)	10.7 [NE, NE]	1.4730 [0.6168, 3.5178] 0.3832 0.3823	
No	85 / 213 (39.9)	15.3 [6.7, NE]	93 / 205 (45.4)	7.6 [5.9, 11.2]	0.8029 [0.5976, 1.0788] 0.1452 0.1447	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.0205
Yes	3 / 20 (15.0)	NE [NE, NE]	9 / 16 (56.3)	6.0 [2.6, NE]	0.1939 [0.0503, 0.7476] 0.0172 0.0088	
No	97 / 224 (43.3)	13.0 [5.9, NE]	92 / 217 (42.4)	8.5 [6.2, 12.3]	0.9401 [0.7060, 1.2519] 0.6727 0.6737	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.0939
Yes	13 / 39 (33.3)	NE [5.1, NE]	21 / 36 (58.3)	6.0 [2.8, 9.2]	0.5182 [0.2583, 1.0397] 0.0643 0.0603	
No	87 / 205 (42.4)	13.0 [6.5, NE]	80 / 197 (40.6)	9.2 [6.3, 13.8]	0.9561 [0.7048, 1.2971] 0.7732 0.7738	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.8020
Yes	56 / 145 (38.6)	NE [5.0, NE]	62 / 149 (41.6)	9.2 [6.3, 12.3]	0.8907 [0.6200, 1.2797] 0.5314 0.5293	
No	44 / 99 (44.4)	13.0 [6.5, NE]	39 / 84 (46.4)	6.2 [4.9, NE]	0.7924 [0.5127, 1.2245] 0.2947 0.2944	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.4437
Normal renal function	48 / 116 (41.4)	13.0 [5.8, NE]	56 / 114 (49.1)	7.1 [4.5, 9.2]	0.7602 [0.5161, 1.1197] 0.1653 0.1655	
Mild impairment	32 / 87 (36.8)	NE [5.5, NE]	31 / 81 (38.3)	10.7 [6.3, NE]	0.8913 [0.5411, 1.4682] 0.6514 0.6512	
Moderate impairment	20 / 41 (48.8)	7.7 [3.5, NE]	14 / 38 (36.8)	NE [5.7, NE]	1.3114 [0.6586, 2.6111] 0.4405 0.4343	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.9403
Normal hepatic function	72 / 185 (38.9)	18.9 [7.7, NE]	71 / 177 (40.1)	9.2 [6.2, 13.8]	0.8747 [0.6293, 1.2157] 0.4255 0.4272	
Mild, Moderate or Severe dysfunction	28 / 59 (47.5)	6.6 [3.0, NE]	29 / 55 (52.7)	6.3 [2.4, 12.3]	0.8438 [0.4990, 1.4268] 0.5262 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 Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.0092
IHC 3+	142 / 205 (69.3)	2.3 [1.4, 3.0]	142 / 196 (72.4)	1.9 [1.1, 2.6]	0.8831 [0.6995, 1.1148] 0.2958 0.2936	
IHC 2+/ISH+	24 / 39 (61.5)	2.4 [1.4, 6.7]	30 / 37 (81.1)	0.6 [0.4, 1.4]	0.4402 [0.2536, 0.7642] 0.0035 0.0026	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.3649
Asia [excluding mainland China]	38 / 57 (66.7)	1.8 [0.7, 4.9]	48 / 59 (81.4)	0.9 [0.5, 1.3]	0.6933 [0.4518, 1.0639] 0.0937 0.0917	
Western Europe	86 / 138 (62.3)	2.9 [2.1, 5.5]	86 / 129 (66.7)	2.1 [1.6, 3.2]	0.7752 [0.5742, 1.0465] 0.0963 0.0938	
Mainland China/Rest of World (ROW)	42 / 49 (85.7)	0.7 [0.5, 1.7]	38 / 45 (84.4)	0.8 [0.5, 2.6]	1.0232 [0.6591, 1.5884] 0.9186 0.9357	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.1549
<6 Months	37 / 61 (60.7)	2.4 [1.3, 4.8]	43 / 57 (75.4)	1.0 [0.5, 2.4]	0.6192 [0.3979, 0.9636] 0.0336 0.0328	
≥ 6 Months	129 / 183 (70.5)	2.3 [1.4, 3.5]	129 / 176 (73.3)	1.6 [1.0, 2.3]	0.8571 [0.6710, 1.0948] 0.2169 0.2133	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.8505
<65	92 / 139 (66.2)	2.8 [1.9, 4.9]	87 / 123 (70.7)	2.0 [0.9, 2.6]	0.8169 [0.6090, 1.0960] 0.1775 0.1754	
≥ 65	74 / 105 (70.5)	1.6 [0.5, 2.8]	85 / 110 (77.3)	1.3 [0.8, 2.0]	0.8092 [0.5911, 1.1076] 0.1861 0.1835	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.4478
<75	148 / 220 (67.3)	2.4 [1.6, 3.6]	145 / 198 (73.2)	1.6 [1.0, 2.3]	0.7789 [0.6190, 0.9800] 0.0330 0.0316	
≥ 75	18 / 24 (75.0)	1.1 [0.4, 2.9]	27 / 35 (77.1)	1.1 [0.5, 4.0]	1.0077 [0.5517, 1.8405] 0.9801 0.9827	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.8081
Male	127 / 186 (68.3)	2.3 [1.4, 3.5]	143 / 194 (73.7)	1.6 [0.9, 2.2]	0.7885 [0.6202, 1.0026] 0.0525 0.0509	
Female	39 / 58 (67.2)	2.1 [1.4, 6.1]	29 / 39 (74.4)	2.3 [0.7, 3.7]	0.8266 [0.5105, 1.3385] 0.4388 0.4371	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.6390
White	70 / 115 (60.9)	3.0 [2.1, 6.1]	76 / 120 (63.3)	2.6 [2.0, 3.8]	0.8411 [0.6074, 1.1648] 0.2976 0.2903	
Asian	74 / 101 (73.3)	1.4 [0.7, 2.3]	80 / 93 (86.0)	0.6 [0.5, 1.2]	0.6917 [0.5030, 0.9512] 0.0233 0.0221	
Other	22 / 28 (78.6)	1.9 [0.5, 5.2]	16 / 20 (80.0)	1.2 [0.5, 3.5]	0.8454 [0.4417, 1.6178] 0.6120 0.6014	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.0705
0	55 / 96 (57.3)	4.1 [2.4, 8.3]	57 / 81 (70.4)	2.0 [0.5, 3.7]	0.6260 [0.4315, 0.9083] 0.0136 0.0129	
≥ 1	111 / 148 (75.0)	1.5 [0.7, 2.3]	115 / 152 (75.7)	1.4 [0.9, 2.1]	0.9436 [0.7266, 1.2254] 0.6633 0.6543	

N: number of subjects 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 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.6242
Gastric	108 / 152 (71.1)	2.3 [1.3, 3.6]	110 / 139 (79.1)	1.2 [0.6, 2.2]	0.7441 [0.5696, 0.9720] 0.0301 0.0278	
GEJ	58 / 92 (63.0)	2.3 [1.5, 6.1]	62 / 94 (66.0)	2.0 [1.2, 3.5]	0.8478 [0.5922, 1.2136] 0.3669 0.3680	

N: number of subjects 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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[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.5905
Intestinal	44 / 68 (64.7)	1.1 [0.5, 5.5]	41 / 63 (65.1)	2.0 [1.0, 3.5]	1.0056 [0.6548, 1.5444] 0.9796 0.9946	
Diffuse	17 / 25 (68.0)	1.6 [0.5, 6.3]	15 / 18 (83.3)	0.9 [0.5, 2.3]	0.7291 [0.3630, 1.4641] 0.3744 0.3781	
Others	105 / 151 (69.5)	2.4 [1.7, 3.5]	116 / 152 (76.3)	1.6 [0.6, 2.4]	0.7365 [0.5652, 0.9597] 0.0235 0.0232	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.2303
<2	48 / 72 (66.7)	2.8 [1.3, 6.2]	60 / 72 (83.3)	1.4 [0.6, 2.3]	0.6527 [0.4459, 0.9554] 0.0282 0.0263	
≥ 2	118 / 172 (68.6)	2.1 [1.4, 3.5]	112 / 161 (69.6)	1.6 [0.9, 2.6]	0.8697 [0.6709, 1.1273] 0.2916 0.2899	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.4908
Yes	22 / 31 (71.0)	2.0 [0.7, 6.2]	18 / 28 (64.3)	2.4 [0.5, NE]	0.9406 [0.5007, 1.7669] 0.8490 0.8485	
No	144 / 213 (67.6)	2.4 [1.5, 3.5]	154 / 205 (75.1)	1.6 [1.0, 2.2]	0.7707 [0.6134, 0.9682] 0.0252 0.0240	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.7270
Yes	13 / 20 (65.0)	2.1 [0.3, 8.5]	14 / 16 (87.5)	2.2 [0.5, 6.0]	0.6146 [0.2815, 1.3419] 0.2218 0.2166	
No	153 / 224 (68.3)	2.3 [1.5, 3.0]	158 / 217 (72.8)	1.6 [1.0, 2.2]	0.8015 [0.6413, 1.0018] 0.0519 0.0503	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.6101
Yes	29 / 39 (74.4)	2.0 [0.5, 4.8]	33 / 36 (91.7)	0.8 [0.5, 2.4]	0.6969 [0.4193, 1.1581] 0.1634 0.1647	
No	137 / 205 (66.8)	2.5 [1.5, 3.6]	139 / 197 (70.6)	1.6 [1.0, 2.3]	0.8164 [0.6443, 1.0345] 0.0931 0.0902	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.1620
Yes	94 / 145 (64.8)	2.1 [1.4, 3.8]	101 / 149 (67.8)	2.0 [1.0, 3.0]	0.8930 [0.6740, 1.1833] 0.4308 0.4304	
No	72 / 99 (72.7)	2.4 [1.4, 4.2]	71 / 84 (84.5)	1.3 [0.5, 2.2]	0.6286 [0.4514, 0.8755] 0.0060 0.0054	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.8525
Normal renal function	72 / 116 (62.1)	2.7 [1.4, 5.9]	82 / 114 (71.9)	1.7 [0.7, 2.4]	0.7528 [0.5480, 1.0341] 0.0796 0.0768	
Mild impairment	64 / 87 (73.6)	2.1 [0.8, 2.9]	60 / 81 (74.1)	1.6 [0.6, 2.6]	0.8343 [0.5857, 1.1884] 0.3156 0.3122	
Moderate impairment	30 / 41 (73.2)	2.0 [0.7, 4.4]	30 / 38 (78.9)	1.3 [0.6, 3.0]	0.7867 [0.4727, 1.3093] 0.3560 0.3556	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) TEAE	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.9153
Normal hepatic function	126 / 185 (68.1)	2.4 [1.5, 3.6]	130 / 177 (73.4)	1.6 [1.0, 2.4]	0.7810 [0.6106, 0.9991] 0.0491 0.0479	
Mild, Moderate or Severe dysfunction	40 / 59 (67.8)	1.7 [0.5, 4.9]	41 / 55 (74.5)	1.0 [0.4, 2.1]	0.8212 [0.5308, 1.2705] 0.3763 0.3755	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.0011
IHC 3+	34 / 205 (16.6)	22.1 [15.2, NE]	31 / 196 (15.8)	NE [NE, NE]	0.7998 [0.4869, 1.3138] 0.3777 0.3768	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	9 / 37 (24.3)	NE [3.7, NE]	0.0685 [0.0085, 0.5487] 0.0116 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.1143
Asia [excluding mainland China]	5 / 57 (8.8)	NE [15.2, NE]	15 / 59 (25.4)	NE [7.4, NE]	0.2519 [0.0901, 0.7046] 0.0086 0.0047	
Western Europe	22 / 138 (15.9)	22.1 [13.7, NE]	18 / 129 (14.0)	NE [NE, NE]	0.7310 [0.3784, 1.4121] 0.3509 0.3500	
Mainland China/Rest of World (ROW)	8 / 49 (16.3)	NE [NE, NE]	7 / 45 (15.6)	NE [10.2, NE]	0.9655 [0.3482, 2.6771] 0.9462 0.9490	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.1485
<6 Months	7 / 61 (11.5)	NE [15.2, NE]	12 / 57 (21.1)	NE [NE, NE]	0.3860 [0.1446, 1.0305] 0.0574 0.0486	
≥ 6 Months	28 / 183 (15.3)	22.1 [17.1, NE]	28 / 176 (15.9)	NE [NE, NE]	0.7199 [0.4217, 1.2291] 0.2286 0.2270	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.0205
<65	9 / 139 (6.5)	NE [18.0, NE]	19 / 123 (15.4)	NE [NE, NE]	0.3222 [0.1449, 0.7164] 0.0055 0.0035	
≥ 65	26 / 105 (24.8)	17.1 [13.6, NE]	21 / 110 (19.1)	NE [10.1, NE]	0.9288 [0.5091, 1.6946] 0.8097 0.8112	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.3465
<75	29 / 220 (13.2)	NE [17.1, NE]	32 / 198 (16.2)	NE [NE, NE]	0.5831 [0.3480, 0.9770] 0.0405 0.0384	
≥ 75	6 / 24 (25.0)	13.7 [5.3, NE]	8 / 35 (22.9)	NE [6.5, NE]	1.0141 [0.3511, 2.9288] 0.9794 0.9794	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.9514
Male	31 / 186 (16.7)	22.1 [15.2, NE]	36 / 194 (18.6)	NE [NE, NE]	0.6052 [0.3674, 0.9970] 0.0486 0.0465	
Female	4 / 58 (6.9)	NE [NE, NE]	4 / 39 (10.3)	NE [7.4, NE]	0.6355 [0.1583, 2.5516] 0.5227 0.5192	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.6233
White	16 / 115 (13.9)	22.1 [17.1, NE]	15 / 120 (12.5)	NE [NE, NE]	0.7611 [0.3615, 1.6021] 0.4722 0.4721	
Asian	13 / 101 (12.9)	NE [15.2, NE]	21 / 93 (22.6)	NE [10.2, NE]	0.4650 [0.2319, 0.9327] 0.0311 0.0273	
Other	6 / 28 (21.4)	13.7 [13.6, NE]	4 / 20 (20.0)	NE [4.5, NE]	0.5936 [0.1480, 2.3815] 0.4619 0.4568	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

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TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.0117
0	10 / 96 (10.4)	NE [17.1, NE]	17 / 81 (21.0)	NE [8.0, NE]	0.2471 [0.1012, 0.6030] 0.0021 0.0009	
≥ 1	25 / 148 (16.9)	15.2 [13.6, NE]	23 / 152 (15.1)	NE [NE, NE]	0.9510 [0.5385, 1.6794] 0.8624 0.8631	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.1719
Gastric	19 / 152 (12.5)	NE [17.1, NE]	28 / 139 (20.1)	NE [10.1, NE]	0.5082 [0.2819, 0.9160] 0.0243 0.0219	
GEJ	16 / 92 (17.4)	22.1 [13.7, NE]	12 / 94 (12.8)	NE [10.2, NE]	0.8377 [0.3818, 1.8380] 0.6587 0.6611	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.8114
Intestinal	15 / 68 (22.1)	15.2 [13.1, NE]	15 / 63 (23.8)	NE [5.7, NE]	0.6402 [0.3093, 1.3251] 0.2295 0.2265	
Diffuse	2 / 25 (8.0)	NE [NE, NE]	3 / 18 (16.7)	NE [6.5, NE]	0.4121 [0.0682, 2.4900] 0.3340 0.3187	
Others	18 / 151 (11.9)	22.1 [18.0, NE]	22 / 152 (14.5)	NE [NE, NE]	0.6223 [0.3280, 1.1809] 0.1467 0.1434	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.0968
<2	13 / 72 (18.1)	18.0 [13.6, NE]	11 / 72 (15.3)	NE [NE, NE]	0.9476 [0.4113, 2.1830] 0.8994 0.8995	
≥ 2	22 / 172 (12.8)	NE [17.1, NE]	29 / 161 (18.0)	NE [10.1, NE]	0.4917 [0.2794, 0.8654] 0.0138 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.1940
Yes	5 / 31 (16.1)	NE [NE, NE]	2 / 28 (7.1)	10.1 [6.0, NE]	1.8785 [0.3627, 9.7287] 0.4524 0.4451	
No	30 / 213 (14.1)	22.1 [17.1, NE]	38 / 205 (18.5)	NE [NE, NE]	0.5550 [0.3398, 0.9064] 0.0186 0.0172	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.6550
Yes	3 / 20 (15.0)	NE [7.7, NE]	2 / 16 (12.5)	NE [6.5, NE]	0.8020 [0.1288, 4.9926] 0.8131 0.8127	
No	32 / 224 (14.3)	22.1 [17.1, NE]	38 / 217 (17.5)	NE [NE, NE]	0.5983 [0.3694, 0.9690] 0.0368 0.0350	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.9722
Yes	6 / 39 (15.4)	NE [NE, NE]	8 / 36 (22.2)	NE [6.5, NE]	0.5781 [0.1992, 1.6780] 0.3135 0.3092	
No	29 / 205 (14.1)	22.1 [17.1, NE]	32 / 197 (16.2)	NE [NE, NE]	0.6136 [0.3646, 1.0324] 0.0658 0.0636	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.8914
Yes	20 / 145 (13.8)	22.1 [17.1, NE]	24 / 149 (16.1)	NE [10.2, NE]	0.6235 [0.3371, 1.1534] 0.1323 0.1291	
No	15 / 99 (15.2)	NE [13.7, NE]	16 / 84 (19.0)	NE [NE, NE]	0.6138 [0.3011, 1.2512] 0.1792 0.1759	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.2876
Normal renal function	13 / 116 (11.2)	NE [15.2, NE]	18 / 114 (15.8)	NE [NE, NE]	0.5557 [0.2698, 1.1442] 0.1109 0.1068	
Mild impairment	16 / 87 (18.4)	NE [18.0, NE]	12 / 81 (14.8)	NE [10.1, NE]	0.9245 [0.4309, 1.9833] 0.8402 0.8419	
Moderate impairment	6 / 41 (14.6)	22.1 [13.6, NE]	10 / 38 (26.3)	NE [5.7, NE]	0.3441 [0.1149, 1.0303] 0.0566 0.0464	

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

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Table 9.13.2 Treatment-Emergent Adverse Events (TEAEs) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
TEAEs associated with discontinuation of study medication	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.3993
Normal hepatic function	27 / 185 (14.6)	22.1 [17.1, NE]	27 / 177 (15.3)	NE [NE, NE]	0.6825 [0.3945, 1.1807] 0.1719 0.1695	
Mild, Moderate or Severe dysfunction	8 / 59 (13.6)	NE [NE, NE]	13 / 55 (23.6)	10.1 [7.4, NE]	0.4729 [0.1953, 1.1448] 0.0969 0.0893	

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

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.13.2_TEAE_SAF_SUB.rtf

Anhang 4-G 4.2 Unerwünschte Ereignisse von besonderem Interesse

Anhang 4-G 4.2.1 Unerwünschte Ereignisse von besonderem Interesse – SAF

Table 9.14.1 Treatment-emergent Adverse Events of Special Interest (AESI) - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Interstitial lung disease (ILD)/pneumonitis	34 (13.9)	NE [NE, NE]	3 (1.3)	NE [NE, NE]	10.0424 [3.0829, 32.7123] 0.0001	<.0001
Serious ILD/pneumonitis	5 (2.0)	NE [NE, NE]	3 (1.3)	NE [NE, NE]	1.4864 [0.3551, 6.2213] 0.5874	0.5849
Severe (CTCAE grade ≥3) ILD/pneumonitis	1 (0.4)	NE [NE, NE]	3 (1.3)	NE [NE, NE]	0.3005 [0.0312, 2.8895] 0.2978	0.2692
Left ventricular (LV) dysfunction	6 (2.5)	NE [NE, NE]	4 (1.7)	NE [NE, NE]	1.1542 [0.3237, 4.1156] 0.8251	0.8249

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:05 (CET); Program name: t_tte_wo_cens.sas; Output name: T.9.14.1_AESI_SAF.rtf

Table 9.14.1 Treatment-emergent Adverse Events of Special Interest (AESI) - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
Serious LV dysfunction	1 (0.4)	NE [NE, NE]	0	NE [NE, NE]	NE [NE, NE] NE	0.3584
Severe (CTCAE grade ≥3) LV dysfunction	3 (1.2)	NE [NE, NE]	0	NE [NE, NE]	NE [NE, NE] NE	0.1374

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from Cox proportional hazards model with treatment as categorical variable in the model. Inclusion of stratification factors is following the pooling strategy described in study SAP. CI and p-value are based on the Wald test.
[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-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
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Anhang 4-G 4.2.2 Unerwünschte Ereignisse von besonderem Interesse – Subgruppenanalyse – SAF

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.5081
IHC 3+	31 / 205 (15.1)	NE [17.8, NE]	3 / 196 (1.5)	NE [NE, NE]	9.3838 [2.8672, 30.7109] 0.0002 <.0001	
IHC 2+/ISH+	3 / 39 (7.7)	NE [NE, NE]	0 / 37	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						0.0879
Asia [excluding mainland China]	13 / 57 (22.8)	17.8 [8.3, NE]	3 / 59 (5.1)	NE [NE, NE]	4.1689 [1.1875, 14.6360] 0.0259 0.0155	
Western Europe	18 / 138 (13.0)	NE [NE, NE]	0 / 129	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	3 / 49 (6.1)	NE [NE, NE]	0 / 45	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.1100
<6 Months	8 / 61 (13.1)	NE [8.3, NE]	2 / 57 (3.5)	NE [NE, NE]	3.0040 [0.6347, 14.2182] 0.1655 0.1453	
≥ 6 Months	26 / 183 (14.2)	NE [17.8, NE]	1 / 176 (0.6)	NE [NE, NE]	23.6322 [3.2055, 174.2236] 0.0019 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.8568
<65	15 / 139 (10.8)	NE [17.8, NE]	1 / 123 (0.8)	NE [NE, NE]	12.0076 [1.5860, 90.9105] 0.0161 0.0021	
≥ 65	19 / 105 (18.1)	NE [NE, NE]	2 / 110 (1.8)	NE [NE, NE]	9.8126 [2.2831, 42.1744] 0.0021 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						0.2991
<75	27 / 220 (12.3)	NE [NE, NE]	1 / 198 (0.5)	NE [NE, NE]	21.9304 [2.9786, 161.4640] 0.0024 <.0001	
≥ 75	7 / 24 (29.2)	11.1 [4.1, NE]	2 / 35 (5.7)	NE [NE, NE]	6.0955 [1.2624, 29.4330] 0.0244 0.0103	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						0.4484
Male	30 / 186 (16.1)	NE [17.8, NE]	3 / 194 (1.5)	NE [NE, NE]	9.2655 [2.8235, 30.4047] 0.0002 <.0001	
Female	4 / 58 (6.9)	NE [NE, NE]	0 / 39	NE [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 Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						0.1343
White	12 / 115 (10.4)	NE [NE, NE]	0 / 120	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	16 / 101 (15.8)	17.8 [17.8, NE]	3 / 93 (3.2)	NE [NE, NE]	4.8044 [1.3990, 16.4991] 0.0127 0.0059	
Other	6 / 28 (21.4)	NE [11.1, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						0.4007
0	17 / 96 (17.7)	NE [17.8, NE]	2 / 81 (2.5)	NE [NE, NE]	6.0741 [1.3987, 26.3779] 0.0160 0.0061	
≥ 1	17 / 148 (11.5)	NE [NE, NE]	1 / 152 (0.7)	NE [NE, NE]	17.4217 [2.3191, 130.8745] 0.0055 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 Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						0.9571
Gastric	23 / 152 (15.1)	NE [17.8, NE]	2 / 139 (1.4)	NE [NE, NE]	10.2357 [2.4121, 43.4359] 0.0016 <.0001	
GEJ	11 / 92 (12.0)	NE [NE, NE]	1 / 94 (1.1)	NE [NE, NE]	9.7467 [1.2573, 75.5606] 0.0293 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 Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						0.0522
Intestinal	13 / 68 (19.1)	NE [11.1, NE]	3 / 63 (4.8)	NE [NE, NE]	3.3305 [0.9461, 11.7242] 0.0610 0.0472	
Diffuse	3 / 25 (12.0)	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	18 / 151 (11.9)	NE [17.8, NE]	0 / 152	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						0.0599
<2	13 / 72 (18.1)	NE [NE, NE]	0 / 72	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 2	21 / 172 (12.2)	NE [17.8, NE]	3 / 161 (1.9)	NE [NE, NE]	5.5130 [1.6412, 18.5193] 0.0058 0.0019	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						0.5061
Yes	3 / 31 (9.7)	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	31 / 213 (14.6)	NE [17.8, NE]	3 / 205 (1.5)	NE [NE, NE]	9.3100 [2.8453, 30.4628] 0.0002 <.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 Brookmeyer-Crowley method.
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Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						0.5125
Yes	3 / 20 (15.0)	NE [4.4, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	31 / 224 (13.8)	NE [NE, NE]	3 / 217 (1.4)	NE [NE, NE]	9.2801 [2.8357, 30.3699] 0.0002 <.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 Brookmeyer-Crowley method.
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Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.3274
Yes	5 / 39 (12.8)	NE [NE, NE]	0 / 36	NE [NE, NE]	NE [NE, NE] NE NE	
No	29 / 205 (14.1)	NE [NE, NE]	3 / 197 (1.5)	NE [NE, NE]	8.4448 [2.5706, 27.7430] 0.0004 <.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 Brookmeyer-Crowley method.
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Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						0.9243
Yes	22 / 145 (15.2)	NE [NE, NE]	2 / 149 (1.3)	NE [NE, NE]	10.8458 [2.5501, 46.1277] 0.0012 <.0001	
No	12 / 99 (12.1)	NE [17.8, NE]	1 / 84 (1.2)	NE [NE, NE]	8.8476 [1.1478, 68.1993] 0.0364 0.0115	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						0.3629
Normal renal function	14 / 116 (12.1)	NE [NE, NE]	2 / 114 (1.8)	NE [NE, NE]	6.3983 [1.4527, 28.1802] 0.0141 0.0048	
Mild impairment	11 / 87 (12.6)	NE [17.8, NE]	0 / 81	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	9 / 41 (22.0)	NE [NE, NE]	1 / 38 (2.6)	NE [NE, NE]	8.4455 [1.0697, 66.6799] 0.0430 0.0151	

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

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Interstitial lung disease (ILD)/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						0.1998
Normal hepatic function	24 / 185 (13.0)	NE [17.8, NE]	1 / 177 (0.6)	NE [NE, NE]	21.0180 [2.8410, 155.4906] 0.0029 <.0001	
Mild, Moderate or Severe dysfunction	10 / 59 (16.9)	NE [NE, NE]	2 / 55 (3.6)	NE [NE, NE]	4.3476 [0.9512, 19.8723] 0.0580 0.0390	

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

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						NE
IHC 3+	5 / 205 (2.4)	NE [NE, NE]	3 / 196 (1.5)	NE [NE, NE]	NE [NE, NE] NE NE	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	0 / 37	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] 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 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						NE
Asia [excluding mainland China]	1 / 57 (1.8)	NE [NE, NE]	3 / 59 (5.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	2 / 138 (1.4)	NE [NE, NE]	0 / 129	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	2 / 49 (4.1)	NE [NE, NE]	0 / 45	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						NE
<6 Months	1 / 61 (1.6)	NE [NE, NE]	2 / 57 (3.5)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 6 Months	4 / 183 (2.2)	NE [NE, NE]	1 / 176 (0.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						NE
<65	2 / 139 (1.4)	NE [NE, NE]	1 / 123 (0.8)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 65	3 / 105 (2.9)	NE [NE, NE]	2 / 110 (1.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						NE
<75	4 / 220 (1.8)	NE [NE, NE]	1 / 198 (0.5)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 75	1 / 24 (4.2)	NE [NE, NE]	2 / 35 (5.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						NE
Male	5 / 186 (2.7)	NE [NE, NE]	3 / 194 (1.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Female	0 / 58	NE [NE, NE]	0 / 39	NE [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 Brookmeyer-Crowley method.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						NE
White	1 / 115 (0.9)	NE [NE, NE]	0 / 120	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	3 / 101 (3.0)	NE [NE, NE]	3 / 93 (3.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	1 / 28 (3.6)	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						NE
0	0 / 96	NE [NE, NE]	2 / 81 (2.5)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 1	5 / 148 (3.4)	NE [NE, NE]	1 / 152 (0.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						NE
Gastric	4 / 152 (2.6)	NE [NE, NE]	2 / 139 (1.4)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	1 / 92 (1.1)	NE [NE, NE]	1 / 94 (1.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						NE
Intestinal	2 / 68 (2.9)	NE [NE, NE]	3 / 63 (4.8)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	3 / 151 (2.0)	NE [NE, NE]	0 / 152	NE [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 Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						NE
<2	2 / 72 (2.8)	NE [NE, NE]	0 / 72	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 2	3 / 172 (1.7)	NE [NE, NE]	3 / 161 (1.9)	NE [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 Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						NE
Yes	3 / 31 (9.7)	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	2 / 213 (0.9)	NE [NE, NE]	3 / 205 (1.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						NE
Yes	0 / 20	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	5 / 224 (2.2)	NE [NE, NE]	3 / 217 (1.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						NE
Yes	1 / 39 (2.6)	NE [NE, NE]	0 / 36	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 205 (2.0)	NE [NE, NE]	3 / 197 (1.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						NE
Yes	3 / 145 (2.1)	NE [NE, NE]	2 / 149 (1.3)	NE [NE, NE]	NE [NE, NE] NE NE	
No	2 / 99 (2.0)	NE [NE, NE]	1 / 84 (1.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						NE
Normal renal function	1 / 116 (0.9)	NE [NE, NE]	2 / 114 (1.8)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	1 / 87 (1.1)	NE [NE, NE]	0 / 81	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	3 / 41 (7.3)	NE [NE, NE]	1 / 38 (2.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						NE
Normal hepatic function	4 / 185 (2.2)	NE [NE, NE]	1 / 177 (0.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	1 / 59 (1.7)	NE [NE, NE]	2 / 55 (3.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						NE
IHC 3+	1 / 205 (0.5)	NE [NE, NE]	3 / 196 (1.5)	NE [NE, NE]	NE [NE, NE] NE NE	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	0 / 37	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						NE
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	3 / 59 (5.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	1 / 138 (0.7)	NE [NE, NE]	0 / 129	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	0 / 45	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						NE
<6 Months	0 / 61	NE [NE, NE]	2 / 57 (3.5)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 6 Months	1 / 183 (0.5)	NE [NE, NE]	1 / 176 (0.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						NE
<65	0 / 139	NE [NE, NE]	1 / 123 (0.8)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 65	1 / 105 (1.0)	NE [NE, NE]	2 / 110 (1.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						NE
<75	0 / 220	NE [NE, NE]	1 / 198 (0.5)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 75	1 / 24 (4.2)	NE [NE, NE]	2 / 35 (5.7)	NE [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 Brookmeyer-Crowley method.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						NE
Male	1 / 186 (0.5)	NE [NE, NE]	3 / 194 (1.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Female	0 / 58	NE [NE, NE]	0 / 39	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						NE
White	0 / 115	NE [NE, NE]	0 / 120	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	0 / 101	NE [NE, NE]	3 / 93 (3.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	1 / 28 (3.6)	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						NE
0	0 / 96	NE [NE, NE]	2 / 81 (2.5)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 1	1 / 148 (0.7)	NE [NE, NE]	1 / 152 (0.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						NE
Gastric	1 / 152 (0.7)	NE [NE, NE]	2 / 139 (1.4)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	0 / 92	NE [NE, NE]	1 / 94 (1.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						NE
Intestinal	1 / 68 (1.5)	NE [NE, NE]	3 / 63 (4.8)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	0 / 151	NE [NE, NE]	0 / 152	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						NE
<2	1 / 72 (1.4)	NE [NE, NE]	0 / 72	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 2	0 / 172	NE [NE, NE]	3 / 161 (1.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						NE
Yes	1 / 31 (3.2)	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 213	NE [NE, NE]	3 / 205 (1.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						NE
Yes	0 / 20	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 224 (0.4)	NE [NE, NE]	3 / 217 (1.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						NE
Yes	0 / 39	NE [NE, NE]	0 / 36	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 205 (0.5)	NE [NE, NE]	3 / 197 (1.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						NE
Yes	0 / 145	NE [NE, NE]	2 / 149 (1.3)	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 99 (1.0)	NE [NE, NE]	1 / 84 (1.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						NE
Normal renal function	0 / 116	NE [NE, NE]	2 / 114 (1.8)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	1 / 87 (1.1)	NE [NE, NE]	0 / 81	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	0 / 41	NE [NE, NE]	1 / 38 (2.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) ILD/pneumonitis	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						NE
Normal hepatic function	1 / 185 (0.5)	NE [NE, NE]	1 / 177 (0.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	0 / 59	NE [NE, NE]	2 / 55 (3.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						NE
IHC 3+	5 / 205 (2.4)	NE [NE, NE]	3 / 196 (1.5)	NE [NE, NE]	NE [NE, NE] NE NE	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	1 / 37 (2.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						NE
Asia [excluding mainland China]	1 / 57 (1.8)	NE [NE, NE]	0 / 59	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	3 / 138 (2.2)	NE [NE, NE]	2 / 129 (1.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	2 / 49 (4.1)	NE [NE, NE]	2 / 45 (4.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						0.9999
<6 Months	0 / 61	NE [NE, NE]	0 / 57	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 6 Months	6 / 183 (3.3)	NE [NE, NE]	4 / 176 (2.3)	NE [NE, NE]	1.2028 [0.3378, 4.2826] 0.7757 0.7754	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						NE
<65	4 / 139 (2.9)	NE [NE, NE]	2 / 123 (1.6)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 65	2 / 105 (1.9)	NE [NE, NE]	2 / 110 (1.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						NE
<75	5 / 220 (2.3)	NE [NE, NE]	4 / 198 (2.0)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 75	1 / 24 (4.2)	NE [NE, NE]	0 / 35	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						NE
Male	5 / 186 (2.7)	NE [NE, NE]	4 / 194 (2.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Female	1 / 58 (1.7)	NE [NE, NE]	0 / 39	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						NE
White	2 / 115 (1.7)	NE [NE, NE]	3 / 120 (2.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	4 / 101 (4.0)	NE [NE, NE]	1 / 93 (1.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						NE
0	2 / 96 (2.1)	NE [NE, NE]	1 / 81 (1.2)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 1	4 / 148 (2.7)	NE [NE, NE]	3 / 152 (2.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						NE
Gastric	4 / 152 (2.6)	NE [NE, NE]	1 / 139 (0.7)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	2 / 92 (2.2)	NE [NE, NE]	3 / 94 (3.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						NE
Intestinal	2 / 68 (2.9)	NE [NE, NE]	1 / 63 (1.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	1 / 25 (4.0)	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	3 / 151 (2.0)	NE [NE, NE]	3 / 152 (2.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						NE
<2	0 / 72	NE [NE, NE]	1 / 72 (1.4)	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 2	6 / 172 (3.5)	NE [NE, NE]	3 / 161 (1.9)	NE [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 Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						NE
Yes	1 / 31 (3.2)	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	5 / 213 (2.3)	NE [NE, NE]	3 / 205 (1.5)	NE [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 Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						NE
Yes	2 / 20 (10.0)	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 224 (1.8)	NE [NE, NE]	4 / 217 (1.8)	NE [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 Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						NE
Yes	3 / 39 (7.7)	NE [NE, NE]	1 / 36 (2.8)	NE [NE, NE]	NE [NE, NE] NE NE	
No	3 / 205 (1.5)	NE [NE, NE]	3 / 197 (1.5)	NE [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 Brookmeyer-Crowley method.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						NE
Yes	3 / 145 (2.1)	NE [NE, NE]	3 / 149 (2.0)	NE [NE, NE]	NE [NE, NE] NE NE	
No	3 / 99 (3.0)	NE [NE, NE]	1 / 84 (1.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						NE
Normal renal function	6 / 116 (5.2)	NE [NE, NE]	3 / 114 (2.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	0 / 87	NE [NE, NE]	1 / 81 (1.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	0 / 41	NE [NE, NE]	0 / 38	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Left ventricular (LV) dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						NE
Normal hepatic function	5 / 185 (2.7)	NE [NE, NE]	4 / 177 (2.3)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	1 / 59 (1.7)	NE [NE, NE]	0 / 55	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						NE
IHC 3+	0 / 205	NE [NE, NE]	0 / 196	NE [NE, NE]	NE [NE, NE] NE NE	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	0 / 37	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						NE
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	0 / 59	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	1 / 138 (0.7)	NE [NE, NE]	0 / 129	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	0 / 45	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						NE
<6 Months	0 / 61	NE [NE, NE]	0 / 57	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 6 Months	1 / 183 (0.5)	NE [NE, NE]	0 / 176	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						NE
<65	0 / 139	NE [NE, NE]	0 / 123	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 65	1 / 105 (1.0)	NE [NE, NE]	0 / 110	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						NE
<75	1 / 220 (0.5)	NE [NE, NE]	0 / 198	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 75	0 / 24	NE [NE, NE]	0 / 35	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						NE
Male	1 / 186 (0.5)	NE [NE, NE]	0 / 194	NE [NE, NE]	NE [NE, NE] NE NE	
Female	0 / 58	NE [NE, NE]	0 / 39	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						NE
White	1 / 115 (0.9)	NE [NE, NE]	0 / 120	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	0 / 101	NE [NE, NE]	0 / 93	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						NE
0	1 / 96 (1.0)	NE [NE, NE]	0 / 81	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 1	0 / 148	NE [NE, NE]	0 / 152	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						NE
Gastric	1 / 152 (0.7)	NE [NE, NE]	0 / 139	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	0 / 92	NE [NE, NE]	0 / 94	NE [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 Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						NE
Intestinal	0 / 68	NE [NE, NE]	0 / 63	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	1 / 151 (0.7)	NE [NE, NE]	0 / 152	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						NE
<2	0 / 72	NE [NE, NE]	0 / 72	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 2	1 / 172 (0.6)	NE [NE, NE]	0 / 161	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						NE
Yes	0 / 31	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 213 (0.5)	NE [NE, NE]	0 / 205	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						NE
Yes	0 / 20	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 224 (0.4)	NE [NE, NE]	0 / 217	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						NE
Yes	0 / 39	NE [NE, NE]	0 / 36	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 205 (0.5)	NE [NE, NE]	0 / 197	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						NE
Yes	0 / 145	NE [NE, NE]	0 / 149	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 99 (1.0)	NE [NE, NE]	0 / 84	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						NE
Normal renal function	1 / 116 (0.9)	NE [NE, NE]	0 / 114	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	0 / 87	NE [NE, NE]	0 / 81	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	0 / 41	NE [NE, NE]	0 / 38	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Serious LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						NE
Normal hepatic function	1 / 185 (0.5)	NE [NE, NE]	0 / 177	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	0 / 59	NE [NE, NE]	0 / 55	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						NE
IHC 3+	2 / 205 (1.0)	NE [NE, NE]	0 / 196	NE [NE, NE]	NE [NE, NE] NE NE	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	0 / 37	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Geography stratification factor						NE
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	0 / 59	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	3 / 138 (2.2)	NE [NE, NE]	0 / 129	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	0 / 45	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Time to progression on first-line therapy from IRT						NE
<6 Months	0 / 61	NE [NE, NE]	0 / 57	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 6 Months	3 / 183 (1.6)	NE [NE, NE]	0 / 176	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						NE
<65	1 / 139 (0.7)	NE [NE, NE]	0 / 123	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 65	2 / 105 (1.9)	NE [NE, NE]	0 / 110	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Age at randomization						NE
<75	2 / 220 (0.9)	NE [NE, NE]	0 / 198	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 75	1 / 24 (4.2)	NE [NE, NE]	0 / 35	NE [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 Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Sex						NE
Male	2 / 186 (1.1)	NE [NE, NE]	0 / 194	NE [NE, NE]	NE [NE, NE] NE NE	
Female	1 / 58 (1.7)	NE [NE, NE]	0 / 39	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
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Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Race						NE
White	2 / 115 (1.7)	NE [NE, NE]	0 / 120	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	1 / 101 (1.0)	NE [NE, NE]	0 / 93	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
ECOG						NE
0	1 / 96 (1.0)	NE [NE, NE]	0 / 81	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 1	2 / 148 (1.4)	NE [NE, NE]	0 / 152	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Primary tumor location						NE
Gastric	2 / 152 (1.3)	NE [NE, NE]	0 / 139	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	1 / 92 (1.1)	NE [NE, NE]	0 / 94	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Histological subtype						NE
Intestinal	1 / 68 (1.5)	NE [NE, NE]	0 / 63	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	2 / 151 (1.3)	NE [NE, NE]	0 / 152	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Number of metastatic sites						NE
<2	0 / 72	NE [NE, NE]	0 / 72	NE [NE, NE]	NE [NE, NE] NE NE	
≥ 2	3 / 172 (1.7)	NE [NE, NE]	0 / 161	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior adjuvant/neoadjuvant therapy						NE
Yes	0 / 31	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	3 / 213 (1.4)	NE [NE, NE]	0 / 205	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior nivolumab or pembrolizumab treatment						NE
Yes	0 / 20	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	3 / 224 (1.3)	NE [NE, NE]	0 / 217	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						NE
Yes	0 / 39	NE [NE, NE]	0 / 36	NE [NE, NE]	NE [NE, NE] NE NE	
No	3 / 205 (1.5)	NE [NE, NE]	0 / 197	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
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Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Presence of liver metastasis at baseline						NE
Yes	2 / 145 (1.4)	NE [NE, NE]	0 / 149	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 99 (1.0)	NE [NE, NE]	0 / 84	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Renal function at baseline						NE
Normal renal function	3 / 116 (2.6)	NE [NE, NE]	0 / 114	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	0 / 87	NE [NE, NE]	0 / 81	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	0 / 41	NE [NE, NE]	0 / 38	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: Confidence Interval; HR: Hazard Ratio; NE: not estimable

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Table 9.14.2 Treatment-emergent Adverse Events of Special Interest (AESI) - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
Severe (CTCAE grade ≥3) LV dysfunction	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
Hepatic function at baseline						NE
Normal hepatic function	2 / 185 (1.1)	NE [NE, NE]	0 / 177	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	1 / 59 (1.7)	NE [NE, NE]	0 / 55	NE [NE, NE]	NE [NE, NE] NE NE	

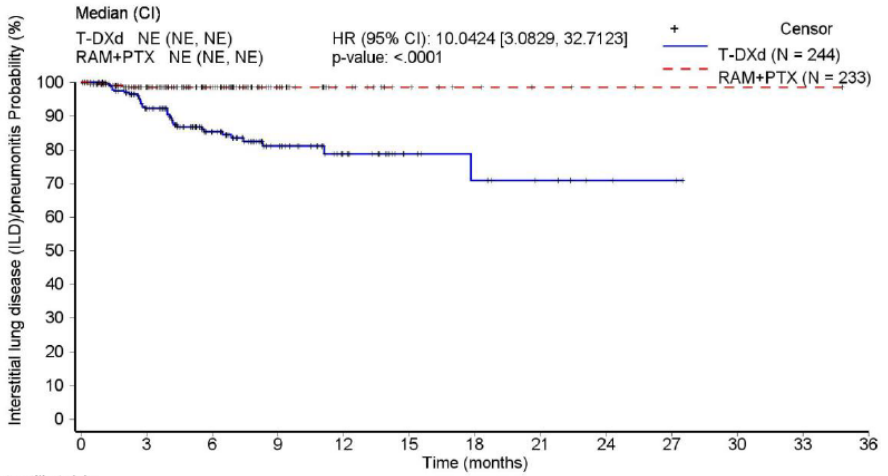
N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:02 (CET); Program name: t_tte_subgroup.sas; Output name: T.9.14.2_AESI_SAF_SUB.rtf

Anhang 4-G 4.2.3 Unerwünschte Ereignisse von besonderem Interesse – Kaplan-Meier-Plot – SAF

Figure 9.14.1 Treatment-emergent Adverse Events of Special Interest (AESI) - Kaplan-Meier plot - Safety Analysis Set

Interstitial lung disease (ILD)/pneumonitis



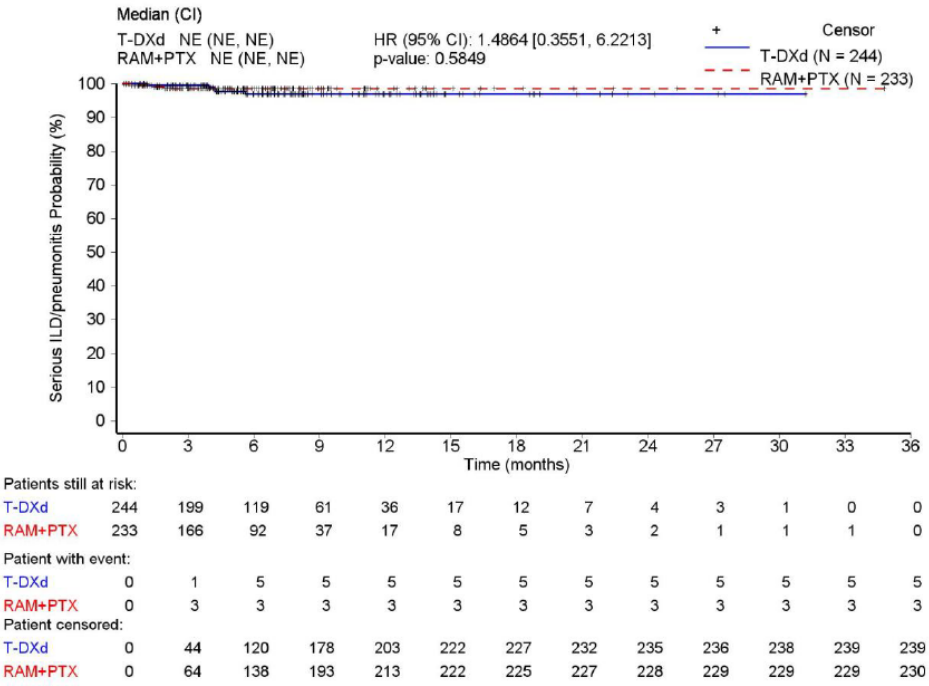
Patients still at risk:													
T-DXd	244	184	108	52	27	13	9	6	3	2	0	0	0
RAM+PTX	233	166	92	37	17	8	5	3	2	1	1	1	0
Patient with event:													
T-DXd	0	17	28	32	33	33	34	34	34	34	34	34	34
RAM+PTX	0	3	3	3	3	3	3	3	3	3	3	3	3
Patient censored:													
T-DXd	0	43	108	160	184	198	201	204	207	208	210	210	210
RAM+PTX	0	64	138	193	213	222	225	227	228	229	229	229	230

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; HR: Hazard Ratio; NE: not estimable

Data source:
DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location:
DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:20 (CET); Program name: f_km.sas; Output name: F.9.14.1_AESI_SAF.rtf

Figure 9.14.1 Treatment-emergent Adverse Events of Special Interest (AESI) - Kaplan-Meier plot - Safety Analysis Set

Serious ILD/pneumonitis



Patients still at risk:													
T-DXd	244	199	119	61	36	17	12	7	4	3	1	0	0
RAM+PTX	233	166	92	37	17	8	5	3	2	1	1	1	0
Patient with event:													
T-DXd	0	1	5	5	5	5	5	5	5	5	5	5	5
RAM+PTX	0	3	3	3	3	3	3	3	3	3	3	3	3
Patient censored:													
T-DXd	0	44	120	178	203	222	227	232	235	236	238	239	239
RAM+PTX	0	64	138	193	213	222	225	227	228	229	229	229	230

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; HR: Hazard Ratio; NE: not estimable

Data source:
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Program Location:
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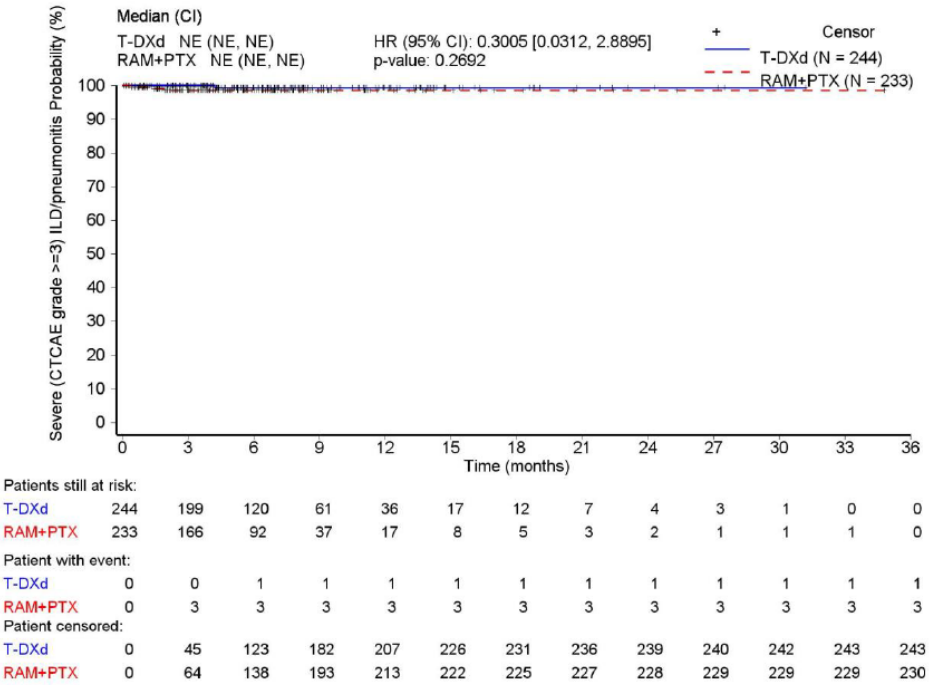
Run date: 12AUG2025 15:20 (CET); Program name: f_km.sas; Output name: F.9.14.1_AESI_SAF.rtf

Figure 9.14.1 Treatment-emergent Adverse Events of Special Interest (AESI) - Kaplan-Meier plot - Safety Analysis Set

Severe (CTCAE grade >=3) ILD/pneumonitis



Patients still at risk:													
T-DXd	244	199	120	61	36	17	12	7	4	3	1	0	0
RAM+PTX	233	166	92	37	17	8	5	3	2	1	1	1	0
Patient with event:													
T-DXd	0	0	1	1	1	1	1	1	1	1	1	1	1
RAM+PTX	0	3	3	3	3	3	3	3	3	3	3	3	3
Patient censored:													
T-DXd	0	45	123	182	207	226	231	236	239	240	242	243	243
RAM+PTX	0	64	138	193	213	222	225	227	228	229	229	229	230

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; HR: Hazard Ratio; NE: not estimable

Data source:
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Program Location:
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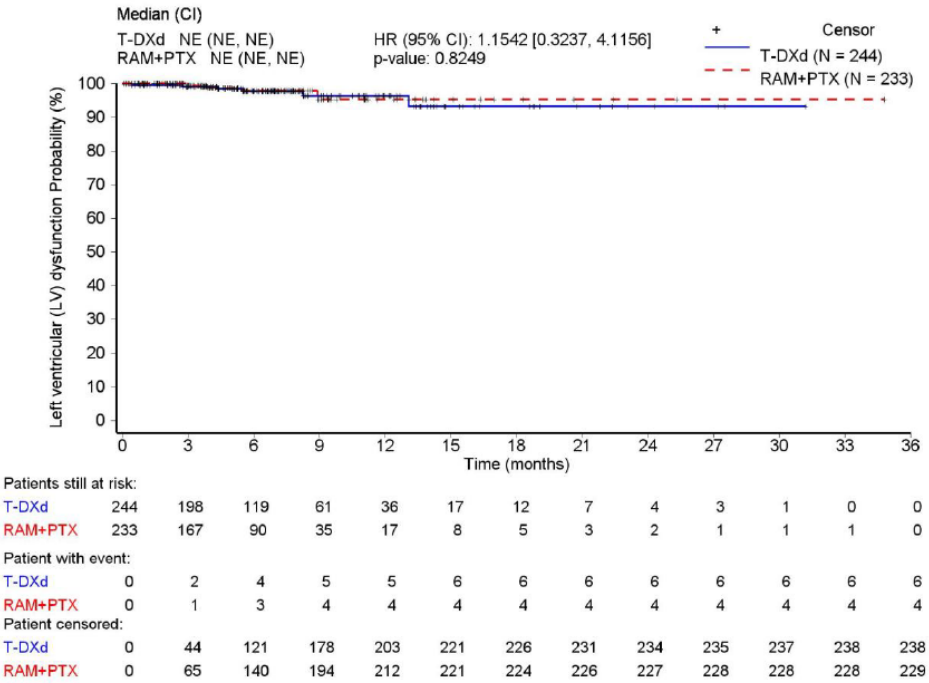
Run date: 12AUG2025 15:20 (CET); Program name: f_km.sas; Output name: F.9.14.1_AESI_SAF.rtf

Figure 9.14.1 Treatment-emergent Adverse Events of Special Interest (AESI) - Kaplan-Meier plot - Safety Analysis Set

Left ventricular (LV) dysfunction



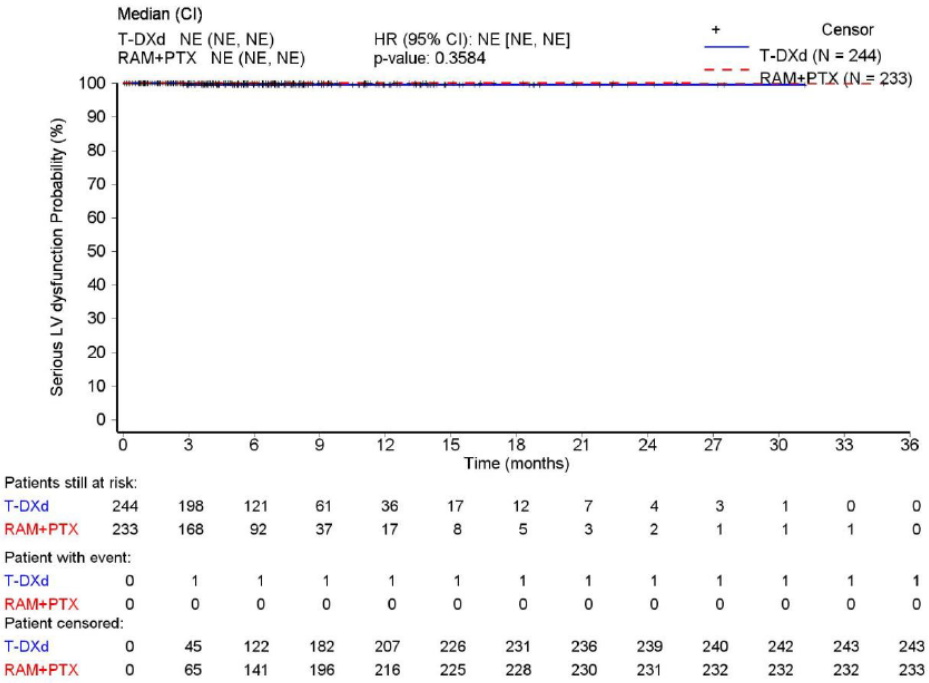
Patients still at risk:													
T-DXd	244	198	119	61	36	17	12	7	4	3	1	0	0
RAM+PTX	233	167	90	35	17	8	5	3	2	1	1	1	0
Patient with event:													
T-DXd	0	2	4	5	5	6	6	6	6	6	6	6	6
RAM+PTX	0	1	3	4	4	4	4	4	4	4	4	4	4
Patient censored:													
T-DXd	0	44	121	178	203	221	226	231	234	235	237	238	238
RAM+PTX	0	65	140	194	212	221	224	226	227	228	228	228	229

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; HR: Hazard Ratio; NE: not estimable

Data source:
DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
Program Location:
DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 12AUG2025 15:20 (CET); Program name: f_km.sas; Output name: F.9.14.1_AESI_SAF.rtf

Figure 9.14.1 Treatment-emergent Adverse Events of Special Interest (AESI) - Kaplan-Meier plot - Safety Analysis Set

Serious LV dysfunction



Patients still at risk:													
T-DXd	244	198	121	61	36	17	12	7	4	3	1	0	0
RAM+PTX	233	168	92	37	17	8	5	3	2	1	1	1	0
Patient with event:													
T-DXd	0	1	1	1	1	1	1	1	1	1	1	1	1
RAM+PTX	0	0	0	0	0	0	0	0	0	0	0	0	0
Patient censored:													
T-DXd	0	45	122	182	207	226	231	236	239	240	242	243	243
RAM+PTX	0	65	141	196	216	225	228	230	231	232	232	232	233

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; HR: Hazard Ratio; NE: not estimable

Data source:
DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
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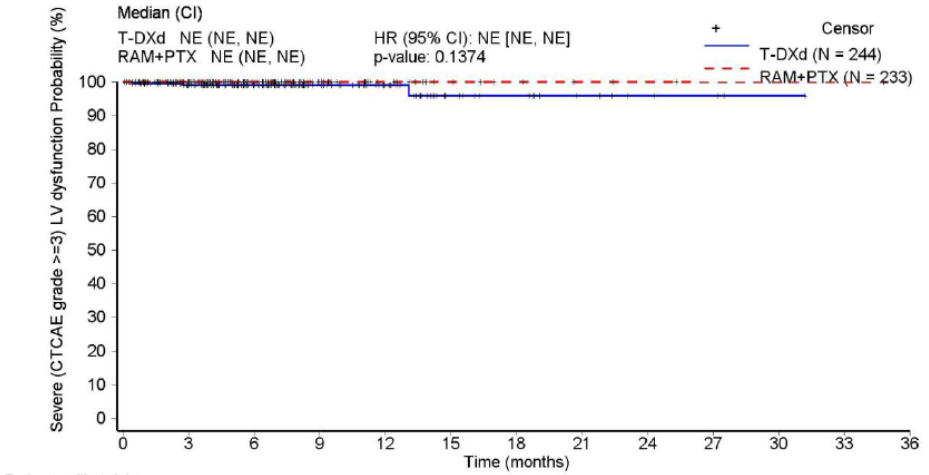
Run date: 12AUG2025 15:20 (CET); Program name: f_km.sas; Output name: F.9.14.1_AESI_SAF.rtf

Figure 9.14.1 Treatment-emergent Adverse Events of Special Interest (AESI) - Kaplan-Meier plot - Safety Analysis Set

Severe (CTCAE grade >=3) LV dysfunction



Patients still at risk:													
T-DXd	244	198	121	61	36	17	12	7	4	3	1	0	0
RAM+PTX	233	168	92	37	17	8	5	3	2	1	1	1	0
Patient with event:													
T-DXd	0	2	2	2	2	3	3	3	3	3	3	3	3
RAM+PTX	0	0	0	0	0	0	0	0	0	0	0	0	0
Patient censored:													
T-DXd	0	44	121	181	206	224	229	234	237	238	240	241	241
RAM+PTX	0	65	141	196	216	225	228	230	231	232	232	232	233

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; HR: Hazard Ratio; NE: not estimable

Data source:
DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADTTESA
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Run date: 12AUG2025 15:20 (CET); Program name: f_km.sas; Output name: F.9.14.1_AESI_SAF.rtf

Anhang 4-G 4.3 Unerwünschte Ereignisse nach SOC und PT

Anhang 4-G 4.3.1 Jegliche Unerwünschte Ereignisse nach SOC und PT – SAF

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	199 (81.6)	0.5 [0.3, 0.7]	180 (77.3)	0.9 [0.6, 1.4]	1.2691 [1.0367, 1.5536] 0.0209	0.0242
PT: Nausea	129 (52.9)	3.5 [1.4, 8.0]	47 (20.2)	NE [15.8, NE]	3.4360 [2.4587, 4.8019] <.0001	<0.0001
PT: Diarrhoea	86 (35.2)	11.5 [10.1, NE]	66 (28.3)	NE [13.7, NE]	1.2217 [0.8862, 1.6842] 0.2215	0.2211
PT: Constipation	66 (27.0)	NE [NE, NE]	43 (18.5)	NE [NE, NE]	1.4108 [0.9603, 2.0728] 0.0795	0.0783
PT: Vomiting	64 (26.2)	NE [NE, NE]	33 (14.2)	NE [NE, NE]	1.9230 [1.2631, 2.9276] 0.0023	0.0019

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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	39 (16.0)	NE [NE, NE]	29 (12.4)	NE [15.8, NE]	1.1881 [0.7338, 1.9238] 0.4833	0.4823
PT: Dysphagia	21 (8.6)	NE [NE, NE]	16 (6.9)	NE [NE, NE]	1.0119 [0.5259, 1.9471] 0.9718	0.9724
PT: Abdominal pain upper	19 (7.8)	NE [NE, NE]	18 (7.7)	NE [NE, NE]	0.9315 [0.4883, 1.7770] 0.8295	0.8303
PT: Ascites	16 (6.6)	NE [NE, NE]	15 (6.4)	NE [NE, NE]	0.8934 [0.4402, 1.8131] 0.7549	0.7556
PT: Abdominal distension	14 (5.7)	NE [NE, NE]	12 (5.2)	NE [NE, NE]	0.9597 [0.4425, 2.0815] 0.9171	0.9169

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Stomatitis	14 (5.7)	NE [NE, NE]	31 (13.3)	NE [NE, NE]	0.3767 [0.1999, 0.7097] 0.0025	0.0017
PT: Gastrooesophageal reflux disease	12 (4.9)	NE [NE, NE]	9 (3.9)	NE [NE, NE]	1.0961 [0.4605, 2.6091] 0.8357	0.8348
PT: Dyspepsia	11 (4.5)	NE [NE, NE]	11 (4.7)	NE [NE, NE]	0.8488 [0.3667, 1.9645] 0.7018	0.7013
PT: Flatulence	7 (2.9)	NE [NE, NE]	3 (1.3)	NE [NE, NE]	2.1055 [0.5441, 8.1473] 0.2808	0.2696
PT: Dry mouth	5 (2.0)	NE [NE, NE]	6 (2.6)	NE [NE, NE]	0.6542 [0.1981, 2.1597] 0.4862	0.4830

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Upper gastrointestinal haemorrhage	5 (2.0)	NE [19.0, NE]	7 (3.0)	NE [NE, NE]	0.5735 [0.1810, 1.8175] 0.3448	0.3390
PT: Haemorrhoids	3 (1.2)	NE [NE, NE]	10 (4.3)	NE [NE, NE]	0.2342 [0.0640, 0.8568] 0.0283	0.0171
PT: Toothache	3 (1.2)	NE [NE, NE]	7 (3.0)	NE [NE, NE]	0.3630 [0.0937, 1.4065] 0.1425	0.1262

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: General disorders and administration site conditions						
PT: Any	167 (68.4)	1.8 [1.1, 2.6]	164 (70.4)	1.7 [1.3, 2.1]	0.9357 [0.7530, 1.1626] 0.5484	0.5216
PT: Asthenia	74 (30.3)	NE [12.8, NE]	53 (22.7)	NE [NE, NE]	1.3266 [0.9321, 1.8880] 0.1165	0.1165
PT: Fatigue	58 (23.8)	NE [16.4, NE]	56 (24.0)	NE [NE, NE]	0.9479 [0.6557, 1.3702] 0.7758	0.7668
PT: Pyrexia	39 (16.0)	NE [20.7, NE]	34 (14.6)	NE [NE, NE]	0.9427 [0.5931, 1.4984] 0.8029	0.8040
PT: Oedema peripheral	25 (10.2)	NE [21.5, NE]	30 (12.9)	NE [14.7, NE]	0.6151 [0.3583, 1.0559] 0.0780	0.0747

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Malaise	17 (7.0)	NE [NE, NE]	10 (4.3)	NE [19.9, NE]	1.5885 [0.7265, 3.4733] 0.2463	0.2434
PT: Disease progression	8 (3.3)	NE [NE, NE]	18 (7.7)	NE [NE, NE]	0.3710 [0.1611, 0.8541] 0.0198	0.0152
PT: Mucosal inflammation	6 (2.5)	NE [NE, NE]	8 (3.4)	NE [NE, NE]	0.6523 [0.2262, 1.8815] 0.4292	0.4256
PT: Influenza like illness	4 (1.6)	NE [NE, NE]	9 (3.9)	NE [NE, NE]	0.3585 [0.1096, 1.1720] 0.0896	0.0767

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	153 (62.7)	2.5 [1.4, 3.5]	113 (48.5)	5.6 [3.6, 8.0]	1.3589 [1.0639, 1.7358] 0.0141	0.0138
PT: Decreased appetite	98 (40.2)	11.1 [10.3, NE]	70 (30.0)	15.6 [8.2, NE]	1.3654 [1.0038, 1.8573] 0.0473	0.0473
PT: Hypoalbuminaemia	39 (16.0)	NE [NE, NE]	23 (9.9)	NE [NE, NE]	1.4824 [0.8847, 2.4840] 0.1350	0.1329
PT: Hypokalaemia	39 (16.0)	NE [NE, NE]	21 (9.0)	NE [NE, NE]	1.6081 [0.9442, 2.7387] 0.0804	0.0778
PT: Hyponatraemia	15 (6.1)	NE [NE, NE]	18 (7.7)	NE [NE, NE]	0.6775 [0.3408, 1.3470] 0.2668	0.2640

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Hyperglycaemia	13 (5.3)	NE [NE, NE]	9 (3.9)	NE [NE, NE]	1.2214 [0.5202, 2.8675] 0.6460	0.6457
PT: Hypocalcaemia	13 (5.3)	NE [NE, NE]	16 (6.9)	NE [NE, NE]	0.6395 [0.3061, 1.3360] 0.2343	0.2300
PT: Hypomagnesaemia	12 (4.9)	NE [21.3, NE]	9 (3.9)	NE [NE, NE]	1.0953 [0.4574, 2.6227] 0.8382	0.8377
PT: Hypoproteinaemia	9 (3.7)	NE [NE, NE]	8 (3.4)	NE [NE, NE]	0.9944 [0.3833, 2.5797] 0.9909	0.9898
PT: Hypophosphataemia	7 (2.9)	NE [NE, NE]	5 (2.1)	NE [NE, NE]	1.1534 [0.3633, 3.6617] 0.8087	0.8085

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Hyperkalaemia	3 (1.2)	NE [NE, NE]	8 (3.4)	NE [NE, NE]	0.3234 [0.0856, 1.2210] 0.0958	0.0793

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	149 (61.1)	2.1 [1.1, 4.0]	123 (52.8)	4.6 [2.3, 5.6]	1.1943 [0.9401, 1.5172] 0.1460	0.1567
PT: Neutrophil count decreased	80 (32.8)	NE [NE, NE]	74 (31.8)	NE [NE, NE]	0.9395 [0.6847, 1.2892] 0.6991	0.6914
PT: White blood cell count decreased	58 (23.8)	NE [NE, NE]	43 (18.5)	NE [NE, NE]	1.2368 [0.8336, 1.8352] 0.2910	0.2817
PT: Weight decreased	53 (21.7)	NE [NE, NE]	26 (11.2)	NE [NE, NE]	1.8403 [1.1506, 2.9435] 0.0109	0.0097
PT: Aspartate aminotransferase increased	52 (21.3)	NE [14.9, NE]	26 (11.2)	NE [NE, NE]	1.8258 [1.1396, 2.9253] 0.0123	0.0111

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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	50 (20.5)	NE [NE, NE]	31 (13.3)	NE [NE, NE]	1.5003 [0.9578, 2.3500] 0.0764	0.0832
PT: Alanine aminotransferase increased	35 (14.3)	NE [NE, NE]	19 (8.2)	NE [NE, NE]	1.6539 [0.9448, 2.8954] 0.0782	0.0758
PT: Blood alkaline phosphatase increased	25 (10.2)	NE [23.1, NE]	16 (6.9)	NE [NE, NE]	1.3525 [0.7207, 2.5380] 0.3472	0.3467
PT: Lymphocyte count decreased	23 (9.4)	NE [NE, NE]	11 (4.7)	NE [NE, NE]	1.8057 [0.8779, 3.7141] 0.1083	0.1032
PT: Gamma-glutamyltransferase increased	22 (9.0)	NE [NE, NE]	14 (6.0)	NE [NE, NE]	1.4266 [0.7296, 2.7895] 0.2990	0.2977

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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 bilirubin increased	14 (5.7)	NE [NE, NE]	14 (6.0)	NE [16.5, NE]	0.8309 [0.3940, 1.7521] 0.6265	0.6260
PT: Blood creatinine increased	11 (4.5)	NE [NE, NE]	6 (2.6)	NE [NE, NE]	1.6445 [0.6078, 4.4496] 0.3274	0.3224
PT: Blood lactate dehydrogenase increased	9 (3.7)	NE [NE, NE]	5 (2.1)	NE [NE, NE]	1.4857 [0.4962, 4.4482] 0.4792	0.4764
PT: C-reactive protein increased	6 (2.5)	NE [NE, NE]	4 (1.7)	NE [NE, NE]	1.3245 [0.3730, 4.7028] 0.6638	0.6632
PT: Electrocardiogram QT prolonged	6 (2.5)	NE [NE, NE]	5 (2.1)	NE [NE, NE]	0.9637 [0.2931, 3.1684] 0.9514	0.9515

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	144 (59.0)	2.8 [1.4, 4.9]	134 (57.5)	2.3 [1.5, 3.7]	0.9617 [0.7597, 1.2173] 0.7454	0.7314
PT: Anaemia	119 (48.8)	6.4 [4.2, 21.4]	103 (44.2)	7.2 [3.7, NE]	1.0441 [0.8017, 1.3598] 0.7490	0.7562
PT: Neutropenia	43 (17.6)	NE [18.4, NE]	43 (18.5)	NE [NE, NE]	0.8748 [0.5727, 1.3360] 0.5358	0.5357
PT: Thrombocytopenia	18 (7.4)	NE [NE, NE]	6 (2.6)	NE [NE, NE]	2.7984 [1.1099, 7.0553] 0.0292	0.0231
PT: Leukopenia	14 (5.7)	NE [NE, NE]	12 (5.2)	NE [NE, NE]	1.0660 [0.4930, 2.3049] 0.8710	0.8710

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Febrile neutropenia	7 (2.9)	NE [NE, NE]	11 (4.7)	NE [NE, NE]	0.5813 [0.2253, 1.5000] 0.2620	0.2562
PT: Lymphopenia	7 (2.9)	NE [NE, NE]	7 (3.0)	NE [NE, NE]	0.8812 [0.3087, 2.5154] 0.8132	0.8135

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	96 (39.3)	11.1 [6.9, NE]	96 (41.2)	7.0 [4.4, NE]	0.7878 [0.5930, 1.0467] 0.1000	0.0989
PT: Cough	31 (12.7)	NE [NE, NE]	34 (14.6)	NE [NE, NE]	0.7451 [0.4565, 1.2162] 0.2392	0.2380
PT: Interstitial lung disease	20 (8.2)	NE [18.8, NE]	3 (1.3)	NE [NE, NE]	5.5500 [1.6460, 18.7138] 0.0057	0.0019
PT: Pneumonitis	19 (7.8)	NE [NE, NE]	2 (0.9)	NE [NE, NE]	8.1164 [1.8890, 34.8734] 0.0049	0.0008
PT: Dyspnoea	17 (7.0)	NE [NE, NE]	21 (9.0)	NE [NE, NE]	0.6763 [0.3555, 1.2868] 0.2334	0.2308

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Hiccups	14 (5.7)	NE [NE, NE]	5 (2.1)	NE [NE, NE]	2.6263 [0.9459, 7.2919] 0.0639	0.0539
PT: Pulmonary embolism	9 (3.7)	NE [NE, NE]	5 (2.1)	NE [NE, NE]	1.5669 [0.5246, 4.6804] 0.4212	0.4172
PT: Productive cough	7 (2.9)	NE [NE, NE]	7 (3.0)	NE [NE, NE]	0.7899 [0.2757, 2.2630] 0.6605	0.6597
PT: Rhinorrhoea	7 (2.9)	NE [NE, NE]	9 (3.9)	NE [NE, NE]	0.6525 [0.2426, 1.7555] 0.3979	0.3946
PT: Oropharyngeal pain	5 (2.0)	NE [NE, NE]	6 (2.6)	NE [NE, NE]	0.6788 [0.2052, 2.2455] 0.5257	0.5232

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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	4 (1.6)	NE [NE, NE]	34 (14.6)	NE [NE, NE]	0.0962 [0.0341, 0.2712] <.0001	<0.0001
PT: Dysphonia	1 (0.4)	NE [NE, NE]	10 (4.3)	NE [NE, NE]	0.0851 [0.0109, 0.6658] 0.0189	0.0028

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	90 (36.9)	9.4 [7.7, 14.1]	87 (37.3)	8.0 [6.1, 10.3]	0.8276 [0.6144, 1.1147] 0.2131	0.2127
PT: Pneumonia	23 (9.4)	NE [NE, NE]	13 (5.6)	NE [NE, NE]	1.4526 [0.7344, 2.8730] 0.2833	0.2806
PT: COVID-19	22 (9.0)	NE [NE, NE]	16 (6.9)	NE [13.6, NE]	1.1031 [0.5772, 2.1084] 0.7665	0.7670
PT: Urinary tract infection	10 (4.1)	NE [NE, NE]	11 (4.7)	NE [NE, NE]	0.7885 [0.3345, 1.8584] 0.5869	0.5865
PT: Upper respiratory tract infection	8 (3.3)	NE [NE, NE]	4 (1.7)	NE [NE, NE]	1.5606 [0.4676, 5.2078] 0.4692	0.4656

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Nasopharyngitis	6 (2.5)	NE [NE, NE]	4 (1.7)	NE [17.9, NE]	1.1589 [0.3230, 4.1580] 0.8210	0.8209

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	87 (35.7)	NE [9.0, NE]	94 (40.3)	NE [4.2, NE]	0.7744 [0.5781, 1.0374] 0.0865	0.0855
PT: Alopecia	61 (25.0)	NE [NE, NE]	62 (26.6)	NE [NE, NE]	0.8856 [0.6218, 1.2612] 0.5006	0.5055
PT: Rash	9 (3.7)	NE [NE, NE]	11 (4.7)	NE [NE, NE]	0.7104 [0.2928, 1.7237] 0.4496	0.4478
PT: Pruritus	8 (3.3)	NE [NE, NE]	8 (3.4)	NE [NE, NE]	0.7904 [0.2953, 2.1158] 0.6397	0.6389
PT: Dry skin	7 (2.9)	NE [NE, NE]	7 (3.0)	NE [NE, NE]	0.7901 [0.2761, 2.2607] 0.6604	0.6597

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders						
PT: Any	62 (25.4)	NE [13.2, NE]	114 (48.9)	5.1 [3.7, 6.6]	0.3872 [0.2835, 0.5287] <.0001	<0.0001
PT: Dizziness	15 (6.1)	NE [NE, NE]	3 (1.3)	NE [NE, NE]	4.4591 [1.2901, 15.4123] 0.0182	0.0097
PT: Headache	10 (4.1)	NE [NE, NE]	14 (6.0)	NE [NE, NE]	0.5613 [0.2477, 1.2719] 0.1665	0.1606
PT: Dysgeusia	8 (3.3)	NE [NE, NE]	11 (4.7)	NE [NE, NE]	0.6479 [0.2604, 1.6116] 0.3505	0.3466
PT: Peripheral sensory neuropathy	8 (3.3)	NE [NE, NE]	35 (15.0)	NE [14.1, NE]	0.1685 [0.0779, 0.3648] <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Neuropathy peripheral	7 (2.9)	NE [NE, NE]	24 (10.3)	NE [NE, NE]	0.2514 [0.1083, 0.5836] 0.0013	0.0005
PT: Paraesthesia	4 (1.6)	NE [NE, NE]	14 (6.0)	NE [NE, NE]	0.2443 [0.0804, 0.7428] 0.0130	0.0071
PT: Hypoaesthesia	3 (1.2)	NE [NE, NE]	9 (3.9)	NE [NE, NE]	0.2920 [0.0790, 1.0791] 0.0649	0.0495
PT: Neurotoxicity	3 (1.2)	NE [NE, NE]	12 (5.2)	NE [NE, NE]	0.2134 [0.0601, 0.7573] 0.0168	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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	41 (16.8)	NE [NE, NE]	63 (27.0)	14.6 [14.6, NE]	0.5101 [0.3430, 0.7587] 0.0009	0.0007
PT: Back pain	10 (4.1)	NE [NE, NE]	18 (7.7)	NE [14.6, NE]	0.4291 [0.1962, 0.9385] 0.0341	0.0294
PT: Arthralgia	6 (2.5)	NE [NE, NE]	11 (4.7)	NE [NE, NE]	0.4417 [0.1623, 1.2026] 0.1098	0.1009
PT: Myalgia	4 (1.6)	NE [NE, NE]	12 (5.2)	NE [NE, NE]	0.2757 [0.0886, 0.8586] 0.0262	0.0175
PT: Pain in extremity	2 (0.8)	NE [NE, NE]	9 (3.9)	NE [NE, NE]	0.1979 [0.0427, 0.9165] 0.0383	0.0212

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Hepatobiliary disorders						
PT: Any	21 (8.6)	29.0 [NE, NE]	17 (7.3)	NE [14.7, NE]	1.1019 [0.5805, 2.0913] 0.7667	0.7660

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	21 (8.6)	NE [NE, NE]	23 (9.9)	NE [NE, NE]	0.7651 [0.4229, 1.3842] 0.3761	0.3752
PT: Insomnia	14 (5.7)	NE [NE, NE]	15 (6.4)	NE [NE, NE]	0.7792 [0.3754, 1.6174] 0.5031	0.5023

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Vascular disorders						
PT: Any	18 (7.4)	NE [NE, NE]	56 (24.0)	NE [12.6, NE]	0.2512 [0.1474, 0.4281] <.0001	<0.0001
PT: Hypertension	6 (2.5)	NE [NE, NE]	44 (18.9)	NE [NE, NE]	0.1098 [0.0468, 0.2580] <.0001	<0.0001
PT: Hypotension	5 (2.0)	NE [NE, NE]	5 (2.1)	NE [NE, NE]	0.8516 [0.2447, 2.9639] 0.8007	0.8005

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Cardiac disorders						
PT: Any	16 (6.6)	NE [19.9, NE]	12 (5.2)	NE [NE, NE]	1.0563 [0.4985, 2.2384] 0.8862	0.8879

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	14 (5.7)	NE [NE, NE]	15 (6.4)	NE [14.4, NE]	0.6765 [0.3221, 1.4209] 0.3020	0.2994

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Renal and urinary disorders						
PT: Any	12 (4.9)	NE [NE, NE]	31 (13.3)	NE [NE, NE]	0.2975 [0.1524, 0.5809] 0.0004	0.0002
PT: Proteinuria	0	NE [NE, NE]	17 (7.3)	NE [NE, NE]	NE [NE, NE] NE	<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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	8 (3.3)	NE [NE, NE]	26 (11.2)	NE [NE, NE]	0.2514 [0.1136, 0.5560]	0.0002
PT: Infusion related reaction	0	NE [NE, NE]	10 (4.3)	NE [NE, NE]	0.0007 NE [NE, NE] NE	0.0010

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
PT: Any	4 (1.6)	NE [NE, NE]	12 (5.2)	NE [NE, NE]	0.2923 [0.0942, 0.9071] 0.0333	0.0235

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Reproductive system and breast disorders						
PT: Any	4 (1.6)	NE [NE, NE]	6 (2.6)	NE [NE, NE]	0.5811 [0.1637, 2.0623] 0.4009	0.3952

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Table 9.16.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Ear and labyrinth disorders						
PT: Any	2 (0.8)	NE [NE, NE]	9 (3.9)	NE [NE, NE]	0.1943 [0.0420, 0.8998] 0.0362	0.0195

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:07 (CET); Program name: t_tte_socpt.sas; Output name: T.9.16.1_10TEAE_SAF.rtf

Anhang 4-G 4.3.2 Jegliche Unerwünschte Ereignisse nach SOC und PT mit statistisch signifikantem Ergebnis auf Endpunktebene – Subgruppenanalyse – SAF

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.4043
IHC 3+	173 / 205 (84.4)	0.5 [0.3, 0.7]	154 / 196 (78.6)	1.0 [0.6, 1.6]	1.3197 [1.0612, 1.6411] 0.0126 0.0145	
IHC 2+/ISH+	26 / 39 (66.7)	0.4 [0.1, 2.8]	26 / 37 (70.3)	0.5 [0.3, 3.3]	1.0859 [0.6297, 1.8725] 0.7669 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Geography stratification factor						0.7080
Asia [excluding mainland China]	43 / 57 (75.4)	0.3 [0.2, 1.3]	41 / 59 (69.5)	1.4 [0.6, 2.6]	1.4022 [0.9122, 2.1553] 0.1233 0.1312	
Western Europe	119 / 138 (86.2)	0.5 [0.3, 0.8]	106 / 129 (82.2)	0.7 [0.4, 1.0]	1.1639 [0.8947, 1.5141] 0.2581 0.2729	
Mainland China/Rest of World (ROW)	37 / 49 (75.5)	0.3 [0.1, 1.6]	33 / 45 (73.3)	2.5 [0.5, 3.3]	1.3860 [0.8635, 2.2246] 0.1764 0.1846	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Time to progression on first-line therapy from IRT						0.8258
<6 Months	47 / 61 (77.0)	0.4 [0.2, 1.4]	43 / 57 (75.4)	0.9 [0.5, 2.1]	1.3774 [0.9047, 2.0971] 0.1354 0.1394	
≥6 Months	152 / 183 (83.1)	0.5 [0.3, 0.7]	137 / 176 (77.8)	0.9 [0.5, 1.6]	1.2549 [0.9952, 1.5822] 0.0549 0.0610	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Age at randomization						0.1346
<65	112 / 139 (80.6)	0.5 [0.3, 1.1]	98 / 123 (79.7)	0.9 [0.5, 1.6]	1.0982 [0.8365, 1.4417] 0.4999 0.5294	
≥65	87 / 105 (82.9)	0.4 [0.2, 0.5]	82 / 110 (74.5)	1.0 [0.5, 1.7]	1.5265 [1.1261, 2.0693] 0.0064 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Age at randomization						0.9119
<75	181 / 220 (82.3)	0.4 [0.3, 0.6]	155 / 198 (78.3)	0.9 [0.6, 1.4]	1.2515 [1.0092, 1.5520] 0.0410 0.0478	
≥75	18 / 24 (75.0)	0.7 [0.4, 3.6]	25 / 35 (71.4)	1.4 [0.5, 3.3]	1.3249 [0.7203, 2.4371] 0.3655 0.3533	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Sex						0.3137
Male	151 / 186 (81.2)	0.5 [0.3, 1.0]	152 / 194 (78.4)	0.9 [0.6, 1.4]	1.2109 [0.9660, 1.5178] 0.0970 0.1062	
Female	48 / 58 (82.8)	0.3 [0.1, 0.5]	28 / 39 (71.8)	1.0 [0.5, 2.2]	1.5207 [0.9518, 2.4295] 0.0795 0.0781	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Race						0.3922
White	96 / 115 (83.5)	0.5 [0.3, 0.8]	97 / 120 (80.8)	0.8 [0.4, 1.4]	1.1975 [0.9016, 1.5904] 0.2132 0.2274	
Asian	78 / 101 (77.2)	0.3 [0.2, 0.8]	66 / 93 (71.0)	1.4 [0.7, 2.6]	1.4560 [1.0479, 2.0230] 0.0252 0.0277	
Other	25 / 28 (89.3)	0.7 [0.1, 2.1]	17 / 20 (85.0)	0.4 [0.0, 1.6]	0.9490 [0.5107, 1.7635] 0.8685 0.8446	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
ECOG						0.3214
0	77 / 96 (80.2)	0.5 [0.3, 1.0]	64 / 81 (79.0)	0.9 [0.5, 2.0]	1.1126 [0.7968, 1.5537] 0.5310 0.5547	
≥1	122 / 148 (82.4)	0.3 [0.2, 0.6]	116 / 152 (76.3)	1.0 [0.6, 1.6]	1.3731 [1.0641, 1.7717] 0.0148 0.0167	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Primary tumor location						0.5733
Gastric	118 / 152 (77.6)	0.5 [0.3, 1.1]	104 / 139 (74.8)	1.2 [0.6, 2.2]	1.2218 [0.9381, 1.5914] 0.1373 0.1442	
GEJ	81 / 92 (88.0)	0.3 [0.1, 0.5]	76 / 94 (80.9)	0.8 [0.5, 1.4]	1.3443 [0.9809, 1.8425] 0.0658 0.0751	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Histological subtype						0.4244
Intestinal	56 / 68 (82.4)	0.3 [0.2, 0.7]	45 / 63 (71.4)	0.9 [0.5, 1.6]	1.4561 [0.9822, 2.1587] 0.0614 0.0602	
Diffuse	17 / 25 (68.0)	0.7 [0.1, 1.4]	16 / 18 (88.9)	1.2 [0.3, 1.6]	0.9269 [0.4672, 1.8390] 0.8281 0.8032	
Others	126 / 151 (83.4)	0.5 [0.3, 0.8]	119 / 152 (78.3)	0.9 [0.5, 1.7]	1.2632 [0.9822, 1.6247] 0.0688 0.0776	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Number of metastatic sites						0.8390
<2	57 / 72 (79.2)	0.5 [0.3, 0.9]	58 / 72 (80.6)	0.9 [0.4, 1.7]	1.2303 [0.8521, 1.7764] 0.2687 0.2811	
≥2	142 / 172 (82.6)	0.4 [0.2, 0.7]	122 / 161 (75.8)	0.9 [0.6, 1.6]	1.2920 [1.0133, 1.6474] 0.0388 0.0437	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Prior adjuvant/neoadjuvant therapy						0.2419
Yes	26 / 31 (83.9)	0.5 [0.1, 2.3]	18 / 28 (64.3)	1.4 [0.5, 6.5]	1.8038 [0.9747, 3.3382] 0.0603 0.0634	
No	173 / 213 (81.2)	0.5 [0.3, 0.7]	162 / 205 (79.0)	0.9 [0.6, 1.4]	1.2185 [0.9828, 1.5107] 0.0715 0.0793	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Prior nivolumab or pembrolizumab treatment						0.1239
Yes	18 / 20 (90.0)	0.2 [0.1, 0.3]	13 / 16 (81.3)	2.1 [0.4, 3.0]	2.4218 [1.1454, 5.1205] 0.0206 0.0177	
No	181 / 224 (80.8)	0.5 [0.3, 0.8]	167 / 217 (77.0)	0.9 [0.6, 1.4]	1.2170 [0.9856, 1.5028] 0.0680 0.0750	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						0.2365
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						
Yes	32 / 39 (82.1)	0.3 [0.1, 1.5]	27 / 36 (75.0)	2.0 [0.5, 5.0]	1.6688 [0.9944, 2.8007] 0.0525 0.0522	
No	167 / 205 (81.5)	0.5 [0.3, 0.7]	153 / 197 (77.7)	0.9 [0.5, 1.4]	1.2092 [0.9702, 1.5069] 0.0909 0.1010	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Presence of liver metastasis at baseline						0.9747
Yes	117 / 145 (80.7)	0.5 [0.3, 0.7]	110 / 149 (73.8)	0.8 [0.5, 1.4]	1.2808 [0.9866, 1.6626] 0.0630 0.0643	
No	82 / 99 (82.8)	0.4 [0.1, 1.0]	70 / 84 (83.3)	1.2 [0.5, 2.1]	1.2705 [0.9220, 1.7507] 0.1434 0.1640	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Renal function at baseline						0.6028
Normal renal function	91 / 116 (78.4)	0.5 [0.2, 1.0]	93 / 114 (81.6)	0.9 [0.6, 1.6]	1.1784 [0.8816, 1.5751] 0.2674 0.2892	
Mild impairment	72 / 87 (82.8)	0.5 [0.3, 0.9]	57 / 81 (70.4)	0.9 [0.5, 2.6]	1.3465 [0.9505, 1.9075] 0.0940 0.0957	
Moderate impairment	36 / 41 (87.8)	0.4 [0.1, 1.3]	30 / 38 (78.9)	1.1 [0.3, 2.7]	1.5866 [0.9720, 2.5898] 0.0648 0.0664	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Any						
Hepatic function at baseline						0.1253
Normal hepatic function	153 / 185 (82.7)	0.4 [0.2, 0.6]	136 / 177 (76.8)	1.2 [0.7, 1.8]	1.3791 [1.0935, 1.7392] 0.0066 0.0079	
Mild, Moderate or Severe dysfunction	46 / 59 (78.0)	0.7 [0.3, 1.6]	43 / 55 (78.2)	0.6 [0.4, 1.0]	0.9564 [0.6301, 1.4515] 0.8340 0.8318	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.1814
IHC 3+	111 / 205 (54.1)	3.1 [1.4, 8.0]	44 / 196 (22.4)	NE [15.8, NE]	3.1885 [2.2468, 4.5248] <.0001 <.0001	
IHC 2+/ISH+	18 / 39 (46.2)	6.3 [0.3, NE]	3 / 37 (8.1)	NE [NE, NE]	7.1649 [2.1073, 24.3610] 0.0016 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Geography stratification factor						0.7202
Asia [excluding mainland China]	29 / 57 (50.9)	6.1 [0.8, NE]	9 / 59 (15.3)	15.8 [15.8, NE]	4.1473 [1.9609, 8.7718] 0.0002 <.0001	
Western Europe	77 / 138 (55.8)	2.1 [0.8, 6.0]	31 / 129 (24.0)	NE [9.2, NE]	3.1896 [2.0973, 4.8509] <.0001 <.0001	
Mainland China/Rest of World (ROW)	23 / 49 (46.9)	3.4 [0.2, NE]	7 / 45 (15.6)	NE [NE, NE]	3.9656 [1.6963, 9.2704] 0.0015 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Time to progression on first-line therapy from IRT						0.7484
<6 Months	29 / 61 (47.5)	6.3 [0.9, NE]	9 / 57 (15.8)	NE [7.0, NE]	3.9772 [1.8793, 8.4170] 0.0003 <.0001	
≥6 Months	100 / 183 (54.6)	3.1 [0.9, 8.0]	38 / 176 (21.6)	NE [15.8, NE]	3.3202 [2.2833, 4.8281] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Age at randomization						0.2867
<65	80 / 139 (57.6)	2.2 [0.8, 6.3]	32 / 123 (26.0)	NE [9.2, NE]	2.9992 [1.9879, 4.5252] <.0001 <.0001	
≥65	49 / 105 (46.7)	4.9 [1.5, NE]	15 / 110 (13.6)	NE [10.1, NE]	4.3481 [2.4345, 7.7658] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Age at randomization						0.6297
<75	120 / 220 (54.5)	3.0 [0.9, 6.3]	41 / 198 (20.7)	NE [15.8, NE]	3.4800 [2.4392, 4.9649] <.0001 <.0001	
≥75	9 / 24 (37.5)	NE [2.6, NE]	6 / 35 (17.1)	NE [10.1, NE]	2.7187 [0.9646, 7.6631] 0.0585 0.0484	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Sex						0.5228
Male	95 / 186 (51.1)	4.4 [1.4, NE]	39 / 194 (20.1)	NE [NE, NE]	3.2244 [2.2196, 4.6841] <.0001 <.0001	
Female	34 / 58 (58.6)	2.1 [0.7, 6.0]	8 / 39 (20.5)	NE [7.0, NE]	4.8543 [2.1427, 10.9971] 0.0002 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Race						0.2658
White	59 / 115 (51.3)	3.8 [0.9, NE]	25 / 120 (20.8)	NE [10.1, NE]	3.3204 [2.0752, 5.3127] <.0001 <.0001	
Asian	51 / 101 (50.5)	6.1 [1.1, NE]	14 / 93 (15.1)	NE [15.8, NE]	4.3857 [2.4252, 7.9312] <.0001 <.0001	
Other	19 / 28 (67.9)	1.0 [0.4, 6.0]	8 / 20 (40.0)	NE [0.5, NE]	1.9830 [0.8676, 4.5321] 0.1045 0.1068	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
ECOG						0.5877
0	50 / 96 (52.1)	4.4 [0.8, NE]	17 / 81 (21.0)	NE [9.2, NE]	3.0598 [1.7630, 5.3103] <.0001 <.0001	
≥1	79 / 148 (53.4)	2.7 [0.9, NE]	30 / 152 (19.7)	15.8 [15.8, NE]	3.6566 [2.3991, 5.5733] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Primary tumor location						0.6170
Gastric	76 / 152 (50.0)	4.9 [2.2, NE]	27 / 139 (19.4)	15.8 [10.1, NE]	3.2876 [2.1173, 5.1048] <.0001 <.0001	
GEJ	53 / 92 (57.6)	0.8 [0.3, NE]	20 / 94 (21.3)	NE [NE, NE]	3.7422 [2.2331, 6.2712] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Histological subtype						0.6599
Intestinal	34 / 68 (50.0)	3.8 [0.4, NE]	15 / 63 (23.8)	15.8 [7.1, NE]	2.7995 [1.5208, 5.1532] 0.0009 0.0006	
Diffuse	12 / 25 (48.0)	NE [0.4, NE]	4 / 18 (22.2)	8.3 [8.3, NE]	2.9285 [0.9402, 9.1215] 0.0638 0.0530	
Others	83 / 151 (55.0)	3.1 [1.4, 6.3]	28 / 152 (18.4)	NE [NE, NE]	3.9199 [2.5508, 6.0239] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Number of metastatic sites						0.0673
<2	37 / 72 (51.4)	2.6 [0.8, NE]	22 / 72 (30.6)	15.8 [8.3, NE]	2.3550 [1.3819, 4.0135] 0.0016 0.0012	
≥2	92 / 172 (53.5)	3.7 [1.4, 11.0]	25 / 161 (15.5)	NE [NE, NE]	4.3928 [2.8214, 6.8393] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Prior adjuvant/neoadjuvant therapy						0.9979
Yes	17 / 31 (54.8)	3.5 [0.1, NE]	6 / 28 (21.4)	10.1 [10.1, NE]	3.1984 [1.2584, 8.1292] 0.0146 0.0105	
No	112 / 213 (52.6)	3.4 [1.4, 11.0]	41 / 205 (20.0)	NE [15.8, NE]	3.4662 [2.4217, 4.9612] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Prior nivolumab or pembrolizumab treatment						0.2637
Yes	12 / 20 (60.0)	0.6 [0.1, NE]	2 / 16 (12.5)	NE [NE, NE]	6.7226 [1.4972, 30.1849] 0.0129 0.0039	
No	117 / 224 (52.2)	3.7 [1.4, 11.0]	45 / 217 (20.7)	NE [15.8, NE]	3.2797 [2.3238, 4.6289] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.0637
Yes	20 / 39 (51.3)	3.4 [0.1, NE]	3 / 36 (8.3)	NE [NE, NE]	8.3378 [2.4714, 28.1297] 0.0006 <.0001	
No	109 / 205 (53.2)	3.5 [1.4, 8.0]	44 / 197 (22.3)	NE [15.8, NE]	3.0930 [2.1777, 4.3932] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Presence of liver metastasis at baseline						0.8158
Yes	75 / 145 (51.7)	3.8 [1.4, NE]	28 / 149 (18.8)	NE [NE, NE]	3.5814 [2.3180, 5.5335] <.0001 <.0001	
No	54 / 99 (54.5)	2.3 [0.7, NE]	19 / 84 (22.6)	15.8 [15.8, NE]	3.1945 [1.8894, 5.4010] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Renal function at baseline						0.7686
Normal renal function	62 / 116 (53.4)	2.3 [0.5, NE]	26 / 114 (22.8)	NE [15.8, NE]	3.2985 [2.0820, 5.2258] <.0001 <.0001	
Mild impairment	44 / 87 (50.6)	6.0 [0.9, NE]	12 / 81 (14.8)	NE [10.1, NE]	4.1903 [2.2110, 7.9414] <.0001 <.0001	
Moderate impairment	23 / 41 (56.1)	2.6 [0.7, NE]	9 / 38 (23.7)	NE [NE, NE]	2.8639 [1.3194, 6.2163] 0.0078 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Hepatic function at baseline						0.6740
Normal hepatic function	98 / 185 (53.0)	3.1 [0.9, NE]	38 / 177 (21.5)	NE [15.8, NE]	3.2540 [2.2352, 4.7371] <.0001 <.0001	
Mild, Moderate or Severe dysfunction	31 / 59 (52.5)	3.5 [0.9, NE]	9 / 55 (16.4)	NE [7.1, NE]	4.1345 [1.9641, 8.7033] 0.0002 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.3221
IHC 3+	56 / 205 (27.3)	NE [NE, NE]	27 / 196 (13.8)	NE [NE, NE]	2.1023 [1.3280, 3.3279] 0.0015 0.0012	
IHC 2+/ISH+	8 / 39 (20.5)	NE [NE, NE]	6 / 37 (16.2)	9.9 [9.9, NE]	1.1886 [0.4079, 3.4635] 0.7516 0.7538	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Geography stratification factor						0.1493
Asia [excluding mainland China]	9 / 57 (15.8)	NE [NE, NE]	5 / 59 (8.5)	NE [NE, NE]	1.8585 [0.6217, 5.5557] 0.2673 0.2605	
Western Europe	38 / 138 (27.5)	NE [12.4, NE]	24 / 129 (18.6)	NE [9.9, NE]	1.4951 [0.8964, 2.4937] 0.1234 0.1212	
Mainland China/Rest of World (ROW)	17 / 49 (34.7)	NE [4.9, NE]	4 / 45 (8.9)	NE [NE, NE]	4.6916 [1.5769, 13.9587] 0.0055 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Time to progression on first-line therapy from IRT						0.5219
<6 Months	13 / 61 (21.3)	NE [NE, NE]	8 / 57 (14.0)	NE [NE, NE]	1.5322 [0.6337, 3.7044] 0.3435 0.3404	
≥6 Months	51 / 183 (27.9)	NE [NE, NE]	25 / 176 (14.2)	NE [NE, NE]	2.0638 [1.2786, 3.3313] 0.0030 0.0024	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Age at randomization						0.9160
<65	42 / 139 (30.2)	NE [NE, NE]	21 / 123 (17.1)	NE [NE, NE]	1.8705 [1.1077, 3.1585] 0.0191 0.0173	
≥65	22 / 105 (21.0)	NE [NE, NE]	12 / 110 (10.9)	NE [NE, NE]	1.9348 [0.9552, 3.9189] 0.0668 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Age at randomization						0.7006
<75	58 / 220 (26.4)	NE [NE, NE]	27 / 198 (13.6)	NE [NE, NE]	2.0034 [1.2685, 3.1640] 0.0029 0.0024	
≥75	6 / 24 (25.0)	NE [9.2, NE]	6 / 35 (17.1)	NE [7.9, NE]	1.5372 [0.4951, 4.7728] 0.4570 0.4537	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Sex						0.8786
Male	48 / 186 (25.8)	NE [NE, NE]	26 / 194 (13.4)	NE [NE, NE]	1.9363 [1.2005, 3.1230] 0.0067 0.0058	
Female	16 / 58 (27.6)	NE [6.9, NE]	7 / 39 (17.9)	NE [7.9, NE]	1.7903 [0.7355, 4.3574] 0.1994 0.1939	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Race						0.1118
White	30 / 115 (26.1)	NE [12.4, NE]	19 / 120 (15.8)	NE [NE, NE]	1.6822 [0.9465, 2.9900] 0.0763 0.0729	
Asian	26 / 101 (25.7)	NE [NE, NE]	8 / 93 (8.6)	NE [NE, NE]	3.2847 [1.4868, 7.2568] 0.0033 0.0019	
Other	8 / 28 (28.6)	NE [5.2, NE]	6 / 20 (30.0)	7.9 [1.5, NE]	0.7714 [0.2629, 2.2638] 0.6366 0.6357	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
ECOG						0.4741
0	23 / 96 (24.0)	NE [12.4, NE]	12 / 81 (14.8)	NE [9.9, NE]	1.5200 [0.7546, 3.0614] 0.2412 0.2378	
≥1	41 / 148 (27.7)	NE [NE, NE]	21 / 152 (13.8)	NE [NE, NE]	2.1920 [1.2953, 3.7096] 0.0035 0.0027	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Primary tumor location						0.5780
Gastric	35 / 152 (23.0)	NE [NE, NE]	19 / 139 (13.7)	NE [NE, NE]	1.7619 [1.0076, 3.0808] 0.0470 0.0447	
GEJ	29 / 92 (31.5)	NE [9.2, NE]	14 / 94 (14.9)	NE [NE, NE]	2.2062 [1.1657, 4.1753] 0.0151 0.0127	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Histological subtype						0.4155
Intestinal	16 / 68 (23.5)	NE [NE, NE]	12 / 63 (19.0)	NE [NE, NE]	1.2842 [0.6068, 2.7178] 0.5132 0.5176	
Diffuse	6 / 25 (24.0)	NE [6.9, NE]	2 / 18 (11.1)	NE [NE, NE]	2.2054 [0.4432, 10.9757] 0.3341 0.3217	
Others	42 / 151 (27.8)	NE [12.4, NE]	19 / 152 (12.5)	NE [NE, NE]	2.3267 [1.3530, 4.0010] 0.0023 0.0017	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Number of metastatic sites						0.0225
<2	15 / 72 (20.8)	NE [12.4, NE]	16 / 72 (22.2)	NE [9.9, NE]	0.9858 [0.4869, 1.9958] 0.9683 0.9663	
≥2	49 / 172 (28.5)	NE [NE, NE]	17 / 161 (10.6)	NE [NE, NE]	2.8274 [1.6280, 4.9107] 0.0002 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Prior adjuvant/neoadjuvant therapy						0.1586
Yes	12 / 31 (38.7)	6.7 [3.5, NE]	3 / 28 (10.7)	NE [NE, NE]	4.2606 [1.2001, 15.1266] 0.0250 0.0147	
No	52 / 213 (24.4)	NE [NE, NE]	30 / 205 (14.6)	NE [NE, NE]	1.7012 [1.0850, 2.6673] 0.0206 0.0192	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Prior nivolumab or pembrolizumab treatment						0.2156
Yes	7 / 20 (35.0)	NE [1.6, NE]	1 / 16 (6.3)	NE [NE, NE]	5.6391 [0.6901, 46.0776] 0.1065 0.0690	
No	57 / 224 (25.4)	NE [NE, NE]	32 / 217 (14.7)	NE [NE, NE]	1.7863 [1.1583, 2.7547] 0.0087 0.0078	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.1139
Yes	13 / 39 (33.3)	NE [5.8, NE]	3 / 36 (8.3)	NE [NE, NE]	4.4637 [1.2714, 15.6718] 0.0196 0.0105	
No	51 / 205 (24.9)	NE [NE, NE]	30 / 197 (15.2)	NE [NE, NE]	1.6611 [1.0577, 2.6087] 0.0275 0.0261	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Presence of liver metastasis at baseline						0.9216
Yes	34 / 145 (23.4)	NE [NE, NE]	19 / 149 (12.8)	NE [NE, NE]	1.8564 [1.0586, 3.2556] 0.0309 0.0284	
No	30 / 99 (30.3)	NE [9.2, NE]	14 / 84 (16.7)	NE [NE, NE]	1.9657 [1.0419, 3.7086] 0.0369 0.0337	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Renal function at baseline						0.0494
Normal renal function	25 / 116 (21.6)	NE [NE, NE]	22 / 114 (19.3)	NE [NE, NE]	1.1824 [0.6666, 2.0974] 0.5666 0.5666	
Mild impairment	30 / 87 (34.5)	NE [6.7, NE]	8 / 81 (9.9)	NE [NE, NE]	3.6740 [1.6842, 8.0149] 0.0011 0.0005	
Moderate impairment	9 / 41 (22.0)	NE [12.4, NE]	3 / 38 (7.9)	NE [7.9, NE]	2.5048 [0.6657, 9.4249] 0.1744 0.1610	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Vomiting						
Hepatic function at baseline						0.6387
Normal hepatic function	49 / 185 (26.5)	NE [NE, NE]	26 / 177 (14.7)	NE [NE, NE]	1.8602 [1.1553, 2.9950] 0.0106 0.0096	
Mild, Moderate or Severe dysfunction	15 / 59 (25.4)	NE [NE, NE]	6 / 55 (10.9)	NE [NE, NE]	2.3723 [0.9194, 6.1213] 0.0741 0.0655	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.6817
IHC 3+	13 / 205 (6.3)	NE [NE, NE]	28 / 196 (14.3)	NE [NE, NE]	0.4023 [0.2083, 0.7770] 0.0067 0.0050	
IHC 2+/ISH+	1 / 39 (2.6)	NE [17.3, NE]	3 / 37 (8.1)	NE [NE, NE]	0.0000 [0.0000, NE] 0.9956 0.0598	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Geography stratification factor						0.5649
Asia [excluding mainland China]	6 / 57 (10.5)	NE [NE, NE]	10 / 59 (16.9)	NE [NE, NE]	0.5744 [0.2086, 1.5814] 0.2832 0.2787	
Western Europe	7 / 138 (5.1)	NE [17.3, NE]	16 / 129 (12.4)	NE [NE, NE]	0.3364 [0.1372, 0.8246] 0.0172 0.0126	
Mainland China/Rest of World (ROW)	1 / 49 (2.0)	NE [NE, NE]	5 / 45 (11.1)	NE [NE, NE]	0.1891 [0.0221, 1.6191] 0.1285 0.0888	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Time to progression on first-line therapy from IRT						0.0962
<6 Months	1 / 61 (1.6)	NE [NE, NE]	8 / 57 (14.0)	NE [NE, NE]	0.1097 [0.0137, 0.8779] 0.0373 0.0113	
≥6 Months	13 / 183 (7.1)	NE [NE, NE]	23 / 176 (13.1)	NE [NE, NE]	0.4754 [0.2401, 0.9411] 0.0328 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Age at randomization						0.4677
<65	9 / 139 (6.5)	NE [17.3, NE]	15 / 123 (12.2)	NE [NE, NE]	0.4489 [0.1958, 1.0293] 0.0585 0.0521	
≥65	5 / 105 (4.8)	NE [NE, NE]	16 / 110 (14.5)	NE [NE, NE]	0.3024 [0.1107, 0.8257] 0.0196 0.0133	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Age at randomization						0.2276
<75	11 / 220 (5.0)	NE [NE, NE]	26 / 198 (13.1)	NE [NE, NE]	0.3234 [0.1591, 0.6576] 0.0018 0.0010	
≥75	3 / 24 (12.5)	NE [NE, NE]	5 / 35 (14.3)	NE [NE, NE]	0.8949 [0.2137, 3.7486] 0.8793 0.8792	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Sex						0.5789
Male	11 / 186 (5.9)	NE [NE, NE]	24 / 194 (12.4)	NE [NE, NE]	0.4319 [0.2114, 0.8823] 0.0212 0.0177	
Female	3 / 58 (5.2)	17.3 [NE, NE]	7 / 39 (17.9)	NE [7.5, NE]	0.2796 [0.0714, 1.0947] 0.0672 0.0513	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Race						0.9403
White	6 / 115 (5.2)	NE [17.3, NE]	14 / 120 (11.7)	NE [NE, NE]	0.3718 [0.1412, 0.9791] 0.0452 0.0375	
Asian	7 / 101 (6.9)	NE [NE, NE]	16 / 93 (17.2)	NE [NE, NE]	0.3688 [0.1516, 0.8971] 0.0278 0.0220	
Other	1 / 28 (3.6)	NE [NE, NE]	1 / 20 (5.0)	NE [NE, NE]	0.5804 [0.0362, 9.3069] 0.7008 0.6973	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
ECOG						0.0380
0	9 / 96 (9.4)	NE [NE, NE]	8 / 81 (9.9)	NE [NE, NE]	0.7890 [0.3009, 2.0683] 0.6298 0.6290	
≥1	5 / 148 (3.4)	NE [NE, NE]	23 / 152 (15.1)	NE [NE, NE]	0.2010 [0.0764, 0.5290] 0.0012 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Primary tumor location						0.8704
Gastric	8 / 152 (5.3)	NE [17.3, NE]	17 / 139 (12.2)	NE [NE, NE]	0.4023 [0.1735, 0.9330] 0.0339 0.0281	
GEJ	6 / 92 (6.5)	NE [NE, NE]	14 / 94 (14.9)	NE [NE, NE]	0.3564 [0.1365, 0.9303] 0.0351 0.0277	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Histological subtype						0.1526
Intestinal	4 / 68 (5.9)	NE [17.3, NE]	11 / 63 (17.5)	NE [NE, NE]	0.2772 [0.0878, 0.8754] 0.0288 0.0196	
Diffuse	0 / 25	NE [NE, NE]	3 / 18 (16.7)	NE [6.8, NE]	NE [NE, NE] NE NE	
Others	10 / 151 (6.6)	NE [NE, NE]	17 / 152 (11.2)	NE [NE, NE]	0.5412 [0.2477, 1.1823] 0.1236 0.1178	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Number of metastatic sites						0.5264
<2	2 / 72 (2.8)	NE [NE, NE]	8 / 72 (11.1)	NE [NE, NE]	0.2485 [0.0527, 1.1705] 0.0783 0.0564	
≥2	12 / 172 (7.0)	NE [17.3, NE]	23 / 161 (14.3)	NE [NE, NE]	0.4030 [0.1997, 0.8132] 0.0112 0.0087	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Prior adjuvant/neoadjuvant therapy						0.7172
Yes	1 / 31 (3.2)	NE [NE, NE]	3 / 28 (10.7)	NE [NE, NE]	0.2792 [0.0290, 2.6858] 0.2693 0.2376	
No	13 / 213 (6.1)	NE [NE, NE]	28 / 205 (13.7)	NE [NE, NE]	0.3897 [0.2015, 0.7540] 0.0051 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Prior nivolumab or pembrolizumab treatment						0.6223
Yes	1 / 20 (5.0)	NE [NE, NE]	3 / 16 (18.8)	NE [NE, NE]	0.2511 [0.0261, 2.4142] 0.2314 0.1931	
No	13 / 224 (5.8)	NE [NE, NE]	28 / 217 (12.9)	NE [NE, NE]	0.3925 [0.2028, 0.7597] 0.0055 0.0040	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.8597
Yes	2 / 39 (5.1)	NE [NE, NE]	4 / 36 (11.1)	NE [NE, NE]	0.4444 [0.0814, 2.4267] 0.3491 0.3350	
No	12 / 205 (5.9)	NE [NE, NE]	27 / 197 (13.7)	NE [NE, NE]	0.3645 [0.1838, 0.7226] 0.0038 0.0026	

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

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Presence of liver metastasis at baseline						0.5170
Yes	8 / 145 (5.5)	NE [17.3, NE]	22 / 149 (14.8)	NE [NE, NE]	0.3132 [0.1378, 0.7119] 0.0056 0.0035	
No	6 / 99 (6.1)	NE [NE, NE]	9 / 84 (10.7)	NE [NE, NE]	0.5110 [0.1817, 1.4370] 0.2032 0.1951	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Renal function at baseline						0.1421
Normal renal function	9 / 116 (7.8)	NE [17.3, NE]	13 / 114 (11.4)	NE [NE, NE]	0.6204 [0.2645, 1.4551] 0.2724 0.2677	
Mild impairment	2 / 87 (2.3)	NE [NE, NE]	12 / 81 (14.8)	NE [NE, NE]	0.1274 [0.0285, 0.5697] 0.0070 0.0014	
Moderate impairment	3 / 41 (7.3)	NE [NE, NE]	6 / 38 (15.8)	NE [NE, NE]	0.4206 [0.1051, 1.6830] 0.2209 0.2062	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Stomatitis						
Hepatic function at baseline						0.9197
Normal hepatic function	10 / 185 (5.4)	NE [NE, NE]	22 / 177 (12.4)	NE [NE, NE]	0.3821 [0.1804, 0.8093] 0.0120 0.0091	
Mild, Moderate or Severe dysfunction	4 / 59 (6.8)	NE [NE, NE]	9 / 55 (16.4)	NE [7.1, NE]	0.3587 [0.1100, 1.1691] 0.0890 0.0762	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.2344
IHC 3+	3 / 205 (1.5)	NE [NE, NE]	8 / 196 (4.1)	NE [NE, NE]	0.3025 [0.0798, 1.1471] 0.0787 0.0626	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	2 / 37 (5.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Geography stratification factor						0.4561
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	2 / 59 (3.4)	NE [13.6, NE]	NE [NE, NE] NE NE	
Western Europe	3 / 138 (2.2)	NE [NE, NE]	7 / 129 (5.4)	NE [NE, NE]	0.3320 [0.0858, 1.2846] 0.1102 0.0931	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	1 / 45 (2.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Time to progression on first-line therapy from IRT						0.2633
<6 Months	0 / 61	NE [NE, NE]	2 / 57 (3.5)	NE [6.9, NE]	NE [NE, NE] NE NE	
≥6 Months	3 / 183 (1.6)	NE [NE, NE]	8 / 176 (4.5)	NE [NE, NE]	0.3033 [0.0798, 1.1520] 0.0798 0.0637	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Age at randomization						NE
<65	2 / 139 (1.4)	NE [NE, NE]	7 / 123 (5.7)	NE [NE, NE]	NE [NE, NE] NE NE	
≥65	1 / 105 (1.0)	NE [NE, NE]	3 / 110 (2.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Age at randomization						0.4253
<75	3 / 220 (1.4)	NE [NE, NE]	8 / 198 (4.0)	NE [13.6, NE]	0.2600 [0.0681, 0.9925] 0.0487	
≥75	0 / 24	NE [NE, NE]	2 / 35 (5.7)	NE [NE, NE]	0.0344 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 Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Sex						0.2507
Male	3 / 186 (1.6)	NE [NE, NE]	8 / 194 (4.1)	NE [13.6, NE]	0.2950 [0.0767, 1.1348] 0.0757 0.0602	
Female	0 / 58	NE [NE, NE]	2 / 39 (5.1)	NE [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 Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Race						NE
White	3 / 115 (2.6)	NE [NE, NE]	5 / 120 (4.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	0 / 101	NE [NE, NE]	3 / 93 (3.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	2 / 20 (10.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
ECOG						NE
0	1 / 96 (1.0)	NE [NE, NE]	5 / 81 (6.2)	NE [NE, NE]	NE [NE, NE] NE NE	
≥1	2 / 148 (1.4)	NE [NE, NE]	5 / 152 (3.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Primary tumor location						NE
Gastric	2 / 152 (1.3)	NE [NE, NE]	7 / 139 (5.0)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	1 / 92 (1.1)	NE [NE, NE]	3 / 94 (3.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Histological subtype						0.3422
Intestinal	0 / 68	NE [NE, NE]	2 / 63 (3.2)	NE [13.6, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	1 / 18 (5.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Others	3 / 151 (2.0)	NE [NE, NE]	7 / 152 (4.6)	NE [NE, NE]	0.3758 [0.0971, 1.4540] 0.1563 0.1401	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Number of metastatic sites						0.4933
<2	1 / 72 (1.4)	NE [NE, NE]	2 / 72 (2.8)	NE [NE, NE]	0.5304 [0.0481, 5.8530] 0.6048 0.5986	
≥2	2 / 172 (1.2)	NE [NE, NE]	8 / 161 (5.0)	NE [13.6, NE]	0.1792 [0.0377, 0.8507] 0.0305 0.0151	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Prior adjuvant/neoadjuvant therapy						0.9997
Yes	0 / 31	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	3 / 213 (1.4)	NE [NE, NE]	10 / 205 (4.9)	NE [NE, NE]	0.2370 [0.0649, 0.8663] 0.0295 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Prior nivolumab or pembrolizumab treatment						0.0901
Yes	1 / 20 (5.0)	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	2 / 224 (0.9)	NE [NE, NE]	10 / 217 (4.6)	NE [NE, NE]	0.1575 [0.0343, 0.7232] 0.0175 0.0065	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.3346
Yes	1 / 39 (2.6)	NE [NE, NE]	1 / 36 (2.8)	NE [NE, NE]	0.9199 [0.0575, 14.7069] 0.9529 0.9530	
No	2 / 205 (1.0)	NE [NE, NE]	9 / 197 (4.6)	NE [NE, NE]	0.1671 [0.0358, 0.7802] 0.0229 0.0099	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Presence of liver metastasis at baseline						NE
Yes	2 / 145 (1.4)	NE [NE, NE]	6 / 149 (4.0)	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 99 (1.0)	NE [NE, NE]	4 / 84 (4.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Renal function at baseline						NE
Normal renal function	2 / 116 (1.7)	NE [NE, NE]	5 / 114 (4.4)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	0 / 87	NE [NE, NE]	5 / 81 (6.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	1 / 41 (2.4)	NE [NE, NE]	0 / 38	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Haemorrhoids						
Hepatic function at baseline						NE
Normal hepatic function	1 / 185 (0.5)	NE [NE, NE]	6 / 177 (3.4)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	2 / 59 (3.4)	NE [NE, NE]	4 / 55 (7.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.4475
IHC 3+	7 / 205 (3.4)	NE [NE, NE]	14 / 196 (7.1)	NE [NE, NE]	0.4254 [0.1716, 1.0550] 0.0651 0.0573	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	4 / 37 (10.8)	NE [NE, NE]	0.2009 [0.0224, 1.8034] 0.1517 0.1118	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Geography stratification factor						0.4363
Asia [excluding mainland China]	2 / 57 (3.5)	NE [NE, NE]	2 / 59 (3.4)	NE [NE, NE]	0.9666 [0.1360, 6.8699] 0.9729 0.9729	
Western Europe	5 / 138 (3.6)	NE [NE, NE]	10 / 129 (7.8)	NE [NE, NE]	0.3994 [0.1363, 1.1703] 0.0943 0.0832	
Mainland China/Rest of World (ROW)	1 / 49 (2.0)	NE [NE, NE]	6 / 45 (13.3)	NE [NE, NE]	0.1476 [0.0177, 1.2287] 0.0768 0.0404	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Time to progression on first-line therapy from IRT						0.7923
<6 Months	2 / 61 (3.3)	NE [NE, NE]	5 / 57 (8.8)	NE [7.3, NE]	0.3159 [0.0607, 1.6437] 0.1709 0.1488	
≥6 Months	6 / 183 (3.3)	NE [NE, NE]	13 / 176 (7.4)	NE [NE, NE]	0.3910 [0.1485, 1.0297] 0.0573 0.0487	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Age at randomization						0.0214
<65	2 / 139 (1.4)	NE [NE, NE]	12 / 123 (9.8)	NE [NE, NE]	0.1245 [0.0278, 0.5568] 0.0064 0.0012	
≥65	6 / 105 (5.7)	NE [NE, NE]	6 / 110 (5.5)	NE [NE, NE]	0.9654 [0.3110, 2.9966] 0.9515 0.9515	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Age at randomization						0.3270
<75	7 / 220 (3.2)	NE [NE, NE]	17 / 198 (8.6)	NE [NE, NE]	0.3206 [0.1328, 0.7739] 0.0114 0.0076	
≥75	1 / 24 (4.2)	NE [NE, NE]	1 / 35 (2.9)	NE [NE, NE]	1.3647 [0.0850, 21.9105] 0.8262 0.8255	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Sex						0.4225
Male	5 / 186 (2.7)	NE [NE, NE]	15 / 194 (7.7)	NE [NE, NE]	0.2997 [0.1088, 0.8257] 0.0198 0.0134	
Female	3 / 58 (5.2)	NE [NE, NE]	3 / 39 (7.7)	NE [NE, NE]	0.6331 [0.1274, 3.1463] 0.5763 0.5730	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Race						0.5714
White	5 / 115 (4.3)	NE [NE, NE]	11 / 120 (9.2)	NE [NE, NE]	0.4080 [0.1417, 1.1749] 0.0967 0.0859	
Asian	3 / 101 (3.0)	NE [NE, NE]	6 / 93 (6.5)	NE [NE, NE]	0.4145 [0.1035, 1.6599] 0.2135 0.1990	
Other	0 / 28	NE [NE, NE]	1 / 20 (5.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
ECOG						0.2311
0	1 / 96 (1.0)	NE [NE, NE]	5 / 81 (6.2)	NE [NE, NE]	0.1323 [0.0154, 1.1360] 0.0652 0.0300	
≥1	7 / 148 (4.7)	NE [NE, NE]	13 / 152 (8.6)	NE [NE, NE]	0.5082 [0.2027, 1.2743] 0.1490 0.1413	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Primary tumor location						0.4727
Gastric	6 / 152 (3.9)	NE [NE, NE]	11 / 139 (7.9)	NE [NE, NE]	0.4514 [0.1667, 1.2224] 0.1176 0.1083	
GEJ	2 / 92 (2.2)	NE [NE, NE]	7 / 94 (7.4)	NE [NE, NE]	0.2460 [0.0510, 1.1855] 0.0805 0.0582	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Histological subtype						0.9394
Intestinal	0 / 68	NE [NE, NE]	0 / 63	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	1 / 25 (4.0)	NE [NE, NE]	1 / 18 (5.6)	NE [NE, NE]	0.6574 [0.0411, 10.5155] 0.7668 0.7651	
Others	7 / 151 (4.6)	NE [NE, NE]	17 / 152 (11.2)	NE [NE, NE]	0.3710 [0.1538, 0.8950] 0.0273 0.0216	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Number of metastatic sites						0.9368
<2	2 / 72 (2.8)	NE [NE, NE]	6 / 72 (8.3)	NE [NE, NE]	0.3465 [0.0699, 1.7172] 0.1944 0.1740	
≥2	6 / 172 (3.5)	NE [NE, NE]	12 / 161 (7.5)	NE [NE, NE]	0.3611 [0.1347, 0.9682] 0.0430 0.0349	

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

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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]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Prior adjuvant/neoadjuvant therapy						0.3722
Yes	0 / 31	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	8 / 213 (3.8)	NE [NE, NE]	17 / 205 (8.3)	NE [NE, NE]	0.3953 [0.1704, 0.9171] 0.0307 0.0251	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Prior nivolumab or pembrolizumab treatment						0.1658
Yes	0 / 20	NE [NE, NE]	2 / 16 (12.5)	NE [6.8, NE]	NE [NE, NE] NE NE	
No	8 / 224 (3.6)	NE [NE, NE]	16 / 217 (7.4)	NE [NE, NE]	0.4282 [0.1831, 1.0015] 0.0504 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.0727
Yes	0 / 39	NE [NE, NE]	4 / 36 (11.1)	NE [NE, NE]	NE [NE, NE] NE NE	
No	8 / 205 (3.9)	NE [NE, NE]	14 / 197 (7.1)	NE [NE, NE]	0.4776 [0.2001, 1.1397] 0.0959 0.0885	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Presence of liver metastasis at baseline						0.3207
Yes	2 / 145 (1.4)	NE [NE, NE]	9 / 149 (6.0)	NE [NE, NE]	0.2066 [0.0446, 0.9570] 0.0438 0.0257	
No	6 / 99 (6.1)	NE [NE, NE]	9 / 84 (10.7)	NE [NE, NE]	0.4866 [0.1728, 1.3702] 0.1727 0.1636	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Renal function at baseline						0.8231
Normal renal function	4 / 116 (3.4)	NE [NE, NE]	9 / 114 (7.9)	NE [NE, NE]	0.3944 [0.1213, 1.2829] 0.1221 0.1091	
Mild impairment	2 / 87 (2.3)	NE [NE, NE]	6 / 81 (7.4)	NE [NE, NE]	0.2625 [0.0529, 1.3026] 0.1017 0.0783	
Moderate impairment	2 / 41 (4.9)	NE [NE, NE]	3 / 38 (7.9)	NE [NE, NE]	0.5387 [0.0893, 3.2491] 0.4999 0.4933	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Hepatic function at baseline						0.8921
Normal hepatic function	5 / 185 (2.7)	NE [NE, NE]	12 / 177 (6.8)	NE [NE, NE]	0.3467 [0.1220, 0.9850] 0.0468 0.0373	
Mild, Moderate or Severe dysfunction	3 / 59 (5.1)	NE [NE, NE]	6 / 55 (10.9)	NE [NE, NE]	0.3951 [0.0985, 1.5844] 0.1900 0.1746	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.2094
IHC 3+	130 / 205 (63.4)	2.5 [1.4, 3.5]	92 / 196 (46.9)	6.0 [3.9, 8.3]	1.4629 [1.1184, 1.9134] 0.0055 0.0052	
IHC 2+/ISH+	23 / 39 (59.0)	4.2 [0.5, 13.2]	21 / 37 (56.8)	3.2 [0.5, 7.1]	0.9333 [0.5079, 1.7148] 0.8240 0.8285	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Geography stratification factor						0.3855
Asia [excluding mainland China]	36 / 57 (63.2)	1.9 [0.8, 13.2]	25 / 59 (42.4)	7.6 [4.6, 8.3]	1.4789 [0.8754, 2.4984] 0.1435 0.1420	
Western Europe	74 / 138 (53.6)	4.7 [2.6, 6.0]	57 / 129 (44.2)	6.0 [3.4, NE]	1.2215 [0.8642, 1.7265] 0.2571 0.2601	
Mainland China/Rest of World (ROW)	43 / 49 (87.8)	0.5 [0.4, 0.8]	31 / 45 (68.9)	1.4 [0.7, 3.2]	1.6459 [1.0309, 2.6279] 0.0369 0.0365	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Time to progression on first-line therapy from IRT						0.5117
<6 Months	41 / 61 (67.2)	2.1 [0.9, 3.5]	25 / 57 (43.9)	5.1 [2.1, NE]	1.5010 [0.9071, 2.4838] 0.1140 0.1118	
≥6 Months	112 / 183 (61.2)	2.6 [1.4, 4.7]	88 / 176 (50.0)	5.6 [3.2, 8.0]	1.3144 [0.9930, 1.7398] 0.0560 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Age at randomization						0.3103
<65	85 / 139 (61.2)	3.0 [1.5, 4.8]	63 / 123 (51.2)	5.6 [3.6, 7.7]	1.2194 [0.8788, 1.6919] 0.2352 0.2351	
≥65	68 / 105 (64.8)	1.9 [0.7, 3.5]	50 / 110 (45.5)	5.6 [2.5, NE]	1.5834 [1.0954, 2.2889] 0.0145 0.0140	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Age at randomization						0.4901
<75	140 / 220 (63.6)	2.5 [1.4, 3.5]	94 / 198 (47.5)	5.7 [3.6, 8.0]	1.4109 [1.0842, 1.8361] 0.0104 0.0102	
≥75	13 / 24 (54.2)	3.1 [0.5, NE]	19 / 35 (54.3)	4.6 [0.9, NE]	1.0864 [0.5351, 2.2058] 0.8186 0.8177	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT:						
Any						
Sex						0.3845
Male	110 / 186 (59.1)	3.0 [1.6, 4.9]	94 / 194 (48.5)	5.6 [3.6, 8.2]	1.2504 [0.9469, 1.6511] 0.1151 0.1160	
Female	43 / 58 (74.1)	1.4 [0.6, 3.1]	19 / 39 (48.7)	6.0 [1.3, NE]	1.7120 [0.9971, 2.9395] 0.0512 0.0479	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT:						
Any						
Race						0.4676
White	56 / 115 (48.7)	4.9 [2.8, NE]	50 / 120 (41.7)	7.1 [3.9, NE]	1.1745 [0.8014, 1.7213] 0.4094 0.4135	
Asian	77 / 101 (76.2)	1.0 [0.5, 1.5]	54 / 93 (58.1)	3.8 [1.4, 7.6]	1.4119 [0.9919, 2.0097] 0.0555 0.0548	
Other	20 / 28 (71.4)	2.1 [0.3, 4.8]	9 / 20 (45.0)	5.1 [0.4, NE]	1.8368 [0.8359, 4.0362] 0.1301 0.1266	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
ECOG						0.7690
0	56 / 96 (58.3)	4.2 [1.6, 6.9]	34 / 81 (42.0)	6.0 [5.1, 8.2]	1.4479 [0.9403, 2.2295] 0.0929 0.0925	
≥1	97 / 148 (65.5)	1.7 [1.1, 3.0]	79 / 152 (52.0)	3.6 [2.3, 8.3]	1.3006 [0.9645, 1.7537] 0.0848 0.0834	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Primary tumor location						0.2069
Gastric	96 / 152 (63.2)	2.8 [1.4, 4.2]	74 / 139 (53.2)	4.5 [2.7, 7.6]	1.1762 [0.8654, 1.5986] 0.2999 0.3040	
GEJ	57 / 92 (62.0)	2.1 [1.2, 4.9]	39 / 94 (41.5)	12.3 [3.2, NE]	1.6907 [1.1243, 2.5425] 0.0116 0.0109	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Histological subtype						0.6609
Intestinal	40 / 68 (58.8)	3.4 [1.0, 8.3]	27 / 63 (42.9)	7.6 [2.7, NE]	1.4369 [0.8759, 2.3574] 0.1512 0.1520	
Diffuse	16 / 25 (64.0)	3.0 [0.5, 6.9]	7 / 18 (38.9)	NE [0.9, NE]	1.8228 [0.7404, 4.4873] 0.1915 0.1820	
Others	97 / 151 (64.2)	2.1 [1.4, 3.4]	79 / 152 (52.0)	4.5 [2.8, 7.1]	1.2962 [0.9624, 1.7457] 0.0877 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Number of metastatic sites						0.3122
<2	43 / 72 (59.7)	2.5 [1.0, 6.4]	42 / 72 (58.3)	5.7 [1.4, 8.2]	1.1426 [0.7437, 1.7555] 0.5429 0.5428	
≥2	110 / 172 (64.0)	2.2 [1.4, 3.5]	71 / 161 (44.1)	5.6 [3.8, NE]	1.4925 [1.1051, 2.0156] 0.0090 0.0087	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT:						
Any						
Prior adjuvant/neoadjuvant therapy						0.7696
Yes	16 / 31 (51.6)	4.9 [0.7, NE]	11 / 28 (39.3)	NE [1.1, NE]	1.3019 [0.6035, 2.8088] 0.5012 0.4974	
No	137 / 213 (64.3)	2.2 [1.4, 3.4]	102 / 205 (49.8)	5.6 [3.4, 7.7]	1.3776 [1.0640, 1.7836] 0.0151 0.0149	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Prior nivolumab or pembrolizumab treatment						0.2862
Yes	12 / 20 (60.0)	4.2 [0.7, NE]	9 / 16 (56.3)	2.8 [0.2, NE]	0.7861 [0.3223, 1.9172] 0.5967 0.5898	
No	141 / 224 (62.9)	2.1 [1.4, 3.5]	104 / 217 (47.9)	5.6 [3.8, 8.0]	1.4184 [1.0994, 1.8301] 0.0072 0.0070	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.0812
Yes	29 / 39 (74.4)	1.4 [0.5, 3.5]	27 / 36 (75.0)	1.0 [0.5, 3.2]	0.8308 [0.4863, 1.4192] 0.4974 0.4967	
No	124 / 205 (60.5)	2.6 [1.5, 4.4]	86 / 197 (43.7)	7.6 [4.6, 8.3]	1.5062 [1.1422, 1.9862] 0.0037 0.0035	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Presence of liver metastasis at baseline						0.4304
Yes	87 / 145 (60.0)	2.6 [1.3, 4.2]	73 / 149 (49.0)	5.6 [3.2, 8.0]	1.2360 [0.9035, 1.6910] 0.1852 0.1840	
No	66 / 99 (66.7)	2.1 [1.4, 4.4]	40 / 84 (47.6)	5.6 [2.7, NE]	1.5927 [1.0736, 2.3628] 0.0207 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Renal function at baseline						0.7511
Normal renal function	67 / 116 (57.8)	4.2 [2.1, 6.0]	55 / 114 (48.2)	5.7 [3.8, 8.2]	1.2411 [0.8649, 1.7810] 0.2411 0.2429	
Mild impairment	61 / 87 (70.1)	1.2 [0.7, 2.5]	40 / 81 (49.4)	3.9 [1.4, NE]	1.5320 [1.0272, 2.2850] 0.0365 0.0350	
Moderate impairment	25 / 41 (61.0)	2.1 [0.4, 13.2]	18 / 38 (47.4)	4.6 [1.4, NE]	1.3015 [0.7059, 2.3996] 0.3985 0.3991	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Any						
Hepatic function at baseline						0.8011
Normal hepatic function	116 / 185 (62.7)	3.0 [1.4, 4.4]	86 / 177 (48.6)	5.6 [3.6, 7.7]	1.3426 [1.0131, 1.7792] 0.0403 0.0404	
Mild, Moderate or Severe dysfunction	37 / 59 (62.7)	1.9 [0.7, 4.8]	26 / 55 (47.3)	8.0 [1.3, NE]	1.4146 [0.8553, 2.3397] 0.1767 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.7798
IHC 3+	82 / 205 (40.0)	NE [5.3, NE]	58 / 196 (29.6)	15.6 [9.4, NE]	1.4046 [1.0029, 1.9671] 0.0480 0.0474	
IHC 2+/ISH+	16 / 39 (41.0)	10.3 [5.7, NE]	12 / 37 (32.4)	7.9 [5.1, NE]	1.1141 [0.5154, 2.4084] 0.7836 0.7846	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Geography stratification factor						0.3949
Asia [excluding mainland China]	29 / 57 (50.9)	10.9 [1.1, NE]	20 / 59 (33.9)	16.2 [4.6, NE]	1.7068 [0.9556, 3.0484] 0.0708 0.0684	
Western Europe	44 / 138 (31.9)	NE [NE, NE]	35 / 129 (27.1)	15.6 [7.9, NE]	1.1504 [0.7368, 1.7961] 0.5377 0.5409	
Mainland China/Rest of World (ROW)	25 / 49 (51.0)	3.5 [1.5, NE]	15 / 45 (33.3)	9.4 [5.5, NE]	1.8243 [0.9566, 3.4789] 0.0680 0.0638	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Time to progression on first-line therapy from IRT						0.7328
<6 Months	25 / 61 (41.0)	10.5 [2.8, NE]	17 / 57 (29.8)	15.6 [5.1, NE]	1.2021 [0.6451, 2.2401] 0.5621 0.5643	
≥6 Months	73 / 183 (39.9)	11.1 [5.7, NE]	53 / 176 (30.1)	16.2 [7.9, NE]	1.4133 [0.9915, 2.0145] 0.0558 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Age at randomization						0.2856
<65	52 / 139 (37.4)	NE [10.9, NE]	40 / 123 (32.5)	9.4 [7.7, NE]	1.1815 [0.7820, 1.7851] 0.4282 0.4300	
≥65	46 / 105 (43.8)	10.3 [4.1, NE]	30 / 110 (27.3)	15.6 [NE, NE]	1.6603 [1.0449, 2.6381] 0.0319 0.0304	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Age at randomization						0.4680
<75	89 / 220 (40.5)	11.1 [6.4, NE]	57 / 198 (28.8)	9.4 [7.9, NE]	1.4434 [1.0337, 2.0154] 0.0312 0.0311	
≥75	9 / 24 (37.5)	NE [1.9, NE]	13 / 35 (37.1)	15.6 [2.7, NE]	1.0985 [0.4623, 2.6103] 0.8316 0.8342	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Sex						0.1835
Male	66 / 186 (35.5)	NE [10.9, NE]	57 / 194 (29.4)	15.6 [8.2, NE]	1.2031 [0.8431, 1.7168] 0.3081 0.3105	
Female	32 / 58 (55.2)	4.7 [1.5, 10.5]	13 / 39 (33.3)	9.4 [7.3, NE]	1.9163 [1.0026, 3.6627] 0.0491 0.0449	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Race						0.5077
White	29 / 115 (25.2)	NE [NE, NE]	27 / 120 (22.5)	15.6 [9.4, NE]	1.0719 [0.6328, 1.8158] 0.7962 0.7970	
Asian	54 / 101 (53.5)	4.8 [1.7, 10.9]	36 / 93 (38.7)	8.2 [6.6, NE]	1.5502 [1.0152, 2.3672] 0.0424 0.0414	
Other	15 / 28 (53.6)	4.2 [0.6, NE]	7 / 20 (35.0)	NE [1.4, NE]	1.7047 [0.6946, 4.1833] 0.2442 0.2419	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
ECOG						0.6857
0	34 / 96 (35.4)	NE [10.9, NE]	22 / 81 (27.2)	9.4 [7.7, NE]	1.2744 [0.7412, 2.1912] 0.3806 0.3867	
≥1	64 / 148 (43.2)	10.3 [4.7, NE]	48 / 152 (31.6)	16.2 [7.9, NE]	1.4534 [0.9993, 2.1139] 0.0504 0.0492	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Primary tumor location						0.1799
Gastric	60 / 152 (39.5)	10.9 [6.4, NE]	48 / 139 (34.5)	8.2 [6.9, 16.2]	1.1471 [0.7835, 1.6794] 0.4806 0.4850	
GEJ	38 / 92 (41.3)	NE [4.2, NE]	22 / 94 (23.4)	NE [9.4, NE]	1.8763 [1.1096, 3.1726] 0.0189 0.0171	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Histological subtype						0.9809
Intestinal	31 / 68 (45.6)	13.2 [2.5, NE]	21 / 63 (33.3)	9.4 [8.2, NE]	1.3947 [0.7985, 2.4358] 0.2423 0.2452	
Diffuse	9 / 25 (36.0)	11.1 [1.9, NE]	4 / 18 (22.2)	NE [NE, NE]	1.5184 [0.4559, 5.0576] 0.4963 0.4960	
Others	58 / 151 (38.4)	10.9 [6.4, NE]	45 / 152 (29.6)	15.6 [7.9, NE]	1.3510 [0.9149, 1.9950] 0.1303 0.1299	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Number of metastatic sites						0.1637
<2	23 / 72 (31.9)	NE [11.1, NE]	26 / 72 (36.1)	16.2 [6.9, NE]	0.9772 [0.5558, 1.7179] 0.9361 0.9327	
≥2	75 / 172 (43.6)	10.5 [4.8, NE]	44 / 161 (27.3)	15.6 [7.9, NE]	1.5652 [1.0772, 2.2744] 0.0188 0.0180	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Prior adjuvant/neoadjuvant therapy						0.7696
Yes	11 / 31 (35.5)	NE [2.1, NE]	6 / 28 (21.4)	NE [5.1, NE]	1.7060 [0.6300, 4.6195] 0.2933 0.2876	
No	87 / 213 (40.8)	10.9 [5.7, NE]	64 / 205 (31.2)	15.6 [7.9, NE]	1.3446 [0.9727, 1.8587] 0.0730 0.0735	

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

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Prior nivolumab or pembrolizumab treatment						0.4385
Yes	6 / 20 (30.0)	NE [2.1, NE]	5 / 16 (31.3)	NE [2.1, NE]	0.9440 [0.2880, 3.0936] 0.9241 0.9264	
No	92 / 224 (41.1)	10.9 [5.7, NE]	65 / 217 (30.0)	15.6 [8.2, NE]	1.4127 [1.0273, 1.9427] 0.0335 0.0333	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.5130
Yes	17 / 39 (43.6)	10.3 [2.2, NE]	15 / 36 (41.7)	7.9 [5.5, NE]	1.0641 [0.5294, 2.1389] 0.8615 0.8598	
No	81 / 205 (39.5)	13.2 [6.4, NE]	55 / 197 (27.9)	15.6 [9.4, NE]	1.4416 [1.0221, 2.0333] 0.0371 0.0369	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Presence of liver metastasis at baseline						0.4716
Yes	55 / 145 (37.9)	11.1 [10.3, NE]	45 / 149 (30.2)	15.6 [9.4, NE]	1.2371 [0.8333, 1.8365] 0.2912 0.2931	
No	43 / 99 (43.4)	NE [4.1, NE]	25 / 84 (29.8)	16.2 [7.3, NE]	1.6471 [1.0052, 2.6990] 0.0476 0.0458	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Renal function at baseline						0.2238
Normal renal function	39 / 116 (33.6)	NE [10.3, NE]	36 / 114 (31.6)	9.4 [7.9, NE]	1.1276 [0.7161, 1.7756] 0.6041 0.6102	
Mild impairment	42 / 87 (48.3)	10.5 [2.8, NE]	21 / 81 (25.9)	15.6 [NE, NE]	1.9056 [1.1276, 3.2204] 0.0160 0.0142	
Moderate impairment	17 / 41 (41.5)	13.2 [4.1, NE]	13 / 38 (34.2)	NE [2.5, NE]	1.0494 [0.4988, 2.2078] 0.8988 0.8957	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Metabolism and nutrition disorders; PT: Decreased appetite						
Hepatic function at baseline						0.2196
Normal hepatic function	74 / 185 (40.0)	11.1 [6.4, NE]	57 / 177 (32.2)	9.4 [7.9, 16.2]	1.2316 [0.8702, 1.7431] 0.2397 0.2436	
Mild, Moderate or Severe dysfunction	24 / 59 (40.7)	NE [2.1, NE]	12 / 55 (21.8)	NE [7.9, NE]	1.9662 [0.9823, 3.9357] 0.0562 0.0512	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.9703
IHC 3+	44 / 205 (21.5)	NE [NE, NE]	22 / 196 (11.2)	NE [NE, NE]	1.8339 [1.0990, 3.0602] 0.0203 0.0184	
IHC 2+/ISH+	9 / 39 (23.1)	NE [6.1, NE]	4 / 37 (10.8)	NE [5.1, NE]	1.8991 [0.5841, 6.1744] 0.2864 0.2816	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Geography stratification factor						0.9336
Asia [excluding mainland China]	7 / 57 (12.3)	NE [NE, NE]	3 / 59 (5.1)	NE [NE, NE]	2.2459 [0.5794, 8.7053] 0.2418 0.2290	
Western Europe	24 / 138 (17.4)	NE [NE, NE]	12 / 129 (9.3)	NE [NE, NE]	1.7314 [0.8654, 3.4640] 0.1208 0.1155	
Mainland China/Rest of World (ROW)	22 / 49 (44.9)	8.0 [3.8, NE]	11 / 45 (24.4)	NE [6.7, NE]	1.9830 [0.9605, 4.0940] 0.0642 0.0582	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Time to progression on first-line therapy from IRT						0.5891
<6 Months	14 / 61 (23.0)	NE [NE, NE]	5 / 57 (8.8)	NE [6.7, NE]	2.4911 [0.8952, 6.9317] 0.0805 0.0706	
≥6 Months	39 / 183 (21.3)	NE [NE, NE]	21 / 176 (11.9)	NE [NE, NE]	1.7036 [1.0019, 2.8967] 0.0492 0.0465	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Age at randomization						0.0415
<65	30 / 139 (21.6)	NE [NE, NE]	19 / 123 (15.4)	NE [10.7, NE]	1.2228 [0.6877, 2.1741] 0.4934 0.4910	
≥65	23 / 105 (21.9)	NE [9.0, NE]	7 / 110 (6.4)	NE [NE, NE]	3.5022 [1.5016, 8.1684] 0.0037 0.0020	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Age at randomization						0.7887
<75	50 / 220 (22.7)	NE [NE, NE]	24 / 198 (12.1)	NE [NE, NE]	1.7462 [1.0727, 2.8424] 0.0249 0.0231	
≥75	3 / 24 (12.5)	NE [9.0, NE]	2 / 35 (5.7)	NE [NE, NE]	2.1204 [0.3535, 12.7179] 0.4109 0.3999	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Sex						0.4494
Male	42 / 186 (22.6)	NE [NE, NE]	20 / 194 (10.3)	NE [NE, NE]	1.9824 [1.1628, 3.3797] 0.0119 0.0103	
Female	11 / 58 (19.0)	NE [NE, NE]	6 / 39 (15.4)	NE [NE, NE]	1.2692 [0.4692, 3.4328] 0.6387 0.6383	

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

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Race						0.2169
White	21 / 115 (18.3)	NE [NE, NE]	9 / 120 (7.5)	NE [NE, NE]	2.3040 [1.0549, 5.0321] 0.0363 0.0311	
Asian	28 / 101 (27.7)	NE [8.3, NE]	13 / 93 (14.0)	NE [NE, NE]	1.9370 [1.0029, 3.7411] 0.0490 0.0449	
Other	4 / 28 (14.3)	NE [NE, NE]	4 / 20 (20.0)	NE [5.1, NE]	0.6802 [0.1697, 2.7263] 0.5864 0.5841	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
ECOG						0.2549
0	12 / 96 (12.5)	NE [NE, NE]	7 / 81 (8.6)	NE [NE, NE]	1.2909 [0.5071, 3.2859] 0.5922 0.5917	
≥1	41 / 148 (27.7)	NE [8.3, NE]	19 / 152 (12.5)	NE [NE, NE]	2.2807 [1.3235, 3.9302] 0.0030 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Primary tumor location						0.3782
Gastric	30 / 152 (19.7)	NE [NE, NE]	17 / 139 (12.2)	NE [NE, NE]	1.5417 [0.8497, 2.7973] 0.1545 0.1510	
GEJ	23 / 92 (25.0)	NE [NE, NE]	9 / 94 (9.6)	NE [NE, NE]	2.3972 [1.1087, 5.1834] 0.0263 0.0217	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Histological subtype						0.2276
Intestinal	12 / 68 (17.6)	NE [8.5, NE]	3 / 63 (4.8)	NE [NE, NE]	3.2419 [0.9124, 11.5180] 0.0690 0.0544	
Diffuse	7 / 25 (28.0)	NE [3.1, NE]	1 / 18 (5.6)	NE [NE, NE]	5.9104 [0.7267, 48.0724] 0.0966 0.0590	
Others	34 / 151 (22.5)	NE [NE, NE]	22 / 152 (14.5)	NE [NE, NE]	1.4631 [0.8556, 2.5021] 0.1645 0.1611	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Number of metastatic sites						0.5587
<2	14 / 72 (19.4)	NE [NE, NE]	7 / 72 (9.7)	NE [NE, NE]	2.2715 [0.9163, 5.6313] 0.0765 0.0682	
≥2	39 / 172 (22.7)	NE [NE, NE]	19 / 161 (11.8)	NE [10.7, NE]	1.6573 [0.9564, 2.8721] 0.0717 0.0688	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Prior adjuvant/neoadjuvant therapy						0.5522
Yes	7 / 31 (22.6)	NE [5.8, NE]	2 / 28 (7.1)	NE [NE, NE]	2.6622 [0.5514, 12.8536] 0.2229 0.2050	
No	46 / 213 (21.6)	NE [NE, NE]	24 / 205 (11.7)	NE [NE, NE]	1.7599 [1.0739, 2.8841] 0.0249 0.0230	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Prior nivolumab or pembrolizumab treatment						0.3619
Yes	6 / 20 (30.0)	NE [3.5, NE]	4 / 16 (25.0)	NE [6.7, NE]	1.0944 [0.3062, 3.9117] 0.8896 0.8896	
No	47 / 224 (21.0)	NE [NE, NE]	22 / 217 (10.1)	NE [NE, NE]	1.9631 [1.1828, 3.2580] 0.0091 0.0078	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.3494
Yes	16 / 39 (41.0)	6.4 [3.8, NE]	11 / 36 (30.6)	10.6 [6.7, NE]	1.3388 [0.6205, 2.8885] 0.4570 0.4475	
No	37 / 205 (18.0)	NE [NE, NE]	15 / 197 (7.6)	NE [NE, NE]	2.2253 [1.2208, 4.0563] 0.0090 0.0073	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Presence of liver metastasis at baseline						0.0885
Yes	23 / 145 (15.9)	NE [NE, NE]	17 / 149 (11.4)	NE [NE, NE]	1.2501 [0.6675, 2.3411] 0.4856 0.4824	
No	30 / 99 (30.3)	NE [8.3, NE]	9 / 84 (10.7)	NE [10.6, NE]	2.9193 [1.3845, 6.1554] 0.0049 0.0032	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Renal function at baseline						0.6142
Normal renal function	25 / 116 (21.6)	NE [NE, NE]	16 / 114 (14.0)	NE [10.7, NE]	1.4647 [0.7816, 2.7452] 0.2337 0.2297	
Mild impairment	20 / 87 (23.0)	NE [9.0, NE]	7 / 81 (8.6)	NE [NE, NE]	2.5204 [1.0651, 5.9641] 0.0354 0.0292	
Moderate impairment	8 / 41 (19.5)	NE [NE, NE]	3 / 38 (7.9)	NE [NE, NE]	2.5613 [0.6794, 9.6556] 0.1648 0.1496	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Weight decreased						
Hepatic function at baseline						0.3279
Normal hepatic function	42 / 185 (22.7)	NE [NE, NE]	18 / 177 (10.2)	NE [NE, NE]	2.1000 [1.2083, 3.6500] 0.0085 0.0071	
Mild, Moderate or Severe dysfunction	11 / 59 (18.6)	NE [NE, NE]	8 / 55 (14.5)	NE [10.7, NE]	1.2448 [0.4998, 3.1000] 0.6381 0.6372	

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

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.1976
IHC 3+	46 / 205 (22.4)	NE [14.9, NE]	21 / 196 (10.7)	NE [NE, NE]	2.0707 [1.2353, 3.4710] 0.0057 0.0048	
IHC 2+/ISH+	6 / 39 (15.4)	NE [NE, NE]	5 / 37 (13.5)	NE [NE, NE]	0.9323 [0.2827, 3.0753] 0.9084 0.9087	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Geography stratification factor						0.2159
Asia [excluding mainland China]	6 / 57 (10.5)	NE [NE, NE]	6 / 59 (10.2)	NE [9.0, NE]	0.9688 [0.3118, 3.0097] 0.9563 0.9562	
Western Europe	23 / 138 (16.7)	NE [11.4, NE]	11 / 129 (8.5)	NE [NE, NE]	1.6588 [0.8072, 3.4087] 0.1684 0.1639	
Mainland China/Rest of World (ROW)	23 / 49 (46.9)	3.8 [2.9, NE]	9 / 45 (20.0)	NE [NE, NE]	3.2713 [1.5057, 7.1074] 0.0028 0.0016	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Time to progression on first-line therapy from IRT						0.1343
<6 Months	11 / 61 (18.0)	NE [11.4, NE]	9 / 57 (15.8)	NE [NE, NE]	1.0081 [0.4149, 2.4492] 0.9858 0.9872	
≥6 Months	41 / 183 (22.4)	NE [14.9, NE]	17 / 176 (9.7)	NE [NE, NE]	2.2706 [1.2894, 3.9983] 0.0045 0.0035	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Age at randomization						0.5444
<65	29 / 139 (20.9)	NE [NE, NE]	15 / 123 (12.2)	NE [NE, NE]	1.6007 [0.8580, 2.9864] 0.1392 0.1359	
≥65	23 / 105 (21.9)	14.9 [11.3, NE]	11 / 110 (10.0)	NE [NE, NE]	1.9967 [0.9663, 4.1262] 0.0619 0.0570	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Age at randomization						0.3157
<75	50 / 220 (22.7)	NE [14.9, NE]	22 / 198 (11.1)	NE [NE, NE]	1.9197 [1.1618, 3.1721] 0.0109 0.0096	
≥75	2 / 24 (8.3)	NE [NE, NE]	4 / 35 (11.4)	NE [9.0, NE]	0.7676 [0.1405, 4.1931] 0.7602 0.7595	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Sex						0.8383
Male	41 / 186 (22.0)	NE [14.9, NE]	21 / 194 (10.8)	NE [NE, NE]	1.8599 [1.0966, 3.1543] 0.0213 0.0194	
Female	11 / 58 (19.0)	NE [10.0, NE]	5 / 39 (12.8)	NE [NE, NE]	1.5705 [0.5441, 4.5326] 0.4039 0.3993	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Race						0.9788
White	21 / 115 (18.3)	14.9 [11.3, NE]	10 / 120 (8.3)	NE [NE, NE]	1.9818 [0.9326, 4.2115] 0.0753 0.0697	
Asian	28 / 101 (27.7)	NE [NE, NE]	15 / 93 (16.1)	NE [NE, NE]	1.8686 [0.9976, 3.4998] 0.0509 0.0474	
Other	3 / 28 (10.7)	NE [NE, NE]	1 / 20 (5.0)	NE [5.0, NE]	1.8610 [0.1933, 17.9178] 0.5909 0.5850	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
ECOG						0.9329
0	19 / 96 (19.8)	NE [11.4, NE]	7 / 81 (8.6)	NE [NE, NE]	1.9110 [0.8012, 4.5580] 0.1442 0.1370	
≥1	33 / 148 (22.3)	NE [NE, NE]	19 / 152 (12.5)	NE [NE, NE]	1.8695 [1.0626, 3.2891] 0.0300 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Primary tumor location						0.3397
Gastric	36 / 152 (23.7)	NE [11.4, NE]	15 / 139 (10.8)	NE [NE, NE]	2.1611 [1.1825, 3.9493] 0.0122 0.0102	
GEJ	16 / 92 (17.4)	NE [NE, NE]	11 / 94 (11.7)	NE [NE, NE]	1.3400 [0.6208, 2.8928] 0.4560 0.4552	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Histological subtype						0.0496
Intestinal	13 / 68 (19.1)	NE [11.3, NE]	1 / 63 (1.6)	NE [NE, NE]	11.1374 [1.4542, 85.2962] 0.0203 0.0035	
Diffuse	5 / 25 (20.0)	NE [4.1, NE]	2 / 18 (11.1)	NE [6.3, NE]	1.8822 [0.3634, 9.7480] 0.4510 0.4436	
Others	34 / 151 (22.5)	NE [NE, NE]	23 / 152 (15.1)	NE [NE, NE]	1.4241 [0.8387, 2.4184] 0.1906 0.1885	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Number of metastatic sites						0.8423
<2	12 / 72 (16.7)	NE [NE, NE]	8 / 72 (11.1)	NE [NE, NE]	1.6731 [0.6832, 4.0976] 0.2601 0.2549	
≥2	40 / 172 (23.3)	NE [11.4, NE]	18 / 161 (11.2)	NE [NE, NE]	1.8354 [1.0502, 3.2076] 0.0330 0.0303	

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

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Prior adjuvant/neoadjuvant therapy						0.6861
Yes	6 / 31 (19.4)	NE [NE, NE]	2 / 28 (7.1)	NE [6.3, NE]	2.5439 [0.5129, 12.6164] 0.2531 0.2362	
No	46 / 213 (21.6)	NE [14.9, NE]	24 / 205 (11.7)	NE [NE, NE]	1.7705 [1.0802, 2.9018] 0.0235 0.0216	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Prior nivolumab or pembrolizumab treatment						0.8201
Yes	6 / 20 (30.0)	9.9 [4.6, NE]	3 / 16 (18.8)	NE [4.7, NE]	1.3835 [0.3303, 5.7949] 0.6569 0.6520	
No	46 / 224 (20.5)	NE [14.9, NE]	23 / 217 (10.6)	NE [NE, NE]	1.8472 [1.1192, 3.0487] 0.0164 0.0148	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.8475
Yes	15 / 39 (38.5)	9.9 [3.5, NE]	9 / 36 (25.0)	NE [NE, NE]	1.7339 [0.7577, 3.9675] 0.1926 0.1861	
No	37 / 205 (18.0)	NE [14.9, NE]	17 / 197 (8.6)	NE [NE, NE]	1.9271 [1.0841, 3.4258] 0.0254 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Presence of liver metastasis at baseline						0.0160
Yes	32 / 145 (22.1)	NE [11.3, NE]	23 / 149 (15.4)	NE [NE, NE]	1.3122 [0.7674, 2.2439] 0.3209 0.3191	
No	20 / 99 (20.2)	NE [NE, NE]	3 / 84 (3.6)	NE [NE, NE]	5.8082 [1.7237, 19.5710] 0.0045 0.0013	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Renal function at baseline						0.5948
Normal renal function	23 / 116 (19.8)	NE [11.3, NE]	12 / 114 (10.5)	NE [NE, NE]	1.8747 [0.9325, 3.7687] 0.0778 0.0733	
Mild impairment	24 / 87 (27.6)	NE [NE, NE]	10 / 81 (12.3)	NE [NE, NE]	2.2446 [1.0726, 4.6974] 0.0319 0.0274	
Moderate impairment	5 / 41 (12.2)	NE [11.4, NE]	4 / 38 (10.5)	NE [9.0, NE]	0.7867 [0.1945, 3.1813] 0.7364 0.7358	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Investigations; PT: Aspartate aminotransferase increased						
Hepatic function at baseline						0.0134
Normal hepatic function	42 / 185 (22.7)	NE [14.9, NE]	14 / 177 (7.9)	NE [NE, NE]	2.7443 [1.4969, 5.0312] 0.0011 0.0007	
Mild, Moderate or Severe dysfunction	10 / 59 (16.9)	NE [10.0, NE]	12 / 55 (21.8)	NE [6.6, NE]	0.7641 [0.3298, 1.7702] 0.5302 0.5296	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.6859
IHC 3+	16 / 205 (7.8)	NE [NE, NE]	5 / 196 (2.6)	NE [NE, NE]	3.0109 [1.1025, 8.2230] 0.0315 0.0241	
IHC 2+/ISH+	2 / 39 (5.1)	NE [NE, NE]	1 / 37 (2.7)	NE [NE, NE]	1.9098 [0.1732, 21.0622] 0.5973 0.5943	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Geography stratification factor						0.1849
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	0 / 59	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	13 / 138 (9.4)	NE [NE, NE]	6 / 129 (4.7)	NE [NE, NE]	1.9394 [0.7362, 5.1086] 0.1801 0.1760	
Mainland China/Rest of World (ROW)	5 / 49 (10.2)	NE [NE, NE]	0 / 45	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Time to progression on first-line therapy from IRT						0.3642
<6 Months	3 / 61 (4.9)	NE [NE, NE]	2 / 57 (3.5)	NE [NE, NE]	1.4159 [0.2366, 8.4750] 0.7032 0.7041	
≥6 Months	15 / 183 (8.2)	NE [NE, NE]	4 / 176 (2.3)	NE [NE, NE]	3.5351 [1.1725, 10.6586] 0.0249 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Age at randomization						0.4684
<65	7 / 139 (5.0)	NE [NE, NE]	3 / 123 (2.4)	NE [NE, NE]	1.9252 [0.4969, 7.4583] 0.3431 0.3359	
≥65	11 / 105 (10.5)	NE [NE, NE]	3 / 110 (2.7)	NE [NE, NE]	3.9102 [1.0904, 14.0217] 0.0364 0.0243	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Age at randomization						0.3407
<75	17 / 220 (7.7)	NE [NE, NE]	6 / 198 (3.0)	NE [NE, NE]	2.4693 [0.9726, 6.2696] 0.0572	
≥75	1 / 24 (4.2)	NE [NE, NE]	0 / 35	NE [NE, NE]	0.0502 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Sex						0.9865
Male	14 / 186 (7.5)	NE [NE, NE]	5 / 194 (2.6)	NE [NE, NE]	2.8685 [1.0320, 7.9730] 0.0433 0.0350	
Female	4 / 58 (6.9)	NE [NE, NE]	1 / 39 (2.6)	NE [NE, NE]	2.6097 [0.2913, 23.3772] 0.3912 0.3740	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Race						0.9652
White	10 / 115 (8.7)	NE [NE, NE]	4 / 120 (3.3)	NE [NE, NE]	2.5810 [0.8092, 8.2321] 0.1091 0.0977	
Asian	4 / 101 (4.0)	NE [NE, NE]	1 / 93 (1.1)	NE [NE, NE]	3.6658 [0.4096, 32.8042] 0.2453 0.2134	
Other	4 / 28 (14.3)	NE [NE, NE]	1 / 20 (5.0)	NE [NE, NE]	2.3863 [0.2582, 22.0545] 0.4433 0.4322	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
ECOG						0.0247
0	4 / 96 (4.2)	NE [NE, NE]	4 / 81 (4.9)	NE [NE, NE]	0.7353 [0.1823, 2.9656] 0.6657 0.6596	
≥1	14 / 148 (9.5)	NE [NE, NE]	2 / 152 (1.3)	NE [NE, NE]	7.2641 [1.6503, 31.9738] 0.0087 0.0021	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Primary tumor location						0.8603
Gastric	10 / 152 (6.6)	NE [NE, NE]	3 / 139 (2.2)	NE [NE, NE]	3.1388 [0.8638, 11.4057] 0.0823 0.0678	
GEJ	8 / 92 (8.7)	NE [NE, NE]	3 / 94 (3.2)	NE [NE, NE]	2.5099 [0.6643, 9.4827] 0.1748 0.1604	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Histological subtype						0.0365
Intestinal	13 / 68 (19.1)	NE [NE, NE]	1 / 63 (1.6)	NE [NE, NE]	12.4440 [1.6260, 95.2356] 0.0152 0.0018	
Diffuse	2 / 25 (8.0)	NE [NE, NE]	1 / 18 (5.6)	NE [5.5, NE]	1.4858 [0.1347, 16.3918] 0.7465 0.7449	
Others	3 / 151 (2.0)	NE [NE, NE]	4 / 152 (2.6)	NE [NE, NE]	0.6962 [0.1556, 3.1142] 0.6357 0.6338	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Number of metastatic sites						0.3156
<2	6 / 72 (8.3)	NE [NE, NE]	1 / 72 (1.4)	NE [NE, NE]	6.3578 [0.7655, 52.8015] 0.0868 0.0497	
≥2	12 / 172 (7.0)	NE [NE, NE]	5 / 161 (3.1)	NE [NE, NE]	2.0341 [0.7139, 5.7953] 0.1838 0.1755	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Prior adjuvant/neoadjuvant therapy						0.0811
Yes	1 / 31 (3.2)	NE [NE, NE]	2 / 28 (7.1)	NE [NE, NE]	0.4490 [0.0407, 4.9520] 0.5132 0.5019	
No	17 / 213 (8.0)	NE [NE, NE]	4 / 205 (2.0)	NE [NE, NE]	4.0042 [1.3463, 11.9089] 0.0126 0.0071	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Prior nivolumab or pembrolizumab treatment						0.2046
Yes	3 / 20 (15.0)	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	15 / 224 (6.7)	NE [NE, NE]	6 / 217 (2.8)	NE [NE, NE]	2.3449 [0.9090, 6.0487] 0.0780 0.0706	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.1087
Yes	4 / 39 (10.3)	NE [NE, NE]	0 / 36	NE [NE, NE]	NE [NE, NE] NE NE	
No	14 / 205 (6.8)	NE [NE, NE]	6 / 197 (3.0)	NE [NE, NE]	2.1416 [0.8220, 5.5794] 0.1190 0.1124	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Presence of liver metastasis at baseline						0.3280
Yes	12 / 145 (8.3)	NE [NE, NE]	3 / 149 (2.0)	NE [NE, NE]	4.2029 [1.1860, 14.8943] 0.0261 0.0160	
No	6 / 99 (6.1)	NE [NE, NE]	3 / 84 (3.6)	NE [NE, NE]	1.5000 [0.3733, 6.0267] 0.5677 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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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]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia Renal function at baseline						0.3144
Normal renal function	12 / 116 (10.3)	NE [NE, NE]	4 / 114 (3.5)	NE [NE, NE]	2.9991 [0.9664, 9.3074] 0.0573 0.0468	
Mild impairment	3 / 87 (3.4)	NE [NE, NE]	2 / 81 (2.5)	NE [NE, NE]	1.3044 [0.2177, 7.8155] 0.7711 0.7721	
Moderate impairment	3 / 41 (7.3)	NE [NE, NE]	0 / 38	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Blood and lymphatic system disorders; PT: Thrombocytopenia						
Hepatic function at baseline						0.0270
Normal hepatic function	11 / 185 (5.9)	NE [NE, NE]	6 / 177 (3.4)	NE [NE, NE]	1.7506 [0.6472, 4.7350] 0.2701 0.2671	
Mild, Moderate or Severe dysfunction	7 / 59 (11.9)	NE [8.5, NE]	0 / 55	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.2748
IHC 3+	18 / 205 (8.8)	NE [18.8, NE]	2 / 196 (1.0)	NE [NE, NE]	7.7265 [1.7894, 33.3629] 0.0062 0.0012	
IHC 2+/ISH+	2 / 39 (5.1)	NE [11.1, NE]	1 / 37 (2.7)	NE [NE, NE]	1.0603 [0.0923, 12.1860] 0.9625 0.9625	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Geography stratification factor						0.1118
Asia [excluding mainland China]	8 / 57 (14.0)	18.8 [11.1, NE]	3 / 59 (5.1)	NE [NE, NE]	2.6341 [0.6987, 9.9304] 0.1526 0.1370	
Western Europe	8 / 138 (5.8)	NE [NE, NE]	0 / 129	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	4 / 49 (8.2)	NE [NE, NE]	0 / 45	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Time to progression on first-line therapy from IRT						0.7200
<6 Months	5 / 61 (8.2)	NE [11.1, NE]	1 / 57 (1.8)	NE [NE, NE]	3.6582 [0.4203, 31.8439] 0.2401 0.2093	
≥6 Months	15 / 183 (8.2)	NE [18.8, NE]	2 / 176 (1.1)	NE [NE, NE]	6.3393 [1.4458, 27.7949] 0.0143 0.0050	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Age at randomization						0.1569
<65	7 / 139 (5.0)	NE [18.8, NE]	0 / 123	NE [NE, NE]	NE [NE, NE] NE NE	
≥65	13 / 105 (12.4)	NE [13.7, NE]	3 / 110 (2.7)	NE [NE, NE]	4.0503 [1.1474, 14.2979] 0.0297 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Age at randomization						0.4292
<75	15 / 220 (6.8)	NE [NE, NE]	1 / 198 (0.5)	NE [NE, NE]	11.4308 [1.5067, 86.7206] 0.0184 0.0029	
≥75	5 / 24 (20.8)	13.7 [5.5, NE]	2 / 35 (5.7)	NE [NE, NE]	3.8258 [0.7421, 19.7226] 0.1088 0.0843	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Sex						0.4616
Male	18 / 186 (9.7)	NE [18.8, NE]	3 / 194 (1.5)	NE [NE, NE]	5.0190 [1.4691, 17.1469] 0.0101	
Female	2 / 58 (3.4)	NE [NE, NE]	0 / 39	NE [NE, NE]	0.0043 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Race						0.2999
White	4 / 115 (3.5)	NE [NE, NE]	0 / 120	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	12 / 101 (11.9)	18.8 [18.8, NE]	3 / 93 (3.2)	NE [NE, NE]	3.4492 [0.9711, 12.2512] 0.0555 0.0417	
Other	4 / 28 (14.3)	13.7 [13.7, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
ECOG						0.1655
0	7 / 96 (7.3)	NE [18.8, NE]	2 / 81 (2.5)	NE [NE, NE]	2.0446 [0.4181, 9.9972] 0.3771 0.3675	
≥1	13 / 148 (8.8)	NE [NE, NE]	1 / 152 (0.7)	NE [NE, NE]	13.3527 [1.7468, 102.0705] 0.0125 0.0011	

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

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Primary tumor location						0.1738
Gastric	14 / 152 (9.2)	NE [18.8, NE]	3 / 139 (2.2)	NE [NE, NE]	3.9945 [1.1463, 13.9188] 0.0297	
GEJ	6 / 92 (6.5)	NE [NE, NE]	0 / 94	NE [NE, NE]	0.0187 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Histological subtype						0.3856
Intestinal	6 / 68 (8.8)	NE [13.7, NE]	2 / 63 (3.2)	NE [NE, NE]	2.1311 [0.4233, 10.7278] 0.3588 0.3480	
Diffuse	2 / 25 (8.0)	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	12 / 151 (7.9)	NE [18.8, NE]	1 / 152 (0.7)	NE [NE, NE]	10.7557 [1.3948, 82.9396] 0.0227 0.0044	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Number of metastatic sites						0.1498
<2	5 / 72 (6.9)	NE [NE, NE]	0 / 72	NE [NE, NE]	NE [NE, NE] NE NE	
≥2	15 / 172 (8.7)	NE [18.8, NE]	3 / 161 (1.9)	NE [NE, NE]	3.7171 [1.0708, 12.9034] 0.0387 0.0267	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Prior adjuvant/neoadjuvant therapy						0.3690
Yes	3 / 31 (9.7)	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	17 / 213 (8.0)	NE [18.8, NE]	3 / 205 (1.5)	NE [NE, NE]	4.7385 [1.3862, 16.1975] 0.0131 0.0062	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Prior nivolumab or pembrolizumab treatment						0.4902
Yes	2 / 20 (10.0)	NE [7.2, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	18 / 224 (8.0)	NE [18.8, NE]	3 / 217 (1.4)	NE [NE, NE]	5.1033 [1.5004, 17.3581] 0.0091 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.2519
Yes	4 / 39 (10.3)	NE [NE, NE]	0 / 36	NE [NE, NE]	NE [NE, NE] NE NE	
No	16 / 205 (7.8)	NE [18.8, NE]	3 / 197 (1.5)	NE [NE, NE]	4.3973 [1.2779, 15.1316] 0.0188 0.0103	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Presence of liver metastasis at baseline						0.9467
Yes	12 / 145 (8.3)	NE [NE, NE]	2 / 149 (1.3)	NE [NE, NE]	5.5419 [1.2398, 24.7733] 0.0250 0.0116	
No	8 / 99 (8.1)	NE [18.8, NE]	1 / 84 (1.2)	NE [NE, NE]	5.6748 [0.7065, 45.5796] 0.1024 0.0654	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Renal function at baseline						0.3522
Normal renal function	6 / 116 (5.2)	NE [NE, NE]	2 / 114 (1.8)	NE [NE, NE]	2.6607 [0.5347, 13.2399] 0.2320 0.2140	
Mild impairment	5 / 87 (5.7)	NE [18.8, NE]	0 / 81	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	9 / 41 (22.0)	NE [11.1, NE]	1 / 38 (2.6)	NE [NE, NE]	8.1282 [1.0283, 64.2474] 0.0470 0.0180	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Interstitial lung disease						
Hepatic function at baseline						0.0043
Normal hepatic function	16 / 185 (8.6)	NE [18.8, NE]	0 / 177	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	4 / 59 (6.8)	NE [NE, NE]	3 / 55 (5.5)	NE [NE, NE]	1.1348 [0.2534, 5.0829] 0.8687 0.8686	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.6861
IHC 3+	18 / 205 (8.8)	NE [NE, NE]	2 / 196 (1.0)	NE [NE, NE]	7.9268 [1.8380, 34.1863] 0.0055 0.0010	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	0 / 37	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Geography stratification factor						0.8984
Asia [excluding mainland China]	6 / 57 (10.5)	NE [15.2, NE]	1 / 59 (1.7)	NE [NE, NE]	5.0152 [0.5990, 41.9883] 0.1369 0.0993	
Western Europe	13 / 138 (9.4)	NE [NE, NE]	1 / 129 (0.8)	NE [NE, NE]	10.8891 [1.4243, 83.2479] 0.0214 0.0039	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	0 / 45	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Time to progression on first-line therapy from IRT						0.4436
<6 Months	5 / 61 (8.2)	NE [15.2, NE]	1 / 57 (1.8)	NE [NE, NE]	3.3217 [0.3793, 29.0898] 0.2782 0.2515	
≥6 Months	14 / 183 (7.7)	NE [NE, NE]	1 / 176 (0.6)	NE [NE, NE]	12.5215 [1.6467, 95.2116] 0.0146 0.0017	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Age at randomization						0.0725
<65	9 / 139 (6.5)	NE [NE, NE]	2 / 123 (1.6)	NE [NE, NE]	3.5044 [0.7566, 16.2311] 0.1089	
≥65	10 / 105 (9.5)	NE [15.2, NE]	0 / 110	NE [NE, NE]	0.0875 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Age at randomization						0.3807
<75	17 / 220 (7.7)	NE [NE, NE]	2 / 198 (1.0)	NE [NE, NE]	6.6689 [1.5390, 28.8987] 0.0112	
≥75	2 / 24 (8.3)	NE [NE, NE]	0 / 35	NE [NE, NE]	0.0034 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Sex						0.4678
Male	16 / 186 (8.6)	NE [NE, NE]	2 / 194 (1.0)	NE [NE, NE]	7.1116 [1.6304, 31.0198] 0.0090 0.0023	
Female	3 / 58 (5.2)	NE [NE, NE]	0 / 39	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Race						0.7839
White	11 / 115 (9.6)	NE [NE, NE]	1 / 120 (0.8)	NE [NE, NE]	10.5748 [1.3651, 81.9200] 0.0240 0.0048	
Asian	6 / 101 (5.9)	NE [15.2, NE]	1 / 93 (1.1)	NE [NE, NE]	4.8487 [0.5813, 40.4442] 0.1446 0.1069	
Other	2 / 28 (7.1)	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
ECOG						0.7499
0	13 / 96 (13.5)	NE [NE, NE]	1 / 81 (1.2)	NE [NE, NE]	9.6293 [1.2585, 73.6758] 0.0292 0.0075	
≥1	6 / 148 (4.1)	NE [15.2, NE]	1 / 152 (0.7)	NE [NE, NE]	5.7180 [0.6877, 47.5424] 0.1066 0.0680	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Primary tumor location						0.0776
Gastric	11 / 152 (7.2)	NE [NE, NE]	0 / 139	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	8 / 92 (8.7)	NE [NE, NE]	2 / 94 (2.1)	NE [NE, NE]	3.5539 [0.7546, 16.7367] 0.1087 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Histological subtype						0.7980
Intestinal	7 / 68 (10.3)	NE [15.2, NE]	1 / 63 (1.6)	NE [NE, NE]	5.5036 [0.6760, 44.8064] 0.1109 0.0730	
Diffuse	2 / 25 (8.0)	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	10 / 151 (6.6)	NE [NE, NE]	1 / 152 (0.7)	NE [NE, NE]	9.2375 [1.1824, 72.1683] 0.0340 0.0098	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Number of metastatic sites						0.7459
<2	10 / 72 (13.9)	NE [15.2, NE]	1 / 72 (1.4)	NE [NE, NE]	10.6991 [1.3672, 83.7232] 0.0239 0.0048	
≥2	9 / 172 (5.2)	NE [NE, NE]	1 / 161 (0.6)	NE [NE, NE]	6.8916 [0.8715, 54.4950] 0.0673 0.0336	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Prior adjuvant/neoadjuvant therapy						0.9995
Yes	0 / 31	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	19 / 213 (8.9)	NE [NE, NE]	2 / 205 (1.0)	NE [NE, NE]	8.2814 [1.9278, 35.5744] 0.0045 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Prior nivolumab or pembrolizumab treatment						0.6916
Yes	1 / 20 (5.0)	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	18 / 224 (8.0)	NE [NE, NE]	2 / 217 (0.9)	NE [NE, NE]	7.8359 [1.8169, 33.7940] 0.0058 0.0011	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.6457
Yes	1 / 39 (2.6)	NE [NE, NE]	0 / 36	NE [NE, NE]	NE [NE, NE] NE NE	
No	18 / 205 (8.8)	NE [NE, NE]	2 / 197 (1.0)	NE [NE, NE]	7.6367 [1.7703, 32.9433] 0.0064 0.0013	

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

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Presence of liver metastasis at baseline						0.0209
Yes	14 / 145 (9.7)	NE [NE, NE]	0 / 149	NE [NE, NE]	NE [NE, NE] NE NE	
No	5 / 99 (5.1)	NE [15.2, NE]	2 / 84 (2.4)	NE [NE, NE]	1.8370 [0.3549, 9.5072] 0.4684 0.4614	

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

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Renal function at baseline						0.2302
Normal renal function	8 / 116 (6.9)	NE [15.2, NE]	2 / 114 (1.8)	NE [NE, NE]	3.5078 [0.7436, 16.5471] 0.1128 0.0910	
Mild impairment	8 / 87 (9.2)	NE [NE, NE]	0 / 81	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	3 / 41 (7.3)	NE [NE, NE]	0 / 38	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Pneumonitis						
Hepatic function at baseline						0.1924
Normal hepatic function	12 / 185 (6.5)	NE [NE, NE]	2 / 177 (1.1)	NE [NE, NE]	5.0830 [1.1359, 22.7465] 0.0335	
Mild, Moderate or Severe dysfunction	7 / 59 (11.9)	NE [NE, NE]	0 / 55	NE [NE, NE]	0.0179 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.6881
IHC 3+	3 / 205 (1.5)	NE [NE, NE]	29 / 196 (14.8)	NE [NE, NE]	0.0864 [0.0263, 0.2839] <.0001 <.0001	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	5 / 37 (13.5)	NE [NE, NE]	0.1445 [0.0168, 1.2454] 0.0784 0.0410	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Geography stratification factor						0.4280
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	6 / 59 (10.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	4 / 138 (2.9)	NE [NE, NE]	26 / 129 (20.2)	NE [NE, NE]	0.1129 [0.0393, 0.3240] <.0001 <.0001	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	2 / 45 (4.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Time to progression on first-line therapy from IRT						0.0585
<6 Months	0 / 61	NE [NE, NE]	12 / 57 (21.1)	NE [4.6, NE]	NE [NE, NE] NE NE	
≥6 Months	4 / 183 (2.2)	NE [NE, NE]	22 / 176 (12.5)	NE [NE, NE]	0.1533 [0.0528, 0.4450] 0.0006 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Age at randomization						0.7530
<65	3 / 139 (2.2)	NE [NE, NE]	21 / 123 (17.1)	NE [NE, NE]	0.1062 [0.0316, 0.3565] 0.0003 <.0001	
≥65	1 / 105 (1.0)	NE [NE, NE]	13 / 110 (11.8)	NE [NE, NE]	0.0725 [0.0095, 0.5546] 0.0115 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Age at randomization						0.4005
<75	4 / 220 (1.8)	NE [NE, NE]	29 / 198 (14.6)	NE [NE, NE]	0.1047 [0.0368, 0.2982] <.0001 <.0001	
≥75	0 / 24	NE [NE, NE]	5 / 35 (14.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Sex						0.2959
Male	2 / 186 (1.1)	NE [NE, NE]	28 / 194 (14.4)	NE [NE, NE]	0.0631 [0.0150, 0.2651] 0.0002 <.0001	
Female	2 / 58 (3.4)	NE [NE, NE]	6 / 39 (15.4)	NE [NE, NE]	0.2029 [0.0409, 1.0066] 0.0510 0.0304	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Race						0.3318
White	3 / 115 (2.6)	NE [NE, NE]	20 / 120 (16.7)	NE [NE, NE]	0.1276 [0.0378, 0.4299] 0.0009 <.0001	
Asian	0 / 101	NE [NE, NE]	9 / 93 (9.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	1 / 28 (3.6)	NE [NE, NE]	5 / 20 (25.0)	NE [3.7, NE]	0.1143 [0.0133, 0.9829] 0.0482 0.0174	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
ECOG						0.2240
0	3 / 96 (3.1)	NE [NE, NE]	13 / 81 (16.0)	NE [NE, NE]	0.1665 [0.0474, 0.5849] 0.0052 0.0015	
≥1	1 / 148 (0.7)	NE [NE, NE]	21 / 152 (13.8)	NE [NE, NE]	0.0428 [0.0057, 0.3180] 0.0021 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Primary tumor location						0.3356
Gastric	1 / 152 (0.7)	NE [NE, NE]	17 / 139 (12.2)	NE [NE, NE]	0.0480 [0.0064, 0.3607] 0.0032 <.0001	
GEJ	3 / 92 (3.3)	NE [NE, NE]	17 / 94 (18.1)	NE [NE, NE]	0.1444 [0.0422, 0.4939] 0.0020 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Histological subtype						0.2327
Intestinal	2 / 68 (2.9)	NE [NE, NE]	5 / 63 (7.9)	NE [NE, NE]	0.3342 [0.0648, 1.7242] 0.1905 0.1690	
Diffuse	0 / 25	NE [NE, NE]	3 / 18 (16.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Others	2 / 151 (1.3)	NE [NE, NE]	26 / 152 (17.1)	NE [NE, NE]	0.0647 [0.0153, 0.2729] 0.0002 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Number of metastatic sites						0.0758
<2	0 / 72	NE [NE, NE]	13 / 72 (18.1)	NE [NE, NE]	NE [NE, NE] NE NE	
≥2	4 / 172 (2.3)	NE [NE, NE]	21 / 161 (13.0)	NE [NE, NE]	0.1459 [0.0499, 0.4259] 0.0004 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Prior adjuvant/neoadjuvant therapy						0.4840
Yes	0 / 31	NE [NE, NE]	2 / 28 (7.1)	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 213 (1.9)	NE [NE, NE]	32 / 205 (15.6)	NE [NE, NE]	0.1023 [0.0362, 0.2896] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Prior nivolumab or pembrolizumab treatment						0.6171
Yes	0 / 20	NE [NE, NE]	1 / 16 (6.3)	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 224 (1.8)	NE [NE, NE]	33 / 217 (15.2)	NE [NE, NE]	0.0996 [0.0353, 0.2813] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.6512
Yes	0 / 39	NE [NE, NE]	1 / 36 (2.8)	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 205 (2.0)	NE [NE, NE]	33 / 197 (16.8)	NE [NE, NE]	0.0967 [0.0342, 0.2732] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Presence of liver metastasis at baseline						0.1980
Yes	1 / 145 (0.7)	NE [NE, NE]	21 / 149 (14.1)	NE [NE, NE]	0.0406 [0.0055, 0.3021] 0.0018 <.0001	
No	3 / 99 (3.0)	NE [NE, NE]	13 / 84 (15.5)	NE [NE, NE]	0.1756 [0.0500, 0.6164] 0.0066 0.0021	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Renal function at baseline						0.4324
Normal renal function	3 / 116 (2.6)	NE [NE, NE]	17 / 114 (14.9)	NE [NE, NE]	0.1564 [0.0458, 0.5337] 0.0031 0.0007	
Mild impairment	1 / 87 (1.1)	NE [NE, NE]	13 / 81 (16.0)	NE [NE, NE]	0.0569 [0.0074, 0.4353] 0.0058 0.0001	
Moderate impairment	0 / 41	NE [NE, NE]	4 / 38 (10.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Epistaxis						
Hepatic function at baseline						0.5656
Normal hepatic function	2 / 185 (1.1)	NE [NE, NE]	23 / 177 (13.0)	NE [NE, NE]	0.0730 [0.0172, 0.3099] 0.0004 <.0001	
Mild, Moderate or Severe dysfunction	2 / 59 (3.4)	NE [NE, NE]	11 / 55 (20.0)	NE [6.7, NE]	0.1347 [0.0297, 0.6098] 0.0093 0.0023	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.6459
IHC 3+	1 / 205 (0.5)	NE [NE, NE]	9 / 196 (4.6)	NE [NE, NE]	0.0960 [0.0122, 0.7589] 0.0263 0.0057	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	1 / 37 (2.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Geography stratification factor						NE
Asia [excluding mainland China]	1 / 57 (1.8)	NE [NE, NE]	1 / 59 (1.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	0 / 138	NE [NE, NE]	9 / 129 (7.0)	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	0 / 45	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Time to progression on first-line therapy from IRT						NE
<6 Months	0 / 61	NE [NE, NE]	0 / 57	NE [NE, NE]	NE [NE, NE] NE NE	
≥6 Months	1 / 183 (0.5)	NE [NE, NE]	10 / 176 (5.7)	NE [NE, NE]	0.0864 [0.0111, 0.6755] 0.0196 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Age at randomization						NE
<65	1 / 139 (0.7)	NE [NE, NE]	6 / 123 (4.9)	NE [NE, NE]	NE [NE, NE] NE NE	
≥65	0 / 105	NE [NE, NE]	4 / 110 (3.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Age at randomization						0.7337
<75	1 / 220 (0.5)	NE [NE, NE]	9 / 198 (4.5)	NE [NE, NE]	0.0886 [0.0112, 0.7001] 0.0216	
≥75	0 / 24	NE [NE, NE]	1 / 35 (2.9)	NE [NE, NE]	0.0037 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Sex						NE
Male	1 / 186 (0.5)	NE [NE, NE]	8 / 194 (4.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Female	0 / 58	NE [NE, NE]	2 / 39 (5.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Race						NE
White	0 / 115	NE [NE, NE]	8 / 120 (6.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	1 / 101 (1.0)	NE [NE, NE]	1 / 93 (1.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	1 / 20 (5.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
ECOG						NE
0	1 / 96 (1.0)	NE [NE, NE]	4 / 81 (4.9)	NE [NE, NE]	NE [NE, NE] NE NE	
≥1	0 / 148	NE [NE, NE]	6 / 152 (3.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Primary tumor location						NE
Gastric	1 / 152 (0.7)	NE [NE, NE]	4 / 139 (2.9)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	0 / 92	NE [NE, NE]	6 / 94 (6.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Histological subtype						NE
Intestinal	0 / 68	NE [NE, NE]	3 / 63 (4.8)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	1 / 151 (0.7)	NE [NE, NE]	7 / 152 (4.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Number of metastatic sites						NE
<2	0 / 72	NE [NE, NE]	4 / 72 (5.6)	NE [NE, NE]	NE [NE, NE] NE NE	
≥2	1 / 172 (0.6)	NE [NE, NE]	6 / 161 (3.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Prior adjuvant/neoadjuvant therapy						NE
Yes	1 / 31 (3.2)	NE [NE, NE]	2 / 28 (7.1)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 213	NE [NE, NE]	8 / 205 (3.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Prior nivolumab or pembrolizumab treatment						0.6186
Yes	0 / 20	NE [NE, NE]	1 / 16 (6.3)	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 224 (0.4)	NE [NE, NE]	9 / 217 (4.1)	NE [NE, NE]	0.0959 [0.0121, 0.7575] 0.0262 0.0057	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.6608
Yes	0 / 39	NE [NE, NE]	1 / 36 (2.8)	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 205 (0.5)	NE [NE, NE]	9 / 197 (4.6)	NE [NE, NE]	0.0932 [0.0118, 0.7365] 0.0245 0.0049	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Presence of liver metastasis at baseline						NE
Yes	1 / 145 (0.7)	NE [NE, NE]	8 / 149 (5.4)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 99	NE [NE, NE]	2 / 84 (2.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Renal function at baseline						NE
Normal renal function	0 / 116	NE [NE, NE]	6 / 114 (5.3)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	0 / 87	NE [NE, NE]	3 / 81 (3.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	1 / 41 (2.4)	NE [NE, NE]	1 / 38 (2.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Respiratory, thoracic and mediastinal disorders; PT: Dysphonia						
Hepatic function at baseline						NE
Normal hepatic function	0 / 185	NE [NE, NE]	8 / 177 (4.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	1 / 59 (1.7)	NE [NE, NE]	2 / 55 (3.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.5096
IHC 3+	55 / 205 (26.8)	NE [13.2, NE]	98 / 196 (50.0)	5.1 [3.0, 6.6]	0.4065 [0.2915, 0.5667] <.0001 <.0001	
IHC 2+/ISH+	7 / 39 (17.9)	NE [6.5, NE]	16 / 37 (43.2)	4.7 [2.3, NE]	0.2977 [0.1219, 0.7272] 0.0078 0.0047	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Geography stratification factor						0.1844
Asia [excluding mainland China]	7 / 57 (12.3)	NE [NE, NE]	26 / 59 (44.1)	5.7 [4.6, NE]	0.1969 [0.0848, 0.4572] 0.0002 <.0001	
Western Europe	42 / 138 (30.4)	13.2 [7.9, NE]	68 / 129 (52.7)	3.8 [1.9, 5.7]	0.3896 [0.2633, 0.5765] <.0001 <.0001	
Mainland China/Rest of World (ROW)	13 / 49 (26.5)	NE [NE, NE]	20 / 45 (44.4)	8.5 [3.7, NE]	0.5766 [0.2867, 1.1598] 0.1226 0.1166	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Time to progression on first-line therapy from IRT						0.4769
<6 Months	13 / 61 (21.3)	NE [9.6, NE]	26 / 57 (45.6)	4.9 [1.5, NE]	0.2979 [0.1466, 0.6051] 0.0008 0.0004	
≥6 Months	49 / 183 (26.8)	NE [13.2, NE]	88 / 176 (50.0)	5.4 [3.7, 6.6]	0.4103 [0.2888, 0.5831] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Age at randomization						0.8744
<65	38 / 139 (27.3)	NE [10.1, NE]	61 / 123 (49.6)	5.0 [2.9, 7.4]	0.3877 [0.2574, 0.5840] <.0001 <.0001	
≥65	24 / 105 (22.9)	NE [NE, NE]	53 / 110 (48.2)	5.4 [2.3, NE]	0.3841 [0.2368, 0.6231] 0.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Age at randomization						0.6268
<75	56 / 220 (25.5)	NE [13.2, NE]	98 / 198 (49.5)	5.0 [3.1, 6.6]	0.3730 [0.2678, 0.5197] <.0001 <.0001	
≥75	6 / 24 (25.0)	NE [5.3, NE]	16 / 35 (45.7)	5.7 [2.1, NE]	0.4847 [0.1889, 1.2433] 0.1318 0.1233	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Sex						0.1645
Male	48 / 186 (25.8)	NE [13.2, NE]	89 / 194 (45.9)	5.7 [4.2, 12.0]	0.4269 [0.2999, 0.6076] <.0001 <.0001	
Female	14 / 58 (24.1)	10.1 [7.9, NE]	25 / 39 (64.1)	2.3 [1.0, 5.7]	0.2273 [0.1136, 0.4545] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Race						0.3784
White	33 / 115 (28.7)	13.2 [7.9, NE]	57 / 120 (47.5)	5.1 [2.3, NE]	0.4465 [0.2888, 0.6904] 0.0003 0.0002	
Asian	21 / 101 (20.8)	NE [NE, NE]	44 / 93 (47.3)	5.7 [4.6, 12.0]	0.3491 [0.2071, 0.5884] <.0001 <.0001	
Other	8 / 28 (28.6)	NE [5.3, NE]	13 / 20 (65.0)	1.4 [0.3, NE]	0.2254 [0.0888, 0.5724] 0.0017 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
ECOG						0.4040
0	27 / 96 (28.1)	NE [9.6, NE]	35 / 81 (43.2)	5.8 [2.4, NE]	0.4838 [0.2905, 0.8058] 0.0053 0.0044	
≥1	35 / 148 (23.6)	NE [10.1, NE]	79 / 152 (52.0)	5.0 [3.0, 6.3]	0.3472 [0.2329, 0.5176] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Primary tumor location						0.1038
Gastric	29 / 152 (19.1)	NE [NE, NE]	66 / 139 (47.5)	5.1 [3.0, NE]	0.3093 [0.1994, 0.4797] <.0001 <.0001	
GEJ	33 / 92 (35.9)	13.2 [6.9, NE]	48 / 94 (51.1)	4.9 [2.3, 6.6]	0.4961 [0.3159, 0.7792] 0.0023 0.0019	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Histological subtype						0.1867
Intestinal	18 / 68 (26.5)	NE [6.9, NE]	28 / 63 (44.4)	5.0 [2.1, NE]	0.4930 [0.2722, 0.8930] 0.0196 0.0168	
Diffuse	3 / 25 (12.0)	NE [NE, NE]	10 / 18 (55.6)	2.1 [1.0, NE]	0.1560 [0.0421, 0.5783] 0.0055 0.0015	
Others	41 / 151 (27.2)	NE [10.1, NE]	76 / 152 (50.0)	5.4 [3.0, 6.6]	0.4002 [0.2732, 0.5864] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Number of metastatic sites						0.5415
<2	16 / 72 (22.2)	NE [10.1, NE]	31 / 72 (43.1)	6.6 [4.9, NE]	0.4257 [0.2315, 0.7828] 0.0060 0.0047	
≥2	46 / 172 (26.7)	NE [NE, NE]	83 / 161 (51.6)	4.6 [2.1, 5.7]	0.3688 [0.2564, 0.5305] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Prior adjuvant/neoadjuvant therapy						0.9955
Yes	6 / 31 (19.4)	NE [NE, NE]	10 / 28 (35.7)	NE [1.4, NE]	0.4580 [0.1663, 1.2616] 0.1309 0.1214	
No	56 / 213 (26.3)	NE [13.2, NE]	104 / 205 (50.7)	5.0 [3.1, 5.8]	0.3837 [0.2766, 0.5322] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Prior nivolumab or pembrolizumab treatment						0.9451
Yes	4 / 20 (20.0)	NE [6.2, NE]	6 / 16 (37.5)	NE [1.8, NE]	0.3949 [0.1063, 1.4667] 0.1652 0.1521	
No	58 / 224 (25.9)	NE [13.2, NE]	108 / 217 (49.8)	5.1 [3.1, 6.3]	0.3881 [0.2815, 0.5352] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						0.8120
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						
Yes	8 / 39 (20.5)	NE [NE, NE]	15 / 36 (41.7)	8.5 [3.0, NE]	0.4224 [0.1787, 0.9988] 0.0497 0.0429	
No	54 / 205 (26.3)	NE [13.2, NE]	99 / 197 (50.3)	5.0 [2.9, 5.8]	0.3820 [0.2734, 0.5338] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Presence of liver metastasis at baseline						0.1402
Yes	35 / 145 (24.1)	NE [NE, NE]	79 / 149 (53.0)	4.4 [2.3, 5.8]	0.3270 [0.2191, 0.4880] <.0001 <.0001	
No	27 / 99 (27.3)	13.2 [9.6, NE]	35 / 84 (41.7)	5.7 [4.7, NE]	0.5209 [0.3137, 0.8651] 0.0117 0.0104	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Renal function at baseline						0.2848
Normal renal function	31 / 116 (26.7)	NE [10.1, NE]	52 / 114 (45.6)	5.7 [3.7, NE]	0.4713 [0.3012, 0.7373] 0.0010 0.0008	
Mild impairment	23 / 87 (26.4)	13.2 [7.4, NE]	40 / 81 (49.4)	5.1 [2.3, 12.0]	0.4083 [0.2441, 0.6831] 0.0006 0.0004	
Moderate impairment	8 / 41 (19.5)	NE [9.6, NE]	22 / 38 (57.9)	4.6 [1.4, 6.6]	0.2124 [0.0927, 0.4866] 0.0002 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Hepatic function at baseline						0.6280
Normal hepatic function	49 / 185 (26.5)	NE [13.2, NE]	89 / 177 (50.3)	5.1 [3.8, 6.6]	0.3968 [0.2789, 0.5645] <.0001 <.0001	
Mild, Moderate or Severe dysfunction	13 / 59 (22.0)	NE [7.1, NE]	25 / 55 (45.5)	3.1 [1.0, NE]	0.3342 [0.1699, 0.6572] 0.0015 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.5650
IHC 3+	14 / 205 (6.8)	NE [NE, NE]	3 / 196 (1.5)	NE [NE, NE]	4.2578 [1.2231, 14.8222] 0.0228 0.0131	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	0 / 37	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Geography stratification factor						0.7674
Asia [excluding mainland China]	1 / 57 (1.8)	NE [NE, NE]	0 / 59	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	8 / 138 (5.8)	NE [NE, NE]	2 / 129 (1.6)	NE [NE, NE]	3.4396 [0.7298, 16.2101] 0.1183 0.0965	
Mainland China/Rest of World (ROW)	6 / 49 (12.2)	NE [NE, NE]	1 / 45 (2.2)	NE [NE, NE]	5.6895 [0.6843, 47.3065] 0.1076 0.0685	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Time to progression on first-line therapy from IRT						0.4001
<6 Months	2 / 61 (3.3)	NE [NE, NE]	0 / 57	NE [NE, NE]	NE [NE, NE] NE NE	
≥6 Months	13 / 183 (7.1)	NE [NE, NE]	3 / 176 (1.7)	NE [NE, NE]	3.9499 [1.1249, 13.8692] 0.0321 0.0206	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Age at randomization						0.2634
<65	11 / 139 (7.9)	NE [NE, NE]	1 / 123 (0.8)	NE [NE, NE]	8.7308 [1.1261, 67.6902] 0.0381 0.0123	
≥65	4 / 105 (3.8)	NE [NE, NE]	2 / 110 (1.8)	NE [NE, NE]	2.0877 [0.3823, 11.4001] 0.3954 0.3854	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Age at randomization						0.3995
<75	14 / 220 (6.4)	NE [NE, NE]	2 / 198 (1.0)	NE [NE, NE]	5.8145 [1.3205, 25.6036] 0.0199 0.0083	
≥75	1 / 24 (4.2)	NE [NE, NE]	1 / 35 (2.9)	NE [NE, NE]	1.4790 [0.0925, 23.6475] 0.7820 0.7806	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Sex						0.3460
Male	12 / 186 (6.5)	NE [NE, NE]	3 / 194 (1.5)	NE [NE, NE]	3.7685 [1.0627, 13.3638] 0.0400	
Female	3 / 58 (5.2)	NE [NE, NE]	0 / 39	NE [NE, NE]	0.0273 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Race						0.8674
White	8 / 115 (7.0)	NE [NE, NE]	2 / 120 (1.7)	NE [NE, NE]	3.9592 [0.8402, 18.6566] 0.0819 0.0602	
Asian	6 / 101 (5.9)	NE [NE, NE]	1 / 93 (1.1)	NE [NE, NE]	5.1842 [0.6236, 43.0984] 0.1278 0.0890	
Other	1 / 28 (3.6)	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
ECOG						0.6475
0	4 / 96 (4.2)	NE [NE, NE]	1 / 81 (1.2)	NE [NE, NE]	3.0714 [0.3427, 27.5230] 0.3159 0.2909	
≥1	11 / 148 (7.4)	NE [NE, NE]	2 / 152 (1.3)	NE [NE, NE]	5.4704 [1.2124, 24.6836] 0.0271 0.0130	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Primary tumor location						0.3923
Gastric	9 / 152 (5.9)	NE [NE, NE]	1 / 139 (0.7)	NE [NE, NE]	7.9795 [1.0104, 63.0158] 0.0489 0.0192	
GEJ	6 / 92 (6.5)	NE [NE, NE]	2 / 94 (2.1)	NE [NE, NE]	2.7116 [0.5458, 13.4708] 0.2226 0.2037	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Histological subtype						NE
Intestinal	7 / 68 (10.3)	NE [NE, NE]	1 / 63 (1.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	1 / 25 (4.0)	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	7 / 151 (4.6)	NE [NE, NE]	2 / 152 (1.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Number of metastatic sites						0.1493
<2	4 / 72 (5.6)	NE [NE, NE]	0 / 72	NE [NE, NE]	NE [NE, NE] NE NE	
≥2	11 / 172 (6.4)	NE [NE, NE]	3 / 161 (1.9)	NE [NE, NE]	3.0097 [0.8367, 10.8259] 0.0916 0.0764	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Prior adjuvant/neoadjuvant therapy						0.2159
Yes	1 / 31 (3.2)	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	0.8311 [0.0519, 13.3189] 0.8960 0.8959	
No	14 / 213 (6.6)	NE [NE, NE]	2 / 205 (1.0)	NE [NE, NE]	6.3049 [1.4319, 27.7615] 0.0149 0.0052	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Prior nivolumab or pembrolizumab treatment						0.3271
Yes	2 / 20 (10.0)	NE [NE, NE]	1 / 16 (6.3)	NE [NE, NE]	1.5592 [0.1414, 17.1979] 0.7169 0.7146	
No	13 / 224 (5.8)	NE [NE, NE]	2 / 217 (0.9)	NE [NE, NE]	5.8954 [1.3296, 26.1396] 0.0195 0.0080	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.4177
Yes	2 / 39 (5.1)	NE [NE, NE]	1 / 36 (2.8)	NE [NE, NE]	1.8351 [0.1664, 20.2392] 0.6201 0.6147	
No	13 / 205 (6.3)	NE [NE, NE]	2 / 197 (1.0)	NE [NE, NE]	5.7911 [1.3059, 25.6812] 0.0208 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Presence of liver metastasis at baseline						0.7817
Yes	8 / 145 (5.5)	NE [NE, NE]	2 / 149 (1.3)	NE [NE, NE]	3.8711 [0.8213, 18.2457] 0.0871 0.0652	
No	7 / 99 (7.1)	NE [NE, NE]	1 / 84 (1.2)	NE [NE, NE]	5.4678 [0.6720, 44.4910] 0.1122 0.0742	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Renal function at baseline						NE
Normal renal function	9 / 116 (7.8)	NE [NE, NE]	0 / 114	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	4 / 87 (4.6)	NE [NE, NE]	2 / 81 (2.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	2 / 41 (4.9)	NE [NE, NE]	1 / 38 (2.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Dizziness						
Hepatic function at baseline						0.2097
Normal hepatic function	11 / 185 (5.9)	NE [NE, NE]	3 / 177 (1.7)	NE [NE, NE]	3.4179 [0.9532, 12.2554] 0.0592 0.0448	
Mild, Moderate or Severe dysfunction	4 / 59 (6.8)	NE [NE, NE]	0 / 55	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.9899
IHC 3+	7 / 205 (3.4)	NE [NE, NE]	31 / 196 (15.8)	NE [NE, NE]	0.1730 [0.0760, 0.3939] <.0001 <.0001	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	4 / 37 (10.8)	14.1 [NE, NE]	0.1535 [0.0167, 1.4144] 0.0981 0.0599	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						0.1620
Geography stratification factor						
Asia [excluding mainland China]	1 / 57 (1.8)	NE [NE, NE]	12 / 59 (20.3)	NE [5.7, NE]	0.0574 [0.0074, 0.4457] 0.0063 0.0002	
Western Europe	7 / 138 (5.1)	NE [NE, NE]	19 / 129 (14.7)	NE [14.1, NE]	0.2634 [0.1100, 0.6305] 0.0027 0.0013	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	4 / 45 (8.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Time to progression on first-line therapy from IRT						0.8745
<6 Months	2 / 61 (3.3)	NE [10.1, NE]	7 / 57 (12.3)	NE [NE, NE]	0.1794 [0.0358, 0.8991] 0.0367 0.0206	
≥6 Months	6 / 183 (3.3)	NE [NE, NE]	28 / 176 (15.9)	NE [14.1, NE]	0.1641 [0.0677, 0.3977] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						0.4984
Age at randomization						
<65	5 / 139 (3.6)	NE [NE, NE]	16 / 123 (13.0)	NE [14.1, NE]	0.2139 [0.0780, 0.5866] 0.0027 0.0010	
≥65	3 / 105 (2.9)	NE [NE, NE]	19 / 110 (17.3)	NE [NE, NE]	0.1374 [0.0406, 0.4650] 0.0014 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Age at randomization						0.7183
<75	7 / 220 (3.2)	NE [NE, NE]	26 / 198 (13.1)	NE [14.1, NE]	0.1859 [0.0802, 0.4309] <.0001 <.0001	
≥75	1 / 24 (4.2)	NE [NE, NE]	9 / 35 (25.7)	NE [5.7, NE]	0.1254 [0.0157, 1.0021] 0.0502 0.0210	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						0.7887
Sex						
Male	5 / 186 (2.7)	NE [NE, NE]	26 / 194 (13.4)	NE [NE, NE]	0.1618 [0.0620, 0.4222] 0.0002 <.0001	
Female	3 / 58 (5.2)	NE [10.1, NE]	9 / 39 (23.1)	14.1 [14.1, NE]	0.1893 [0.0509, 0.7041] 0.0130 0.0056	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Race						0.3098
White	5 / 115 (4.3)	NE [NE, NE]	14 / 120 (11.7)	NE [14.1, NE]	0.3037 [0.1088, 0.8473] 0.0228 0.0160	
Asian	2 / 101 (2.0)	NE [NE, NE]	17 / 93 (18.3)	NE [NE, NE]	0.0831 [0.0191, 0.3618] 0.0009 <.0001	
Other	1 / 28 (3.6)	NE [NE, NE]	4 / 20 (20.0)	NE [NE, NE]	0.0875 [0.0079, 0.9736] 0.0475 0.0212	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
ECOG						0.1768
0	4 / 96 (4.2)	NE [NE, NE]	7 / 81 (8.6)	NE [NE, NE]	0.3975 [0.1155, 1.3683] 0.1435 0.1302	
≥1	4 / 148 (2.7)	NE [NE, NE]	28 / 152 (18.4)	14.1 [14.1, NE]	0.1110 [0.0386, 0.3190] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						0.0563
Primary tumor location						
Gastric	3 / 152 (2.0)	NE [NE, NE]	25 / 139 (18.0)	NE [NE, NE]	0.0885 [0.0266, 0.2943] <.0001 <.0001	
GEJ	5 / 92 (5.4)	NE [NE, NE]	10 / 94 (10.6)	NE [14.1, NE]	0.3695 [0.1252, 1.0903] 0.0713 0.0607	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Histological subtype						0.0119
Intestinal	0 / 68	NE [NE, NE]	11 / 63 (17.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	3 / 18 (16.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Others	8 / 151 (5.3)	NE [NE, NE]	21 / 152 (13.8)	NE [14.1, NE]	0.3024 [0.1334, 0.6854] 0.0042 0.0024	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Number of metastatic sites						0.7212
<2	3 / 72 (4.2)	NE [NE, NE]	13 / 72 (18.1)	14.1 [NE, NE]	0.1788 [0.0493, 0.6485] 0.0088 0.0036	
≥2	5 / 172 (2.9)	NE [NE, NE]	22 / 161 (13.7)	NE [NE, NE]	0.1576 [0.0593, 0.4188] 0.0002 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Prior adjuvant/neoadjuvant therapy						0.2393
Yes	0 / 31	NE [NE, NE]	3 / 28 (10.7)	NE [NE, NE]	NE [NE, NE] NE NE	
No	8 / 213 (3.8)	NE [NE, NE]	32 / 205 (15.6)	NE [14.1, NE]	0.1868 [0.0857, 0.4069] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Prior nivolumab or pembrolizumab treatment						0.9588
Yes	1 / 20 (5.0)	NE [6.2, NE]	3 / 16 (18.8)	NE [NE, NE]	0.1702 [0.0161, 1.7975] 0.1409 0.1037	
No	7 / 224 (3.1)	NE [NE, NE]	32 / 217 (14.7)	NE [14.1, NE]	0.1649 [0.0725, 0.3751] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.9283
Yes	1 / 39 (2.6)	NE [NE, NE]	5 / 36 (13.9)	NE [8.5, NE]	0.1615 [0.0188, 1.3854] 0.0964 0.0574	
No	7 / 205 (3.4)	NE [NE, NE]	30 / 197 (15.2)	NE [14.1, NE]	0.1705 [0.0745, 0.3902] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Presence of liver metastasis at baseline						0.4401
Yes	6 / 145 (4.1)	NE [NE, NE]	23 / 149 (15.4)	NE [14.1, NE]	0.2079 [0.0842, 0.5131] 0.0007 0.0002	
No	2 / 99 (2.0)	NE [NE, NE]	12 / 84 (14.3)	NE [NE, NE]	0.1121 [0.0248, 0.5067] 0.0045 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Peripheral sensory neuropathy						
Renal function at baseline						0.3541
Normal renal function	3 / 116 (2.6)	NE [NE, NE]	13 / 114 (11.4)	NE [14.1, NE]	0.1886 [0.0534, 0.6654] 0.0095 0.0038	
Mild impairment	4 / 87 (4.6)	NE [NE, NE]	11 / 81 (13.6)	NE [NE, NE]	0.2468 [0.0783, 0.7778] 0.0169 0.0097	
Moderate impairment	1 / 41 (2.4)	NE [NE, NE]	11 / 38 (28.9)	NE [5.7, NE]	0.0676 [0.0087, 0.5247] 0.0100 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT:						
Peripheral sensory neuropathy						0.2245
Hepatic function at baseline						
Normal hepatic function	7 / 185 (3.8)	NE [NE, NE]	24 / 177 (13.6)	NE [NE, NE]	0.2153 [0.0924, 0.5021] 0.0004 <.0001	
Mild, Moderate or Severe dysfunction	1 / 59 (1.7)	NE [NE, NE]	11 / 55 (20.0)	14.1 [NE, NE]	0.0645 [0.0083, 0.5035] 0.0089 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.9317
IHC 3+	6 / 205 (2.9)	NE [NE, NE]	21 / 196 (10.7)	NE [NE, NE]	0.2499 [0.1009, 0.6194] 0.0028 0.0012	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	3 / 37 (8.1)	NE [NE, NE]	0.2577 [0.0268, 2.4816] 0.2406 0.2059	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Geography stratification factor						0.5977
Asia [excluding mainland China]	2 / 57 (3.5)	NE [NE, NE]	6 / 59 (10.2)	NE [NE, NE]	0.3127 [0.0631, 1.5506] 0.1547 0.1330	
Western Europe	5 / 138 (3.6)	NE [NE, NE]	16 / 129 (12.4)	NE [NE, NE]	0.2586 [0.0947, 0.7062] 0.0083 0.0045	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	2 / 45 (4.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Time to progression on first-line therapy from IRT						0.2858
<6 Months	3 / 61 (4.9)	NE [NE, NE]	5 / 57 (8.8)	NE [NE, NE]	0.5012 [0.1196, 2.1003] 0.3447 0.3352	
≥6 Months	4 / 183 (2.2)	NE [NE, NE]	19 / 176 (10.8)	NE [NE, NE]	0.1844 [0.0627, 0.5421] 0.0021 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 Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Age at randomization						0.5389
<65	3 / 139 (2.2)	NE [NE, NE]	12 / 123 (9.8)	NE [NE, NE]	0.1923 [0.0542, 0.6821] 0.0107 0.0044	
≥65	4 / 105 (3.8)	NE [NE, NE]	12 / 110 (10.9)	NE [NE, NE]	0.3335 [0.1075, 1.0341] 0.0572 0.0456	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Age at randomization						0.0212
<75	4 / 220 (1.8)	NE [NE, NE]	21 / 198 (10.6)	NE [NE, NE]	0.1525 [0.0523, 0.4444] 0.0006 <.0001	
≥75	3 / 24 (12.5)	NE [NE, NE]	3 / 35 (8.6)	NE [NE, NE]	1.5441 [0.3115, 7.6533] 0.5948 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Sex						0.4863
Male	5 / 186 (2.7)	NE [NE, NE]	21 / 194 (10.8)	NE [NE, NE]	0.2182 [0.0822, 0.5788] 0.0022 0.0008	
Female	2 / 58 (3.4)	NE [NE, NE]	3 / 39 (7.7)	NE [NE, NE]	0.4471 [0.0747, 2.6760] 0.3779 0.3651	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Race						0.9308
White	3 / 115 (2.6)	NE [NE, NE]	12 / 120 (10.0)	NE [NE, NE]	0.2361 [0.0666, 0.8371] 0.0254 0.0150	
Asian	2 / 101 (2.0)	NE [NE, NE]	6 / 93 (6.5)	NE [NE, NE]	0.2864 [0.0578, 1.4195] 0.1258 0.1028	
Other	2 / 28 (7.1)	NE [NE, NE]	6 / 20 (30.0)	NE [1.9, NE]	0.1927 [0.0387, 0.9607] 0.0445 0.0253	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
ECOG						0.0925
0	6 / 96 (6.3)	NE [NE, NE]	11 / 81 (13.6)	NE [NE, NE]	0.4094 [0.1513, 1.1083] 0.0788 0.0695	
≥1	1 / 148 (0.7)	NE [NE, NE]	13 / 152 (8.6)	NE [NE, NE]	0.0729 [0.0095, 0.5575] 0.0116 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Primary tumor location						0.7259
Gastric	4 / 152 (2.6)	NE [NE, NE]	12 / 139 (8.6)	NE [NE, NE]	0.2910 [0.0939, 0.9025] 0.0326 0.0229	
GEJ	3 / 92 (3.3)	NE [NE, NE]	12 / 94 (12.8)	NE [NE, NE]	0.2086 [0.0588, 0.7408] 0.0153 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Histological subtype						0.7549
Intestinal	2 / 68 (2.9)	NE [NE, NE]	4 / 63 (6.3)	NE [NE, NE]	0.4279 [0.0783, 2.3373] 0.3271 0.3127	
Diffuse	1 / 25 (4.0)	NE [NE, NE]	2 / 18 (11.1)	NE [NE, NE]	0.3430 [0.0310, 3.7900] 0.3827 0.3602	
Others	4 / 151 (2.6)	NE [NE, NE]	18 / 152 (11.8)	NE [NE, NE]	0.1995 [0.0675, 0.5898] 0.0036 0.0012	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Number of metastatic sites						0.8391
<2	1 / 72 (1.4)	NE [NE, NE]	5 / 72 (6.9)	NE [NE, NE]	0.2013 [0.0235, 1.7236] 0.1434 0.1042	
≥2	6 / 172 (3.5)	NE [NE, NE]	19 / 161 (11.8)	NE [NE, NE]	0.2565 [0.1024, 0.6428] 0.0037 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Prior adjuvant/neoadjuvant therapy						0.4597
Yes	0 / 31	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	7 / 213 (3.3)	NE [NE, NE]	23 / 205 (11.2)	NE [NE, NE]	0.2633 [0.1129, 0.6137] 0.0020 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Prior nivolumab or pembrolizumab treatment						NE
Yes	0 / 20	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	7 / 224 (3.1)	NE [NE, NE]	24 / 217 (11.1)	NE [NE, NE]	0.2539 [0.1094, 0.5894] 0.0014 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.9994
Yes	0 / 39	NE [NE, NE]	0 / 36	NE [NE, NE]	NE [NE, NE] NE NE	
No	7 / 205 (3.4)	NE [NE, NE]	24 / 197 (12.2)	NE [NE, NE]	0.2485 [0.1070, 0.5770] 0.0012 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neuropathy peripheral						
Presence of liver metastasis at baseline						0.1629
Yes	3 / 145 (2.1)	NE [NE, NE]	18 / 149 (12.1)	NE [NE, NE]	0.1529 [0.0450, 0.5192] 0.0026 0.0005	
No	4 / 99 (4.0)	NE [NE, NE]	6 / 84 (7.1)	NE [NE, NE]	0.5185 [0.1461, 1.8397] 0.3094 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT:						
Neuropathy peripheral						
Renal function at baseline						0.6463
Normal renal function	4 / 116 (3.4)	NE [NE, NE]	10 / 114 (8.8)	NE [NE, NE]	0.3724 [0.1168, 1.1876] 0.0950 0.0822	
Mild impairment	2 / 87 (2.3)	NE [NE, NE]	10 / 81 (12.3)	NE [NE, NE]	0.1582 [0.0346, 0.7227] 0.0174 0.0064	
Moderate impairment	1 / 41 (2.4)	NE [NE, NE]	4 / 38 (10.5)	NE [NE, NE]	0.2125 [0.0237, 1.9026] 0.1661 0.1267	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT:						
Neuropathy peripheral						
Hepatic function at baseline						0.4697
Normal hepatic function	6 / 185 (3.2)	NE [NE, NE]	18 / 177 (10.2)	NE [NE, NE]	0.2897 [0.1150, 0.7302] 0.0086 0.0052	
Mild, Moderate or Severe dysfunction	1 / 59 (1.7)	NE [NE, NE]	6 / 55 (10.9)	NE [NE, NE]	0.1430 [0.0172, 1.1890] 0.0719 0.0362	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.6932
IHC 3+	3 / 205 (1.5)	NE [NE, NE]	12 / 196 (6.1)	NE [NE, NE]	0.2165 [0.0611, 0.7677] 0.0178 0.0091	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	2 / 37 (5.4)	NE [NE, NE]	0.4238 [0.0382, 4.6966] 0.4842 0.4709	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Geography stratification factor						0.3549
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	2 / 59 (3.4)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	4 / 138 (2.9)	NE [NE, NE]	10 / 129 (7.8)	NE [NE, NE]	0.3208 [0.1005, 1.0241] 0.0549 0.0429	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	2 / 45 (4.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Time to progression on first-line therapy from IRT						0.9390
<6 Months	1 / 61 (1.6)	NE [NE, NE]	3 / 57 (5.3)	NE [NE, NE]	0.2871 [0.0299, 2.7615] 0.2799 0.2494	
≥6 Months	3 / 183 (1.6)	NE [NE, NE]	11 / 176 (6.3)	NE [NE, NE]	0.2373 [0.0661, 0.8510] 0.0273 0.0163	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Age at randomization						0.6552
<65	2 / 139 (1.4)	NE [NE, NE]	8 / 123 (6.5)	NE [NE, NE]	0.1907 [0.0404, 0.9000] 0.0363 0.0193	
≥65	2 / 105 (1.9)	NE [NE, NE]	6 / 110 (5.5)	NE [NE, NE]	0.3263 [0.0658, 1.6170] 0.1702 0.1487	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Age at randomization						0.3738
<75	3 / 220 (1.4)	NE [NE, NE]	12 / 198 (6.1)	NE [NE, NE]	0.1989 [0.0561, 0.7054] 0.0124 0.0054	
≥75	1 / 24 (4.2)	NE [NE, NE]	2 / 35 (5.7)	NE [NE, NE]	0.7597 [0.0689, 8.3796] 0.8225 0.8219	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Sex						0.9046
Male	2 / 186 (1.1)	NE [NE, NE]	8 / 194 (4.1)	NE [NE, NE]	0.2301 [0.0488, 1.0853] 0.0634 0.0427	
Female	2 / 58 (3.4)	NE [NE, NE]	6 / 39 (15.4)	NE [NE, NE]	0.2013 [0.0406, 0.9987] 0.0498 0.0295	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Race						0.3088
White	2 / 115 (1.7)	NE [NE, NE]	9 / 120 (7.5)	NE [NE, NE]	0.2049 [0.0442, 0.9490] 0.0427 0.0248	
Asian	0 / 101	NE [NE, NE]	3 / 93 (3.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	2 / 28 (7.1)	NE [NE, NE]	2 / 20 (10.0)	NE [NE, NE]	0.6477 [0.0911, 4.6063] 0.6644 0.6619	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
ECOG						0.3663
0	2 / 96 (2.1)	NE [NE, NE]	3 / 81 (3.7)	NE [NE, NE]	0.4977 [0.0830, 2.9845] 0.4452 0.4360	
≥1	2 / 148 (1.4)	NE [NE, NE]	11 / 152 (7.2)	NE [NE, NE]	0.1681 [0.0372, 0.7585] 0.0204 0.0083	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Primary tumor location						0.7913
Gastric	2 / 152 (1.3)	NE [NE, NE]	8 / 139 (5.8)	NE [NE, NE]	0.2117 [0.0449, 0.9978] 0.0497 0.0304	
GEJ	2 / 92 (2.2)	NE [NE, NE]	6 / 94 (6.4)	NE [NE, NE]	0.2901 [0.0585, 1.4387] 0.1298 0.1068	

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

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Histological subtype						NE
Intestinal	1 / 68 (1.5)	NE [NE, NE]	4 / 63 (6.3)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	4 / 18 (22.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Others	3 / 151 (2.0)	NE [NE, NE]	6 / 152 (3.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Number of metastatic sites						0.9576
<2	1 / 72 (1.4)	NE [NE, NE]	4 / 72 (5.6)	NE [NE, NE]	0.2504 [0.0280, 2.2403] 0.2155 0.1803	
≥2	3 / 172 (1.7)	NE [NE, NE]	10 / 161 (6.2)	NE [NE, NE]	0.2428 [0.0668, 0.8829] 0.0316 0.0197	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Prior adjuvant/neoadjuvant therapy						0.4568
Yes	0 / 31	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 213 (1.9)	NE [NE, NE]	13 / 205 (6.3)	NE [NE, NE]	0.2640 [0.0860, 0.8104] 0.0199 0.0123	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Prior nivolumab or pembrolizumab treatment						0.4470
Yes	0 / 20	NE [NE, NE]	1 / 16 (6.3)	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 224 (1.8)	NE [NE, NE]	13 / 217 (6.0)	NE [NE, NE]	0.2664 [0.0868, 0.8177] 0.0208 0.0130	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.4837
Yes	0 / 39	NE [NE, NE]	1 / 36 (2.8)	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 205 (2.0)	NE [NE, NE]	13 / 197 (6.6)	NE [NE, NE]	0.2608 [0.0850, 0.8005] 0.0188 0.0115	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Presence of liver metastasis at baseline						0.7919
Yes	3 / 145 (2.1)	NE [NE, NE]	10 / 149 (6.7)	NE [NE, NE]	0.2711 [0.0745, 0.9857] 0.0475 0.0336	
No	1 / 99 (1.0)	NE [NE, NE]	4 / 84 (4.8)	NE [NE, NE]	0.1961 [0.0219, 1.7566] 0.1453 0.1048	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Renal function at baseline						NE
Normal renal function	2 / 116 (1.7)	NE [NE, NE]	6 / 114 (5.3)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	2 / 87 (2.3)	NE [NE, NE]	3 / 81 (3.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	0 / 41	NE [NE, NE]	5 / 38 (13.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Paraesthesia						
Hepatic function at baseline						0.3768
Normal hepatic function	3 / 185 (1.6)	NE [NE, NE]	13 / 177 (7.3)	NE [NE, NE]	0.1997 [0.0569, 0.7013] 0.0120 0.0052	
Mild, Moderate or Severe dysfunction	1 / 59 (1.7)	NE [NE, NE]	1 / 55 (1.8)	NE [NE, NE]	0.8018 [0.0501, 12.8278] 0.8759 0.8756	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						NE
IHC 3+	2 / 205 (1.0)	NE [NE, NE]	7 / 196 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	2 / 37 (5.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Geography stratification factor						0.7624
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	1 / 59 (1.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	0 / 138	NE [NE, NE]	0 / 129	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	3 / 49 (6.1)	NE [NE, NE]	8 / 45 (17.8)	NE [NE, NE]	0.3179 [0.0843, 1.1989] 0.0906 0.0741	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Time to progression on first-line therapy from IRT						NE
<6 Months	0 / 61	NE [NE, NE]	4 / 57 (7.0)	NE [NE, NE]	NE [NE, NE] NE NE	
≥6 Months	3 / 183 (1.6)	NE [NE, NE]	5 / 176 (2.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Age at randomization						NE
<65	2 / 139 (1.4)	NE [NE, NE]	6 / 123 (4.9)	NE [NE, NE]	NE [NE, NE] NE NE	
≥65	1 / 105 (1.0)	NE [NE, NE]	3 / 110 (2.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Age at randomization						0.5512
<75	3 / 220 (1.4)	NE [NE, NE]	8 / 198 (4.0)	NE [NE, NE]	0.3019 [0.0800, 1.1384] 0.0770	
≥75	0 / 24	NE [NE, NE]	1 / 35 (2.9)	NE [NE, NE]	0.0607 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Sex						NE
Male	2 / 186 (1.1)	NE [NE, NE]	7 / 194 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Female	1 / 58 (1.7)	NE [NE, NE]	2 / 39 (5.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Race						1.0000
White	0 / 115	NE [NE, NE]	0 / 120	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	3 / 101 (3.0)	NE [NE, NE]	9 / 93 (9.7)	NE [NE, NE]	0.2849 [0.0771, 1.0525] 0.0597 0.0445	
Other	0 / 28	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
ECOG						0.3941
0	0 / 96	NE [NE, NE]	1 / 81 (1.2)	NE [NE, NE]	NE [NE, NE] NE NE	
≥1	3 / 148 (2.0)	NE [NE, NE]	8 / 152 (5.3)	NE [NE, NE]	0.3593 [0.0953, 1.3546] 0.1306 0.1144	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Primary tumor location						NE
Gastric	1 / 152 (0.7)	NE [NE, NE]	6 / 139 (4.3)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	2 / 92 (2.2)	NE [NE, NE]	3 / 94 (3.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Histological subtype						NE
Intestinal	1 / 68 (1.5)	NE [NE, NE]	2 / 63 (3.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	2 / 151 (1.3)	NE [NE, NE]	7 / 152 (4.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Number of metastatic sites						0.3256
<2	1 / 72 (1.4)	NE [NE, NE]	1 / 72 (1.4)	NE [NE, NE]	1.0166 [0.0636, 16.2531] 0.9907 0.9907	
≥2	2 / 172 (1.2)	NE [NE, NE]	8 / 161 (5.0)	NE [NE, NE]	0.2060 [0.0437, 0.9708] 0.0458 0.0270	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Prior adjuvant/neoadjuvant therapy						0.4173
Yes	1 / 31 (3.2)	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	0.8102 [0.0507, 12.9545] 0.8817 0.8815	
No	2 / 213 (0.9)	NE [NE, NE]	8 / 205 (3.9)	NE [NE, NE]	0.2213 [0.0470, 1.0428] 0.0565 0.0364	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Prior nivolumab or pembrolizumab treatment						0.4042
Yes	0 / 20	NE [NE, NE]	1 / 16 (6.3)	NE [NE, NE]	NE [NE, NE] NE NE	
No	3 / 224 (1.3)	NE [NE, NE]	8 / 217 (3.7)	NE [NE, NE]	0.3337 [0.0885, 1.2582] 0.1051 0.0885	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						NE
Yes	3 / 39 (7.7)	NE [NE, NE]	6 / 36 (16.7)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 205	NE [NE, NE]	3 / 197 (1.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Presence of liver metastasis at baseline						NE
Yes	2 / 145 (1.4)	NE [NE, NE]	5 / 149 (3.4)	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 99 (1.0)	NE [NE, NE]	4 / 84 (4.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Renal function at baseline						NE
Normal renal function	1 / 116 (0.9)	NE [NE, NE]	6 / 114 (5.3)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	2 / 87 (2.3)	NE [NE, NE]	3 / 81 (3.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	0 / 41	NE [NE, NE]	0 / 38	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Hypoaesthesia						
Hepatic function at baseline						0.2439
Normal hepatic function	3 / 185 (1.6)	NE [NE, NE]	7 / 177 (4.0)	NE [NE, NE]	0.3761 [0.0972, 1.4551] 0.1566	
Mild, Moderate or Severe dysfunction	0 / 59	NE [NE, NE]	2 / 55 (3.6)	NE [NE, NE]	0.1405 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.9996
IHC 3+	3 / 205 (1.5)	NE [NE, NE]	12 / 196 (6.1)	NE [NE, NE]	0.2167 [0.0611, 0.7686] 0.0179 0.0092	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	0 / 37	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Geography stratification factor						0.4825
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	0 / 59	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	3 / 138 (2.2)	NE [NE, NE]	9 / 129 (7.0)	NE [NE, NE]	0.2772 [0.0749, 1.0255] 0.0546 0.0398	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	3 / 45 (6.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Time to progression on first-line therapy from IRT						0.3208
<6 Months	1 / 61 (1.6)	NE [NE, NE]	1 / 57 (1.8)	NE [NE, NE]	0.9031 [0.0564, 14.4511] 0.9426 0.9427	
≥6 Months	2 / 183 (1.1)	NE [NE, NE]	11 / 176 (6.3)	NE [NE, NE]	0.1574 [0.0349, 0.7107] 0.0162 0.0058	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Age at randomization						0.6312
<65	2 / 139 (1.4)	NE [NE, NE]	9 / 123 (7.3)	NE [NE, NE]	0.1641 [0.0353, 0.7623] 0.0211 0.0086	
≥65	1 / 105 (1.0)	NE [NE, NE]	3 / 110 (2.7)	NE [NE, NE]	0.3432 [0.0357, 3.2992] 0.3543 0.3315	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Age at randomization						0.5978
<75	3 / 220 (1.4)	NE [NE, NE]	11 / 198 (5.6)	NE [NE, NE]	0.2161 [0.0602, 0.7759] 0.0188	
≥75	0 / 24	NE [NE, NE]	1 / 35 (2.9)	NE [NE, NE]	0.0098 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Sex						NE
Male	2 / 186 (1.1)	NE [NE, NE]	7 / 194 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Female	1 / 58 (1.7)	NE [NE, NE]	5 / 39 (12.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Race						0.9708
White	2 / 115 (1.7)	NE [NE, NE]	9 / 120 (7.5)	NE [NE, NE]	0.2109 [0.0455, 0.9768] 0.0466 0.0280	
Asian	1 / 101 (1.0)	NE [NE, NE]	3 / 93 (3.2)	NE [NE, NE]	0.2749 [0.0286, 2.6438] 0.2635 0.2312	
Other	0 / 28	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
ECOG						NE
0	3 / 96 (3.1)	NE [NE, NE]	4 / 81 (4.9)	NE [NE, NE]	NE [NE, NE] NE NE	
≥1	0 / 148	NE [NE, NE]	8 / 152 (5.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Primary tumor location						NE
Gastric	1 / 152 (0.7)	NE [NE, NE]	7 / 139 (5.0)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	2 / 92 (2.2)	NE [NE, NE]	5 / 94 (5.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Histological subtype						0.5828
Intestinal	0 / 68	NE [NE, NE]	2 / 63 (3.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	3 / 151 (2.0)	NE [NE, NE]	10 / 152 (6.6)	NE [NE, NE]	0.2715 [0.0747, 0.9874] 0.0478 0.0339	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Number of metastatic sites						0.1863
<2	0 / 72	NE [NE, NE]	4 / 72 (5.6)	NE [NE, NE]	NE [NE, NE] NE NE	
≥2	3 / 172 (1.7)	NE [NE, NE]	8 / 161 (5.0)	NE [NE, NE]	0.3108 [0.0823, 1.1734] 0.0847 0.0682	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Prior adjuvant/neoadjuvant therapy						0.8257
Yes	1 / 31 (3.2)	NE [NE, NE]	3 / 28 (10.7)	NE [NE, NE]	0.2728 [0.0283, 2.6259] 0.2609 0.2283	
No	2 / 213 (0.9)	NE [NE, NE]	9 / 205 (4.4)	NE [NE, NE]	0.1898 [0.0409, 0.8801] 0.0337 0.0176	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Prior nivolumab or pembrolizumab treatment						0.4448
Yes	0 / 20	NE [NE, NE]	1 / 16 (6.3)	NE [4.4, NE]	NE [NE, NE] NE NE	
No	3 / 224 (1.3)	NE [NE, NE]	11 / 217 (5.1)	NE [NE, NE]	0.2379 [0.0663, 0.8538] 0.0276 0.0166	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.3210
Yes	0 / 39	NE [NE, NE]	2 / 36 (5.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	3 / 205 (1.5)	NE [NE, NE]	10 / 197 (5.1)	NE [NE, NE]	0.2590 [0.0712, 0.9426] 0.0404 0.0272	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Presence of liver metastasis at baseline						0.8773
Yes	2 / 145 (1.4)	NE [NE, NE]	9 / 149 (6.0)	NE [NE, NE]	0.2029 [0.0438, 0.9401] 0.0415 0.0238	
No	1 / 99 (1.0)	NE [NE, NE]	3 / 84 (3.6)	NE [NE, NE]	0.2657 [0.0276, 2.5583] 0.2514 0.2172	

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

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Renal function at baseline						0.0795
Normal renal function	2 / 116 (1.7)	NE [NE, NE]	8 / 114 (7.0)	NE [NE, NE]	0.2276 [0.0483, 1.0727] 0.0613 0.0406	
Mild impairment	0 / 87	NE [NE, NE]	4 / 81 (4.9)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	1 / 41 (2.4)	NE [NE, NE]	0 / 38	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Neurotoxicity						
Hepatic function at baseline						0.0353
Normal hepatic function	1 / 185 (0.5)	NE [NE, NE]	11 / 177 (6.2)	NE [NE, NE]	0.0756 [0.0097, 0.5869] 0.0135 0.0013	
Mild, Moderate or Severe dysfunction	2 / 59 (3.4)	NE [NE, NE]	1 / 55 (1.8)	NE [NE, NE]	1.6673 [0.1510, 18.4087] 0.6765 0.6732	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.7354
IHC 3+	36 / 205 (17.6)	NE [NE, NE]	55 / 196 (28.1)	14.6 [9.5, NE]	0.5300 [0.3474, 0.8085] 0.0032 0.0028	
IHC 2+/ISH+	5 / 39 (12.8)	NE [15.9, NE]	8 / 37 (21.6)	NE [NE, NE]	0.3932 [0.1176, 1.3149] 0.1296 0.1182	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Geography stratification factor						0.2328
Asia [excluding mainland China]	4 / 57 (7.0)	NE [NE, NE]	11 / 59 (18.6)	14.6 [8.5, NE]	0.2426 [0.0742, 0.7931] 0.0191 0.0121	
Western Europe	29 / 138 (21.0)	NE [15.9, NE]	45 / 129 (34.9)	NE [5.8, NE]	0.4666 [0.2915, 0.7468] 0.0015 0.0012	
Mainland China/Rest of World (ROW)	8 / 49 (16.3)	NE [NE, NE]	7 / 45 (15.6)	NE [NE, NE]	1.0961 [0.3970, 3.0268] 0.8594 0.8590	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Time to progression on first-line therapy from IRT						0.5087
<6 Months	10 / 61 (16.4)	NE [15.9, NE]	12 / 57 (21.1)	6.5 [6.4, NE]	0.5916 [0.2468, 1.4177] 0.2391 0.2377	
≥6 Months	31 / 183 (16.9)	NE [NE, NE]	51 / 176 (29.0)	14.6 [14.6, NE]	0.4794 [0.3060, 0.7511] 0.0013 0.0011	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Age at randomization						0.6204
<65	26 / 139 (18.7)	NE [15.9, NE]	34 / 123 (27.6)	14.6 [9.5, NE]	0.5464 [0.3266, 0.9142] 0.0214 0.0196	
≥65	15 / 105 (14.3)	NE [NE, NE]	29 / 110 (26.4)	NE [8.5, NE]	0.4750 [0.2544, 0.8870] 0.0195 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Age at randomization						0.5235
<75	39 / 220 (17.7)	NE [NE, NE]	55 / 198 (27.8)	14.6 [9.5, NE]	0.5199 [0.3436, 0.7867] 0.0020 0.0017	
≥75	2 / 24 (8.3)	NE [8.3, NE]	8 / 35 (22.9)	NE [5.8, NE]	0.3108 [0.0657, 1.4708] 0.1406 0.1195	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Sex						0.7230
Male	31 / 186 (16.7)	NE [NE, NE]	52 / 194 (26.8)	NE [NE, NE]	0.5009 [0.3193, 0.7855] 0.0026 0.0022	
Female	10 / 58 (17.2)	NE [NE, NE]	11 / 39 (28.2)	14.6 [9.5, NE]	0.5865 [0.2490, 1.3815] 0.2222 0.2168	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Race						0.2612
White	25 / 115 (21.7)	NE [NE, NE]	35 / 120 (29.2)	NE [9.5, NE]	0.6284 [0.3758, 1.0509] 0.0766 0.0751	
Asian	11 / 101 (10.9)	NE [NE, NE]	18 / 93 (19.4)	14.6 [14.6, NE]	0.4801 [0.2248, 1.0251] 0.0580 0.0528	
Other	5 / 28 (17.9)	15.9 [8.3, NE]	10 / 20 (50.0)	5.2 [1.2, NE]	0.1991 [0.0605, 0.6554] 0.0079 0.0035	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
ECOG						0.0189
0	10 / 96 (10.4)	NE [NE, NE]	23 / 81 (28.4)	9.5 [6.5, NE]	0.2349 [0.1098, 0.5027] 0.0002 <.0001	
≥1	31 / 148 (20.9)	NE [NE, NE]	40 / 152 (26.3)	14.6 [14.6, NE]	0.7275 [0.4545, 1.1644] 0.1849 0.1837	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Primary tumor location						0.1654
Gastric	17 / 152 (11.2)	NE [NE, NE]	34 / 139 (24.5)	14.6 [9.5, NE]	0.3781 [0.2095, 0.6823] 0.0012 0.0008	
GEJ	24 / 92 (26.1)	NE [15.9, NE]	29 / 94 (30.9)	NE [6.4, NE]	0.6727 [0.3903, 1.1593] 0.1534 0.1535	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Histological subtype						0.9813
Intestinal	9 / 68 (13.2)	NE [NE, NE]	13 / 63 (20.6)	14.6 [9.5, NE]	0.5194 [0.2198, 1.2276] 0.1355 0.1295	
Diffuse	2 / 25 (8.0)	NE [11.8, NE]	3 / 18 (16.7)	NE [NE, NE]	0.2579 [0.0268, 2.4809] 0.2407 0.2059	
Others	30 / 151 (19.9)	NE [15.9, NE]	47 / 152 (30.9)	NE [8.5, NE]	0.5339 [0.3368, 0.8462] 0.0076 0.0067	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Number of metastatic sites						0.6991
<2	10 / 72 (13.9)	NE [15.9, NE]	16 / 72 (22.2)	14.6 [NE, NE]	0.5110 [0.2231, 1.1702] 0.1122 0.1058	
≥2	31 / 172 (18.0)	NE [NE, NE]	47 / 161 (29.2)	NE [8.5, NE]	0.4819 [0.3050, 0.7614] 0.0018 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Prior adjuvant/neoadjuvant therapy						0.2482
Yes	8 / 31 (25.8)	15.9 [6.6, NE]	7 / 28 (25.0)	NE [NE, NE]	0.8556 [0.3000, 2.4400] 0.7706 0.7745	
No	33 / 213 (15.5)	NE [NE, NE]	56 / 205 (27.3)	14.6 [9.5, NE]	0.4637 [0.3006, 0.7152] 0.0005 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Prior nivolumab or pembrolizumab treatment						0.6962
Yes	4 / 20 (20.0)	NE [11.8, NE]	4 / 16 (25.0)	NE [3.6, NE]	0.5493 [0.1228, 2.4567] 0.4331 0.4263	
No	37 / 224 (16.5)	NE [NE, NE]	59 / 217 (27.2)	14.6 [14.6, NE]	0.5026 [0.3321, 0.7608] 0.0011 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.3236
Yes	6 / 39 (15.4)	NE [11.8, NE]	6 / 36 (16.7)	NE [NE, NE]	0.8491 [0.2728, 2.6428] 0.7777 0.7774	
No	35 / 205 (17.1)	NE [NE, NE]	57 / 197 (28.9)	14.6 [9.5, NE]	0.4716 [0.3079, 0.7222] 0.0005 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Presence of liver metastasis at baseline						0.2324
Yes	23 / 145 (15.9)	NE [NE, NE]	44 / 149 (29.5)	NE [8.5, NE]	0.4334 [0.2609, 0.7197] 0.0012 0.0009	
No	18 / 99 (18.2)	NE [15.9, NE]	19 / 84 (22.6)	14.6 [9.5, NE]	0.6768 [0.3523, 1.3002] 0.2412 0.2381	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Renal function at baseline						0.7501
Normal renal function	23 / 116 (19.8)	NE [NE, NE]	36 / 114 (31.6)	14.6 [9.5, NE]	0.5223 [0.3088, 0.8834] 0.0154 0.0139	
Mild impairment	13 / 87 (14.9)	NE [15.9, NE]	17 / 81 (21.0)	NE [8.5, NE]	0.5619 [0.2680, 1.1780] 0.1269 0.1220	
Moderate impairment	5 / 41 (12.2)	NE [NE, NE]	10 / 38 (26.3)	NE [NE, NE]	0.4109 [0.1403, 1.2035] 0.1048 0.0935	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Any						
Hepatic function at baseline						0.3558
Normal hepatic function	29 / 185 (15.7)	NE [NE, NE]	50 / 177 (28.2)	14.6 [9.5, NE]	0.4568 [0.2875, 0.7257] 0.0009 0.0007	
Mild, Moderate or Severe dysfunction	12 / 59 (20.3)	NE [7.5, NE]	13 / 55 (23.6)	NE [5.2, NE]	0.6896 [0.3139, 1.5146] 0.3545 0.3518	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.6834
IHC 3+	8 / 205 (3.9)	NE [NE, NE]	14 / 196 (7.1)	NE [14.6, NE]	0.4745 [0.1979, 1.1375] 0.0947 0.0878	
IHC 2+/ISH+	2 / 39 (5.1)	NE [15.9, NE]	4 / 37 (10.8)	NE [7.8, NE]	0.1629 [0.0177, 1.5016] 0.1093 0.0705	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Geography stratification factor						0.0319
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	3 / 59 (5.1)	NE [14.6, NE]	NE [NE, NE] NE NE	
Western Europe	10 / 138 (7.2)	NE [NE, NE]	11 / 129 (8.5)	NE [NE, NE]	0.6961 [0.2927, 1.6551] 0.4123 0.4099	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	4 / 45 (8.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Time to progression on first-line therapy from IRT						0.2154
<6 Months	4 / 61 (6.6)	NE [15.9, NE]	3 / 57 (5.3)	NE [6.5, NE]	0.8419 [0.1823, 3.8885] 0.8255 0.8369	
≥6 Months	6 / 183 (3.3)	NE [NE, NE]	15 / 176 (8.5)	NE [14.6, NE]	0.3236 [0.1246, 0.8405] 0.0205 0.0149	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Age at randomization						0.7422
<65	7 / 139 (5.0)	NE [15.9, NE]	13 / 123 (10.6)	NE [14.6, NE]	0.3735 [0.1479, 0.9435] 0.0373 0.0305	
≥65	3 / 105 (2.9)	NE [NE, NE]	5 / 110 (4.5)	NE [NE, NE]	0.6047 [0.1445, 2.5310] 0.4911 0.4862	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Age at randomization						0.0715
<75	9 / 220 (4.1)	NE [NE, NE]	18 / 198 (9.1)	NE [14.6, NE]	0.3456 [0.1530, 0.7806] 0.0106	
≥75	1 / 24 (4.2)	NE [NE, NE]	0 / 35	NE [NE, NE]	0.0077 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Sex						0.5055
Male	5 / 186 (2.7)	NE [NE, NE]	12 / 194 (6.2)	NE [NE, NE]	0.3532 [0.1224, 1.0193] 0.0543 0.0449	
Female	5 / 58 (8.6)	NE [NE, NE]	6 / 39 (15.4)	14.6 [9.5, NE]	0.5538 [0.1689, 1.8162] 0.3295 0.3223	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Race						0.0262
White	8 / 115 (7.0)	NE [NE, NE]	9 / 120 (7.5)	NE [NE, NE]	0.8166 [0.3145, 2.1205] 0.6773 0.6770	
Asian	0 / 101	NE [NE, NE]	7 / 93 (7.5)	NE [14.6, NE]	NE [NE, NE] NE NE	
Other	2 / 28 (7.1)	15.9 [NE, NE]	2 / 20 (10.0)	NE [NE, NE]	0.3655 [0.0331, 4.0319] 0.4113 0.3916	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
ECOG						0.3846
0	1 / 96 (1.0)	NE [NE, NE]	3 / 81 (3.7)	NE [NE, NE]	0.1455 [0.0148, 1.4333] 0.0986 0.0575	
≥1	9 / 148 (6.1)	NE [NE, NE]	15 / 152 (9.9)	NE [14.6, NE]	0.5609 [0.2449, 1.2846] 0.1715 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Primary tumor location						0.0483
Gastric	3 / 152 (2.0)	NE [NE, NE]	12 / 139 (8.6)	NE [14.6, NE]	0.1811 [0.0501, 0.6551] 0.0092 0.0037	
GEJ	7 / 92 (7.6)	NE [15.9, NE]	6 / 94 (6.4)	NE [NE, NE]	0.9532 [0.3173, 2.8638] 0.9319 0.9321	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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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]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Histological subtype						0.0461
Intestinal	0 / 68	NE [NE, NE]	3 / 63 (4.8)	14.6 [9.5, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	2 / 18 (11.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Others	10 / 151 (6.6)	NE [15.9, NE]	13 / 152 (8.6)	NE [NE, NE]	0.6822 [0.2980, 1.5617] 0.3654 0.3638	

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

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Number of metastatic sites						0.4905
<2	3 / 72 (4.2)	NE [15.9, NE]	4 / 72 (5.6)	14.6 [NE, NE]	0.3701 [0.0609, 2.2468] 0.2800 0.2648	
≥2	7 / 172 (4.1)	NE [NE, NE]	14 / 161 (8.7)	NE [NE, NE]	0.3877 [0.1558, 0.9647] 0.0416 0.0347	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Prior adjuvant/neoadjuvant therapy						0.0409
Yes	2 / 31 (6.5)	15.9 [15.9, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	8 / 213 (3.8)	NE [NE, NE]	18 / 205 (8.8)	NE [14.6, NE]	0.3577 [0.1547, 0.8273] 0.0163 0.0122	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Prior nivolumab or pembrolizumab treatment						0.3043
Yes	0 / 20	NE [NE, NE]	1 / 16 (6.3)	NE [NE, NE]	NE [NE, NE] NE NE	
No	10 / 224 (4.5)	NE [NE, NE]	17 / 217 (7.8)	NE [14.6, NE]	0.4639 [0.2104, 1.0227] 0.0569 0.0514	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.1931
Yes	0 / 39	NE [NE, NE]	2 / 36 (5.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	10 / 205 (4.9)	NE [NE, NE]	16 / 197 (8.1)	NE [14.6, NE]	0.4737 [0.2121, 1.0575] 0.0682 0.0626	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Presence of liver metastasis at baseline						0.0865
Yes	4 / 145 (2.8)	NE [NE, NE]	14 / 149 (9.4)	NE [NE, NE]	0.2601 [0.0855, 0.7908] 0.0176 0.0106	
No	6 / 99 (6.1)	NE [15.9, NE]	4 / 84 (4.8)	14.6 [9.5, NE]	0.8255 [0.2209, 3.0844] 0.7755 0.7752	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Renal function at baseline						0.8604
Normal renal function	5 / 116 (4.3)	NE [NE, NE]	11 / 114 (9.6)	NE [14.6, NE]	0.3770 [0.1300, 1.0935] 0.0726 0.0625	
Mild impairment	3 / 87 (3.4)	NE [15.9, NE]	5 / 81 (6.2)	NE [NE, NE]	0.3886 [0.0905, 1.6679] 0.2035 0.1883	
Moderate impairment	2 / 41 (4.9)	NE [NE, NE]	2 / 38 (5.3)	NE [NE, NE]	0.9276 [0.1307, 6.5853] 0.9401 0.9402	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Back pain						
Hepatic function at baseline						0.0850
Normal hepatic function	6 / 185 (3.2)	NE [NE, NE]	16 / 177 (9.0)	NE [14.6, NE]	0.2863 [0.1108, 0.7399] 0.0098 0.0061	
Mild, Moderate or Severe dysfunction	4 / 59 (6.8)	NE [NE, NE]	2 / 55 (3.6)	NE [7.8, NE]	1.6471 [0.3014, 9.0019] 0.5647 0.5606	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.2289
IHC 3+	4 / 205 (2.0)	NE [NE, NE]	10 / 196 (5.1)	NE [NE, NE]	0.3366 [0.1052, 1.0767] 0.0664 0.0541	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	2 / 37 (5.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Geography stratification factor						NE
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	4 / 59 (6.8)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	2 / 138 (1.4)	NE [NE, NE]	7 / 129 (5.4)	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	2 / 49 (4.1)	NE [NE, NE]	1 / 45 (2.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Time to progression on first-line therapy from IRT						0.4339
<6 Months	1 / 61 (1.6)	NE [NE, NE]	1 / 57 (1.8)	NE [NE, NE]	0.8423 [0.0525, 13.5167] 0.9035 0.9034	
≥6 Months	3 / 183 (1.6)	NE [NE, NE]	11 / 176 (6.3)	NE [NE, NE]	0.2281 [0.0634, 0.8203] 0.0236 0.0135	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Age at randomization						0.6393
<65	3 / 139 (2.2)	NE [NE, NE]	7 / 123 (5.7)	NE [NE, NE]	0.3432 [0.0887, 1.3283] 0.1214 0.1044	
≥65	1 / 105 (1.0)	NE [NE, NE]	5 / 110 (4.5)	NE [NE, NE]	0.1514 [0.0172, 1.3309] 0.0887 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 Brookmeyer-Crowley method.
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[c] Two-sided p-value from unstratified log-rank test.
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CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Age at randomization						0.5507
<75	4 / 220 (1.8)	NE [NE, NE]	11 / 198 (5.6)	NE [NE, NE]	0.2761 [0.0874, 0.8722] 0.0283	
≥75	0 / 24	NE [NE, NE]	1 / 35 (2.9)	NE [NE, NE]	0.0192 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Sex						0.8522
Male	3 / 186 (1.6)	NE [NE, NE]	10 / 194 (5.2)	NE [NE, NE]	0.2555 [0.0697, 0.9367] 0.0395 0.0268	
Female	1 / 58 (1.7)	NE [NE, NE]	2 / 39 (5.1)	NE [NE, NE]	0.3451 [0.0313, 3.8079] 0.3851 0.3628	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Race						NE
White	3 / 115 (2.6)	NE [NE, NE]	5 / 120 (4.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	1 / 101 (1.0)	NE [NE, NE]	5 / 93 (5.4)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	2 / 20 (10.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
ECOG						NE
0	1 / 96 (1.0)	NE [NE, NE]	6 / 81 (7.4)	NE [NE, NE]	NE [NE, NE] NE NE	
≥1	3 / 148 (2.0)	NE [NE, NE]	6 / 152 (3.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Primary tumor location						NE
Gastric	2 / 152 (1.3)	NE [NE, NE]	7 / 139 (5.0)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	2 / 92 (2.2)	NE [NE, NE]	5 / 94 (5.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Histological subtype						0.2611
Intestinal	1 / 68 (1.5)	NE [NE, NE]	4 / 63 (6.3)	NE [NE, NE]	0.2206 [0.0247, 1.9746] 0.1765 0.1379	
Diffuse	1 / 25 (4.0)	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	2 / 151 (1.3)	NE [NE, NE]	8 / 152 (5.3)	NE [NE, NE]	0.2166 [0.0458, 1.0243] 0.0536 0.0341	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Number of metastatic sites						0.5877
<2	1 / 72 (1.4)	NE [NE, NE]	2 / 72 (2.8)	NE [NE, NE]	0.4922 [0.0446, 5.4291] 0.5627 0.5545	
≥2	3 / 172 (1.7)	NE [NE, NE]	10 / 161 (6.2)	NE [NE, NE]	0.2173 [0.0591, 0.7986] 0.0215 0.0119	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Prior adjuvant/neoadjuvant therapy						0.1371
Yes	0 / 31	NE [NE, NE]	3 / 28 (10.7)	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 213 (1.9)	NE [NE, NE]	9 / 205 (4.4)	NE [NE, NE]	0.3666 [0.1123, 1.1963] 0.0963 0.0833	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Prior nivolumab or pembrolizumab treatment						0.2036
Yes	0 / 20	NE [NE, NE]	2 / 16 (12.5)	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 224 (1.8)	NE [NE, NE]	10 / 217 (4.6)	NE [NE, NE]	0.3347 [0.1045, 1.0716] 0.0653 0.0530	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.2659
Yes	0 / 39	NE [NE, NE]	2 / 36 (5.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 205 (2.0)	NE [NE, NE]	10 / 197 (5.1)	NE [NE, NE]	0.3251 [0.1014, 1.0420] 0.0587 0.0467	

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

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Presence of liver metastasis at baseline						NE
Yes	1 / 145 (0.7)	NE [NE, NE]	8 / 149 (5.4)	NE [NE, NE]	NE [NE, NE] NE NE	
No	3 / 99 (3.0)	NE [NE, NE]	4 / 84 (4.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Renal function at baseline						NE
Normal renal function	3 / 116 (2.6)	NE [NE, NE]	6 / 114 (5.3)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	1 / 87 (1.1)	NE [NE, NE]	4 / 81 (4.9)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	0 / 41	NE [NE, NE]	2 / 38 (5.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Myalgia						
Hepatic function at baseline						0.9865
Normal hepatic function	3 / 185 (1.6)	NE [NE, NE]	9 / 177 (5.1)	NE [NE, NE]	0.2770 [0.0745, 1.0299] 0.0554 0.0408	
Mild, Moderate or Severe dysfunction	1 / 59 (1.7)	NE [NE, NE]	3 / 55 (5.5)	NE [8.5, NE]	0.2796 [0.0290, 2.6936] 0.2702 0.2387	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.5120
IHC 3+	2 / 205 (1.0)	NE [NE, NE]	8 / 196 (4.1)	NE [NE, NE]	0.2236 [0.0475, 1.0536] 0.0582 0.0380	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	1 / 37 (2.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Geography stratification factor						NE
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	0 / 59	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	1 / 138 (0.7)	NE [NE, NE]	8 / 129 (6.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	1 / 49 (2.0)	NE [NE, NE]	1 / 45 (2.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Time to progression on first-line therapy from IRT						NE
<6 Months	0 / 61	NE [NE, NE]	4 / 57 (7.0)	NE [NE, NE]	NE [NE, NE] NE NE	
≥6 Months	2 / 183 (1.1)	NE [NE, NE]	5 / 176 (2.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Age at randomization						NE
<65	1 / 139 (0.7)	NE [NE, NE]	6 / 123 (4.9)	NE [NE, NE]	NE [NE, NE] NE NE	
≥65	1 / 105 (1.0)	NE [NE, NE]	3 / 110 (2.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Age at randomization						0.6145
<75	2 / 220 (0.9)	NE [NE, NE]	8 / 198 (4.0)	NE [NE, NE]	0.2081 [0.0442, 0.9804] 0.0471 0.0282	
≥75	0 / 24	NE [NE, NE]	1 / 35 (2.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Sex						0.4458
Male	2 / 186 (1.1)	NE [NE, NE]	8 / 194 (4.1)	NE [NE, NE]	0.2390 [0.0507, 1.1263] 0.0704 0.0491	
Female	0 / 58	NE [NE, NE]	1 / 39 (2.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Race						NE
White	2 / 115 (1.7)	NE [NE, NE]	5 / 120 (4.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	0 / 101	NE [NE, NE]	1 / 93 (1.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	3 / 20 (15.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
ECOG						NE
0	0 / 96	NE [NE, NE]	3 / 81 (3.7)	NE [NE, NE]	NE [NE, NE] NE NE	
≥1	2 / 148 (1.4)	NE [NE, NE]	6 / 152 (3.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Primary tumor location						NE
Gastric	1 / 152 (0.7)	NE [NE, NE]	4 / 139 (2.9)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	1 / 92 (1.1)	NE [NE, NE]	5 / 94 (5.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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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]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Histological subtype						NE
Intestinal	1 / 68 (1.5)	NE [NE, NE]	1 / 63 (1.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	1 / 151 (0.7)	NE [NE, NE]	8 / 152 (5.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
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CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Number of metastatic sites						NE
<2	0 / 72	NE [NE, NE]	5 / 72 (6.9)	NE [NE, NE]	NE [NE, NE] NE NE	
≥2	2 / 172 (1.2)	NE [NE, NE]	4 / 161 (2.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Prior adjuvant/neoadjuvant therapy						0.5062
Yes	0 / 31	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	2 / 213 (0.9)	NE [NE, NE]	8 / 205 (3.9)	NE [NE, NE]	0.2236 [0.0475, 1.0538] 0.0583 0.0380	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Prior nivolumab or pembrolizumab treatment						0.0556
Yes	1 / 20 (5.0)	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 224 (0.4)	NE [NE, NE]	9 / 217 (4.1)	NE [NE, NE]	0.1001 [0.0127, 0.7902] 0.0290 0.0070	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						NE
Yes	1 / 39 (2.6)	NE [NE, NE]	1 / 36 (2.8)	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 205 (0.5)	NE [NE, NE]	8 / 197 (4.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Presence of liver metastasis at baseline						NE
Yes	2 / 145 (1.4)	NE [NE, NE]	5 / 149 (3.4)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 99	NE [NE, NE]	4 / 84 (4.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Renal function at baseline						NE
Normal renal function	2 / 116 (1.7)	NE [NE, NE]	6 / 114 (5.3)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	0 / 87	NE [NE, NE]	3 / 81 (3.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	0 / 41	NE [NE, NE]	0 / 38	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Musculoskeletal and connective tissue disorders; PT: Pain in extremity						
Hepatic function at baseline						NE
Normal hepatic function	0 / 185	NE [NE, NE]	6 / 177 (3.4)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	2 / 59 (3.4)	NE [NE, NE]	3 / 55 (5.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.4826
IHC 3+	14 / 205 (6.8)	NE [NE, NE]	48 / 196 (24.5)	NE [12.6, NE]	0.2308 [0.1270, 0.4191] <.0001 <.0001	
IHC 2+/ISH+	4 / 39 (10.3)	NE [NE, NE]	8 / 37 (21.6)	NE [5.4, NE]	0.3734 [0.1117, 1.2484] 0.1097 0.0958	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Geography stratification factor						0.1364
Asia [excluding mainland China]	3 / 57 (5.3)	NE [NE, NE]	18 / 59 (30.5)	NE [NE, NE]	0.1421 [0.0418, 0.4836] 0.0018 0.0003	
Western Europe	14 / 138 (10.1)	NE [NE, NE]	28 / 129 (21.7)	12.6 [12.6, NE]	0.3704 [0.1937, 0.7081] 0.0027 0.0018	
Mainland China/Rest of World (ROW)	1 / 49 (2.0)	NE [NE, NE]	10 / 45 (22.2)	NE [NE, NE]	0.0868 [0.0111, 0.6782] 0.0198 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Time to progression on first-line therapy from IRT						0.2740
<6 Months	4 / 61 (6.6)	NE [NE, NE]	7 / 57 (12.3)	NE [NE, NE]	0.4662 [0.1361, 1.5977] 0.2246 0.2137	
≥6 Months	14 / 183 (7.7)	NE [NE, NE]	49 / 176 (27.8)	NE [12.6, NE]	0.2212 [0.1219, 0.4013] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Age at randomization						0.9315
<65	9 / 139 (6.5)	NE [NE, NE]	25 / 123 (20.3)	NE [12.6, NE]	0.2525 [0.1175, 0.5426] 0.0004 0.0001	
≥65	9 / 105 (8.6)	NE [NE, NE]	31 / 110 (28.2)	NE [NE, NE]	0.2618 [0.1245, 0.5503] 0.0004 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Age at randomization						0.3678
<75	17 / 220 (7.7)	NE [NE, NE]	45 / 198 (22.7)	NE [12.6, NE]	0.2736 [0.1562, 0.4793] <.0001 <.0001	
≥75	1 / 24 (4.2)	NE [NE, NE]	11 / 35 (31.4)	NE [5.0, NE]	0.1202 [0.0155, 0.9314] 0.0426 0.0152	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Sex						0.2097
Male	16 / 186 (8.6)	NE [NE, NE]	46 / 194 (23.7)	NE [NE, NE]	0.3017 [0.1706, 0.5336] <.0001 <.0001	
Female	2 / 58 (3.4)	NE [NE, NE]	10 / 39 (25.6)	NE [12.6, NE]	0.1108 [0.0242, 0.5081] 0.0046 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Race						0.1149
White	10 / 115 (8.7)	NE [NE, NE]	26 / 120 (21.7)	12.6 [12.6, NE]	0.3149 [0.1508, 0.6575] 0.0021 0.0012	
Asian	4 / 101 (4.0)	NE [NE, NE]	26 / 93 (28.0)	NE [NE, NE]	0.1185 [0.0413, 0.3400] <.0001 <.0001	
Other	4 / 28 (14.3)	NE [NE, NE]	4 / 20 (20.0)	NE [NE, NE]	0.6503 [0.1624, 2.6042] 0.5433 0.5402	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
ECOG						0.6869
0	8 / 96 (8.3)	NE [NE, NE]	19 / 81 (23.5)	NE [12.6, NE]	0.2753 [0.1195, 0.6344] 0.0025 0.0012	
≥1	10 / 148 (6.8)	NE [NE, NE]	37 / 152 (24.3)	NE [NE, NE]	0.2331 [0.1158, 0.4692] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Primary tumor location						0.1449
Gastric	8 / 152 (5.3)	NE [NE, NE]	35 / 139 (25.2)	NE [12.6, NE]	0.1739 [0.0805, 0.3758] <.0001 <.0001	
GEJ	10 / 92 (10.9)	NE [NE, NE]	21 / 94 (22.3)	NE [NE, NE]	0.3914 [0.1839, 0.8329] 0.0149 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Histological subtype						0.7286
Intestinal	4 / 68 (5.9)	NE [NE, NE]	16 / 63 (25.4)	NE [NE, NE]	0.1900 [0.0633, 0.5699] 0.0030 0.0009	
Diffuse	2 / 25 (8.0)	NE [7.5, NE]	5 / 18 (27.8)	NE [1.9, NE]	0.2355 [0.0451, 1.2281] 0.0861 0.0624	
Others	12 / 151 (7.9)	NE [NE, NE]	35 / 152 (23.0)	NE [12.6, NE]	0.2876 [0.1490, 0.5552] 0.0002 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Number of metastatic sites						0.5798
<2	7 / 72 (9.7)	NE [NE, NE]	21 / 72 (29.2)	NE [12.6, NE]	0.3011 [0.1277, 0.7100] 0.0061 0.0036	
≥2	11 / 172 (6.4)	NE [NE, NE]	35 / 161 (21.7)	NE [NE, NE]	0.2368 [0.1201, 0.4670] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Prior adjuvant/neoadjuvant therapy						0.1623
Yes	4 / 31 (12.9)	NE [NE, NE]	5 / 28 (17.9)	NE [NE, NE]	0.6209 [0.1661, 2.3218] 0.4788 0.4747	
No	14 / 213 (6.6)	NE [NE, NE]	51 / 205 (24.9)	NE [12.6, NE]	0.2151 [0.1188, 0.3894] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						0.0244
Prior nivolumab or pembrolizumab treatment						
Yes	3 / 20 (15.0)	NE [7.5, NE]	1 / 16 (6.3)	NE [NE, NE]	1.9507 [0.1953, 19.4889] 0.5694 0.5627	
No	15 / 224 (6.7)	NE [NE, NE]	55 / 217 (25.3)	NE [12.6, NE]	0.2135 [0.1204, 0.3785] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						0.2353
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						
Yes	4 / 39 (10.3)	NE [NE, NE]	7 / 36 (19.4)	NE [NE, NE]	0.4816 [0.1403, 1.6527] 0.2455 0.2348	
No	14 / 205 (6.8)	NE [NE, NE]	49 / 197 (24.9)	NE [12.6, NE]	0.2199 [0.1211, 0.3992] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Presence of liver metastasis at baseline						0.8373
Yes	10 / 145 (6.9)	NE [NE, NE]	35 / 149 (23.5)	NE [12.6, NE]	0.2344 [0.1157, 0.4750] <.0001 <.0001	
No	8 / 99 (8.1)	NE [NE, NE]	21 / 84 (25.0)	NE [NE, NE]	0.2708 [0.1197, 0.6128] 0.0017 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Renal function at baseline						0.2320
Normal renal function	5 / 116 (4.3)	NE [NE, NE]	23 / 114 (20.2)	NE [NE, NE]	0.1855 [0.0705, 0.4884] 0.0006 0.0001	
Mild impairment	10 / 87 (11.5)	NE [NE, NE]	19 / 81 (23.5)	12.6 [12.6, NE]	0.3841 [0.1776, 0.8305] 0.0150 0.0117	
Moderate impairment	3 / 41 (7.3)	NE [NE, NE]	14 / 38 (36.8)	NE [1.8, NE]	0.1536 [0.0439, 0.5368] 0.0033 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Hepatic function at baseline						0.6302
Normal hepatic function	13 / 185 (7.0)	NE [NE, NE]	44 / 177 (24.9)	NE [12.6, NE]	0.2311 [0.1242, 0.4301] <.0001 <.0001	
Mild, Moderate or Severe dysfunction	5 / 59 (8.5)	NE [NE, NE]	12 / 55 (21.8)	NE [NE, NE]	0.3225 [0.1134, 0.9169] 0.0338 0.0255	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.7565
IHC 3+	5 / 205 (2.4)	NE [NE, NE]	39 / 196 (19.9)	NE [NE, NE]	0.1043 [0.0411, 0.2649] <.0001 <.0001	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	5 / 37 (13.5)	NE [NE, NE]	0.1587 [0.0185, 1.3631] 0.0934 0.0547	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Geography stratification factor						0.4600
Asia [excluding mainland China]	2 / 57 (3.5)	NE [NE, NE]	15 / 59 (25.4)	NE [NE, NE]	0.1143 [0.0261, 0.5007] 0.0040 0.0005	
Western Europe	4 / 138 (2.9)	NE [NE, NE]	23 / 129 (17.8)	NE [NE, NE]	0.1340 [0.0463, 0.3880] 0.0002 <.0001	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	6 / 45 (13.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Time to progression on first-line therapy from IRT						0.6873
<6 Months	1 / 61 (1.6)	NE [NE, NE]	5 / 57 (8.8)	NE [NE, NE]	0.1595 [0.0185, 1.3731] 0.0947 0.0560	
≥6 Months	5 / 183 (2.7)	NE [NE, NE]	39 / 176 (22.2)	NE [NE, NE]	0.1027 [0.0404, 0.2608] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Age at randomization						0.3643
<65	2 / 139 (1.4)	NE [NE, NE]	21 / 123 (17.1)	NE [NE, NE]	0.0675 [0.0158, 0.2888] 0.0003 <.0001	
≥65	4 / 105 (3.8)	NE [NE, NE]	23 / 110 (20.9)	NE [NE, NE]	0.1614 [0.0558, 0.4668] 0.0008 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Age at randomization						0.2359
<75	6 / 220 (2.7)	NE [NE, NE]	36 / 198 (18.2)	NE [NE, NE]	0.1250 [0.0526, 0.2970] <.0001 <.0001	
≥75	0 / 24	NE [NE, NE]	8 / 35 (22.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Sex						0.6390
Male	5 / 186 (2.7)	NE [NE, NE]	36 / 194 (18.6)	NE [NE, NE]	0.1219 [0.0478, 0.3108] <.0001 <.0001	
Female	1 / 58 (1.7)	NE [NE, NE]	8 / 39 (20.5)	NE [NE, NE]	0.0701 [0.0087, 0.5638] 0.0125 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Race						0.3342
White	2 / 115 (1.7)	NE [NE, NE]	22 / 120 (18.3)	NE [NE, NE]	0.0768 [0.0180, 0.3270] 0.0005 <.0001	
Asian	2 / 101 (2.0)	NE [NE, NE]	19 / 93 (20.4)	NE [NE, NE]	0.0840 [0.0195, 0.3607] 0.0009 <.0001	
Other	2 / 28 (7.1)	NE [NE, NE]	3 / 20 (15.0)	NE [NE, NE]	0.4540 [0.0758, 2.7183] 0.3872 0.3749	

N: number of subjects in analysis set; Nsub: number of subjects in subgroup category; n: number of subjects with events; %: proportion of number of subjects in subgroup category
[a] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
ECOG						0.1906
0	4 / 96 (4.2)	NE [NE, NE]	15 / 81 (18.5)	NE [NE, NE]	0.1856 [0.0614, 0.5615] 0.0029 0.0008	
≥1	2 / 148 (1.4)	NE [NE, NE]	29 / 152 (19.1)	NE [NE, NE]	0.0606 [0.0144, 0.2539] 0.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Primary tumor location						0.8377
Gastric	4 / 152 (2.6)	NE [NE, NE]	27 / 139 (19.4)	NE [NE, NE]	0.1177 [0.0411, 0.3366] <.0001 <.0001	
GEJ	2 / 92 (2.2)	NE [NE, NE]	17 / 94 (18.1)	NE [NE, NE]	0.0974 [0.0225, 0.4224] 0.0019 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Histological subtype						0.7551
Intestinal	3 / 68 (4.4)	NE [NE, NE]	16 / 63 (25.4)	NE [NE, NE]	0.1470 [0.0428, 0.5050] 0.0023 0.0004	
Diffuse	1 / 25 (4.0)	NE [7.5, NE]	4 / 18 (22.2)	NE [NE, NE]	0.1450 [0.0159, 1.3225] 0.0869 0.0485	
Others	2 / 151 (1.3)	NE [NE, NE]	24 / 152 (15.8)	NE [NE, NE]	0.0721 [0.0170, 0.3051] 0.0004 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Number of metastatic sites						0.5161
<2	3 / 72 (4.2)	NE [NE, NE]	18 / 72 (25.0)	NE [NE, NE]	0.1491 [0.0439, 0.5066] 0.0023 0.0004	
≥2	3 / 172 (1.7)	NE [NE, NE]	26 / 161 (16.1)	NE [NE, NE]	0.0919 [0.0278, 0.3037] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Prior adjuvant/neoadjuvant therapy						0.2065
Yes	2 / 31 (6.5)	NE [NE, NE]	5 / 28 (17.9)	NE [NE, NE]	0.3113 [0.0602, 1.6100] 0.1639 0.1411	
No	4 / 213 (1.9)	NE [NE, NE]	39 / 205 (19.0)	NE [NE, NE]	0.0829 [0.0296, 0.2324] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Prior nivolumab or pembrolizumab treatment						0.0188
Yes	2 / 20 (10.0)	NE [7.5, NE]	1 / 16 (6.3)	NE [NE, NE]	1.1552 [0.0979, 13.6365] 0.9088 0.9087	
No	4 / 224 (1.8)	NE [NE, NE]	43 / 217 (19.8)	NE [NE, NE]	0.0760 [0.0273, 0.2118] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						0.0693
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						
Yes	2 / 39 (5.1)	NE [NE, NE]	3 / 36 (8.3)	NE [NE, NE]	0.5302 [0.0875, 3.2128] 0.4900 0.4830	
No	4 / 205 (2.0)	NE [NE, NE]	41 / 197 (20.8)	NE [NE, NE]	0.0779 [0.0279, 0.2176] <.0001 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Presence of liver metastasis at baseline						0.6380
Yes	4 / 145 (2.8)	NE [NE, NE]	27 / 149 (18.1)	NE [NE, NE]	0.1303 [0.0456, 0.3726] 0.0001 <.0001	
No	2 / 99 (2.0)	NE [NE, NE]	17 / 84 (20.2)	NE [NE, NE]	0.0819 [0.0189, 0.3556] 0.0008 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Renal function at baseline						0.0014
Normal renal function	0 / 116	NE [NE, NE]	19 / 114 (16.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	6 / 87 (6.9)	NE [NE, NE]	13 / 81 (16.0)	NE [NE, NE]	0.3524 [0.1337, 0.9289] 0.0349 0.0275	
Moderate impairment	0 / 41	NE [NE, NE]	12 / 38 (31.6)	NE [2.8, 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Hepatic function at baseline						0.6724
Normal hepatic function	5 / 185 (2.7)	NE [NE, NE]	34 / 177 (19.2)	NE [NE, NE]	0.1199 [0.0469, 0.3070] <.0001 <.0001	
Mild, Moderate or Severe dysfunction	1 / 59 (1.7)	NE [NE, NE]	10 / 55 (18.2)	NE [NE, NE]	0.0765 [0.0098, 0.5979] 0.0143 0.0015	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.0106
IHC 3+	12 / 205 (5.9)	NE [NE, NE]	24 / 196 (12.2)	NE [NE, NE]	0.4031 [0.2012, 0.8075] 0.0104	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	7 / 37 (18.9)	NE [6.0, NE]	0.0080 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Geography stratification factor						0.1272
Asia [excluding mainland China]	2 / 57 (3.5)	NE [NE, NE]	8 / 59 (13.6)	NE [8.0, NE]	0.1993 [0.0421, 0.9432] 0.0420 0.0241	
Western Europe	4 / 138 (2.9)	NE [NE, NE]	17 / 129 (13.2)	NE [NE, NE]	0.1676 [0.0556, 0.5050] 0.0015 0.0003	
Mainland China/Rest of World (ROW)	6 / 49 (12.2)	NE [NE, NE]	6 / 45 (13.3)	NE [9.2, NE]	0.8422 [0.2688, 2.6386] 0.7682 0.7680	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Time to progression on first-line therapy from IRT						0.3988
<6 Months	1 / 61 (1.6)	NE [NE, NE]	5 / 57 (8.8)	NE [NE, NE]	0.1522 [0.0176, 1.3176] 0.0874 0.0497	
≥6 Months	11 / 183 (6.0)	NE [NE, NE]	26 / 176 (14.8)	NE [NE, NE]	0.3362 [0.1658, 0.6817] 0.0025 0.0015	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Age at randomization						0.7470
<65	7 / 139 (5.0)	NE [NE, NE]	15 / 123 (12.2)	NE [NE, NE]	0.3378 [0.1374, 0.8303] 0.0180 0.0131	
≥65	5 / 105 (4.8)	NE [NE, NE]	16 / 110 (14.5)	NE [NE, NE]	0.2456 [0.0878, 0.6868] 0.0075 0.0040	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Age at randomization						0.9043
<75	11 / 220 (5.0)	NE [NE, NE]	26 / 198 (13.1)	NE [NE, NE]	0.3021 [0.1487, 0.6136] 0.0009 0.0005	
≥75	1 / 24 (4.2)	NE [NE, NE]	5 / 35 (14.3)	NE [7.3, NE]	0.2497 [0.0291, 2.1461] 0.2062 0.1717	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Sex						0.1598
Male	7 / 186 (3.8)	NE [NE, NE]	26 / 194 (13.4)	NE [NE, NE]	0.2062 [0.0888, 0.4784] 0.0002 <.0001	
Female	5 / 58 (8.6)	NE [NE, NE]	5 / 39 (12.8)	NE [NE, NE]	0.6017 [0.1739, 2.0823] 0.4226 0.4176	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Race						0.3776
White	3 / 115 (2.6)	NE [NE, NE]	16 / 120 (13.3)	NE [NE, NE]	0.1637 [0.0476, 0.5626] 0.0041 0.0010	
Asian	7 / 101 (6.9)	NE [NE, NE]	13 / 93 (14.0)	NE [NE, NE]	0.4221 [0.1679, 1.0614] 0.0668 0.0588	
Other	2 / 28 (7.1)	NE [13.6, NE]	2 / 20 (10.0)	NE [NE, NE]	0.3520 [0.0319, 3.8824] 0.3939 0.3725	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
ECOG						0.1324
0	3 / 96 (3.1)	NE [NE, NE]	13 / 81 (16.0)	NE [NE, NE]	0.1313 [0.0372, 0.4639] 0.0016 0.0002	
≥1	9 / 148 (6.1)	NE [NE, NE]	18 / 152 (11.8)	NE [NE, NE]	0.4391 [0.1967, 0.9804] 0.0446 0.0390	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						0.5002
Primary tumor location						
Gastric	9 / 152 (5.9)	NE [NE, NE]	20 / 139 (14.4)	NE [NE, NE]	0.3389 [0.1538, 0.7466] 0.0073 0.0049	
GEJ	3 / 92 (3.3)	NE [NE, NE]	11 / 94 (11.7)	NE [NE, NE]	0.2223 [0.0618, 0.7998] 0.0213 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Histological subtype						0.0346
Intestinal	0 / 68	NE [NE, NE]	6 / 63 (9.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	1 / 25 (4.0)	NE [6.9, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	11 / 151 (7.3)	NE [NE, NE]	25 / 152 (16.4)	NE [NE, NE]	0.3591 [0.1763, 0.7312] 0.0048 0.0032	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Number of metastatic sites						0.3896
<2	5 / 72 (6.9)	NE [13.6, NE]	11 / 72 (15.3)	NE [NE, NE]	0.4321 [0.1492, 1.2514] 0.1220 0.1115	
≥2	7 / 172 (4.1)	NE [NE, NE]	20 / 161 (12.4)	NE [NE, NE]	0.2426 [0.1018, 0.5781] 0.0014 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Prior adjuvant/neoadjuvant therapy						0.8900
Yes	2 / 31 (6.5)	NE [NE, NE]	5 / 28 (17.9)	NE [NE, NE]	0.3061 [0.0593, 1.5813] 0.1576 0.1356	
No	10 / 213 (4.7)	NE [NE, NE]	26 / 205 (12.7)	NE [NE, NE]	0.2961 [0.1424, 0.6158] 0.0011 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Prior nivolumab or pembrolizumab treatment						0.9988
Yes	2 / 20 (10.0)	NE [6.9, NE]	4 / 16 (25.0)	NE [3.1, NE]	0.3164 [0.0567, 1.7648] 0.1895 0.1674	
No	10 / 224 (4.5)	NE [NE, NE]	27 / 217 (12.4)	NE [NE, NE]	0.2899 [0.1400, 0.6005] 0.0009 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						0.9650
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						
Yes	3 / 39 (7.7)	NE [NE, NE]	8 / 36 (22.2)	NE [9.2, NE]	0.2807 [0.0734, 1.0731] 0.0633 0.0481	
No	9 / 205 (4.4)	NE [NE, NE]	23 / 197 (11.7)	NE [NE, NE]	0.3017 [0.1391, 0.6544] 0.0024 0.0013	

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

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Presence of liver metastasis at baseline						0.2689
Yes	5 / 145 (3.4)	NE [NE, NE]	20 / 149 (13.4)	NE [NE, NE]	0.2139 [0.0801, 0.5708] 0.0021 0.0007	
No	7 / 99 (7.1)	NE [NE, NE]	11 / 84 (13.1)	NE [NE, NE]	0.4353 [0.1678, 1.1290] 0.0872 0.0786	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Renal function at baseline						0.5700
Normal renal function	3 / 116 (2.6)	NE [NE, NE]	14 / 114 (12.3)	NE [NE, NE]	0.1824 [0.0523, 0.6360] 0.0076 0.0027	
Mild impairment	7 / 87 (8.0)	NE [NE, NE]	13 / 81 (16.0)	NE [NE, NE]	0.3823 [0.1522, 0.9602] 0.0407 0.0337	
Moderate impairment	2 / 41 (4.9)	NE [13.6, NE]	4 / 38 (10.5)	NE [NE, NE]	0.3072 [0.0517, 1.8256] 0.1943 0.1740	

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

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Any						
Hepatic function at baseline						0.3163
Normal hepatic function	10 / 185 (5.4)	NE [NE, NE]	22 / 177 (12.4)	NE [NE, NE]	0.3509 [0.1656, 0.7437] 0.0063 0.0043	
Mild, Moderate or Severe dysfunction	2 / 59 (3.4)	NE [NE, NE]	9 / 55 (16.4)	NE [8.0, NE]	0.1653 [0.0357, 0.7663] 0.0214 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.9999
IHC 3+	0 / 205	NE [NE, NE]	14 / 196 (7.1)	NE [NE, NE]	NE [NE, NE] NE NE	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	3 / 37 (8.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Geography stratification factor						NE
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	6 / 59 (10.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	0 / 138	NE [NE, NE]	8 / 129 (6.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	3 / 45 (6.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Time to progression on first-line therapy from IRT						0.9997
<6 Months	0 / 61	NE [NE, NE]	2 / 57 (3.5)	NE [NE, NE]	NE [NE, NE] NE NE	
≥6 Months	0 / 183	NE [NE, NE]	15 / 176 (8.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Age at randomization						0.9996
<65	0 / 139	NE [NE, NE]	7 / 123 (5.7)	NE [NE, NE]	NE [NE, NE] NE NE	
≥65	0 / 105	NE [NE, NE]	10 / 110 (9.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Age at randomization						0.9999
<75	0 / 220	NE [NE, NE]	14 / 198 (7.1)	NE [NE, NE]	NE [NE, NE] NE NE	
≥75	0 / 24	NE [NE, NE]	3 / 35 (8.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Sex						0.9998
Male	0 / 186	NE [NE, NE]	15 / 194 (7.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Female	0 / 58	NE [NE, NE]	2 / 39 (5.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Race						NE
White	0 / 115	NE [NE, NE]	8 / 120 (6.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	0 / 101	NE [NE, NE]	8 / 93 (8.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	1 / 20 (5.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
ECOG						0.9998
0	0 / 96	NE [NE, NE]	7 / 81 (8.6)	NE [NE, NE]	NE [NE, NE] NE NE	
≥1	0 / 148	NE [NE, NE]	10 / 152 (6.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Primary tumor location						NE
Gastric	0 / 152	NE [NE, NE]	9 / 139 (6.5)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	0 / 92	NE [NE, NE]	8 / 94 (8.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Histological subtype						1.0000
Intestinal	0 / 68	NE [NE, NE]	5 / 63 (7.9)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	0 / 151	NE [NE, NE]	12 / 152 (7.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Number of metastatic sites						NE
<2	0 / 72	NE [NE, NE]	8 / 72 (11.1)	NE [NE, NE]	NE [NE, NE] NE NE	
≥2	0 / 172	NE [NE, NE]	9 / 161 (5.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Prior adjuvant/neoadjuvant therapy						1.0000
Yes	0 / 31	NE [NE, NE]	2 / 28 (7.1)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 213	NE [NE, NE]	15 / 205 (7.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Prior nivolumab or pembrolizumab treatment						0.9997
Yes	0 / 20	NE [NE, NE]	2 / 16 (12.5)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 224	NE [NE, NE]	15 / 217 (6.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.9997
Yes	0 / 39	NE [NE, NE]	4 / 36 (11.1)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 205	NE [NE, NE]	13 / 197 (6.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Presence of liver metastasis at baseline						0.9999
Yes	0 / 145	NE [NE, NE]	11 / 149 (7.4)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 99	NE [NE, NE]	6 / 84 (7.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Renal function at baseline						NE
Normal renal function	0 / 116	NE [NE, NE]	6 / 114 (5.3)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	0 / 87	NE [NE, NE]	8 / 81 (9.9)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	0 / 41	NE [NE, NE]	3 / 38 (7.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Renal and urinary disorders; PT: Proteinuria						
Hepatic function at baseline						0.9999
Normal hepatic function	0 / 185	NE [NE, NE]	13 / 177 (7.3)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	0 / 59	NE [NE, NE]	4 / 55 (7.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.1080
IHC 3+	8 / 205 (3.9)	NE [NE, NE]	22 / 196 (11.2)	NE [NE, NE]	0.3055 [0.1359, 0.6868] 0.0041 0.0024	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	4 / 37 (10.8)	NE [7.4, 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						0.0965
Geography stratification factor						
Asia [excluding mainland China]	2 / 57 (3.5)	NE [NE, NE]	9 / 59 (15.3)	NE [NE, NE]	0.2027 [0.0437, 0.9394] 0.0414 0.0238	
Western Europe	6 / 138 (4.3)	NE [NE, NE]	11 / 129 (8.5)	NE [NE, NE]	0.4367 [0.1612, 1.1833] 0.1033 0.0941	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	6 / 45 (13.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
Time to progression on first-line therapy from IRT						0.0181
<6 Months	0 / 61	NE [NE, NE]	8 / 57 (14.0)	NE [6.7, NE]	NE [NE, NE] NE NE	
≥6 Months	8 / 183 (4.4)	NE [NE, NE]	18 / 176 (10.2)	NE [NE, NE]	0.3736 [0.1622, 0.8601] 0.0207 0.0161	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
Age at randomization						0.0483
<65	2 / 139 (1.4)	NE [NE, NE]	15 / 123 (12.2)	NE [NE, NE]	0.0999 [0.0228, 0.4378] 0.0022 0.0002	
≥65	6 / 105 (5.7)	NE [NE, NE]	11 / 110 (10.0)	NE [NE, NE]	0.5082 [0.1875, 1.3775] 0.1834 0.1755	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						0.5839
Age at randomization						
<75	7 / 220 (3.2)	NE [NE, NE]	23 / 198 (11.6)	NE [NE, NE]	0.2322 [0.0994, 0.5421] 0.0007 0.0002	
≥75	1 / 24 (4.2)	NE [NE, NE]	3 / 35 (8.6)	NE [NE, NE]	0.4751 [0.0493, 4.5764] 0.5196 0.5100	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
Sex						0.0101
Male	8 / 186 (4.3)	NE [NE, NE]	18 / 194 (9.3)	NE [NE, NE]	0.3965 [0.1720, 0.9137] 0.0299	
Female	0 / 58	NE [NE, NE]	8 / 39 (20.5)	NE [7.4, NE]	0.0246 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
Race						0.1940
White	5 / 115 (4.3)	NE [NE, NE]	10 / 120 (8.3)	NE [NE, NE]	0.4637 [0.1583, 1.3580] 0.1610 0.1512	
Asian	2 / 101 (2.0)	NE [NE, NE]	15 / 93 (16.1)	NE [NE, NE]	0.1080 [0.0247, 0.4729] 0.0031 0.0003	
Other	1 / 28 (3.6)	NE [NE, NE]	1 / 20 (5.0)	NE [NE, NE]	0.6547 [0.0408, 10.4939] 0.7647 0.7630	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
ECOG						0.8473
0	3 / 96 (3.1)	NE [NE, NE]	9 / 81 (11.1)	NE [NE, NE]	0.2154 [0.0580, 0.8003] 0.0219 0.0118	
≥1	5 / 148 (3.4)	NE [NE, NE]	17 / 152 (11.2)	NE [NE, NE]	0.2680 [0.0988, 0.7275] 0.0098 0.0056	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						0.2902
Primary tumor location						
Gastric	4 / 152 (2.6)	NE [NE, NE]	18 / 139 (12.9)	NE [NE, NE]	0.1808 [0.0611, 0.5348] 0.0020 0.0005	
GEJ	4 / 92 (4.3)	NE [NE, NE]	8 / 94 (8.5)	NE [NE, NE]	0.4156 [0.1247, 1.3845] 0.1527 0.1411	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						0.4206
Histological subtype						
Intestinal	3 / 68 (4.4)	NE [NE, NE]	6 / 63 (9.5)	NE [NE, NE]	0.3544 [0.0874, 1.4368] 0.1464 0.1302	
Diffuse	0 / 25	NE [NE, NE]	2 / 18 (11.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Others	5 / 151 (3.3)	NE [NE, NE]	18 / 152 (11.8)	NE [NE, NE]	0.2433 [0.0903, 0.6561] 0.0052 0.0025	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
Number of metastatic sites						0.1822
<2	4 / 72 (5.6)	NE [NE, NE]	8 / 72 (11.1)	NE [NE, NE]	0.4974 [0.1498, 1.6519] 0.2541 0.2450	
≥2	4 / 172 (2.3)	NE [NE, NE]	18 / 161 (11.2)	NE [NE, NE]	0.1649 [0.0556, 0.4888] 0.0011 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
Prior adjuvant/neoadjuvant therapy						0.4489
Yes	0 / 31	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	8 / 213 (3.8)	NE [NE, NE]	25 / 205 (12.2)	NE [NE, NE]	0.2630 [0.1185, 0.5839] 0.0010 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
Prior nivolumab or pembrolizumab treatment						0.6200
Yes	1 / 20 (5.0)	NE [NE, NE]	4 / 16 (25.0)	NE [1.2, NE]	0.1918 [0.0214, 1.7161] 0.1397 0.0988	
No	7 / 224 (3.1)	NE [NE, NE]	22 / 217 (10.1)	NE [NE, NE]	0.2619 [0.1117, 0.6139] 0.0021 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.3241
Yes	1 / 39 (2.6)	NE [NE, NE]	7 / 36 (19.4)	NE [NE, NE]	0.1226 [0.0151, 0.9964] 0.0496 0.0192	
No	7 / 205 (3.4)	NE [NE, NE]	19 / 197 (9.6)	NE [NE, NE]	0.2986 [0.1253, 0.7117] 0.0064 0.0038	

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

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
Presence of liver metastasis at baseline						0.4506
Yes	3 / 145 (2.1)	NE [NE, NE]	15 / 149 (10.1)	NE [NE, NE]	0.1763 [0.0510, 0.6098] 0.0061 0.0020	
No	5 / 99 (5.1)	NE [NE, NE]	11 / 84 (13.1)	NE [NE, NE]	0.3259 [0.1128, 0.9416] 0.0384 0.0295	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
Renal function at baseline						0.3510
Normal renal function	4 / 116 (3.4)	NE [NE, NE]	15 / 114 (13.2)	NE [NE, NE]	0.2186 [0.0723, 0.6605] 0.0070 0.0031	
Mild impairment	1 / 87 (1.1)	NE [NE, NE]	7 / 81 (8.6)	NE [NE, NE]	0.1157 [0.0142, 0.9414] 0.0438 0.0152	
Moderate impairment	3 / 41 (7.3)	NE [NE, NE]	4 / 38 (10.5)	NE [NE, NE]	0.6593 [0.1475, 2.9477] 0.5856 0.5829	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Any						
Hepatic function at baseline						0.6690
Normal hepatic function	7 / 185 (3.8)	NE [NE, NE]	24 / 177 (13.6)	NE [NE, NE]	0.2372 [0.1020, 0.5515] 0.0008 0.0003	
Mild, Moderate or Severe dysfunction	1 / 59 (1.7)	NE [NE, NE]	2 / 55 (3.6)	NE [7.4, NE]	0.3789 [0.0337, 4.2593] 0.4318 0.4146	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						NE
IHC 3+	0 / 205	NE [NE, NE]	9 / 196 (4.6)	NE [NE, NE]	NE [NE, NE] NE NE	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	1 / 37 (2.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Geography stratification factor						NE
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	2 / 59 (3.4)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	0 / 138	NE [NE, NE]	5 / 129 (3.9)	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	3 / 45 (6.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Time to progression on first-line therapy from IRT						NE
<6 Months	0 / 61	NE [NE, NE]	4 / 57 (7.0)	NE [NE, NE]	NE [NE, NE] NE NE	
≥6 Months	0 / 183	NE [NE, NE]	6 / 176 (3.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Age at randomization						NE
<65	0 / 139	NE [NE, NE]	8 / 123 (6.5)	NE [NE, NE]	NE [NE, NE] NE NE	
≥65	0 / 105	NE [NE, NE]	2 / 110 (1.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Age at randomization						0.9996
<75	0 / 220	NE [NE, NE]	10 / 198 (5.1)	NE [NE, NE]	NE [NE, NE] NE NE	
≥75	0 / 24	NE [NE, NE]	0 / 35	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Sex						NE
Male	0 / 186	NE [NE, NE]	7 / 194 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Female	0 / 58	NE [NE, NE]	3 / 39 (7.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Race						NE
White	0 / 115	NE [NE, NE]	5 / 120 (4.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	0 / 101	NE [NE, NE]	5 / 93 (5.4)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
ECOG						NE
0	0 / 96	NE [NE, NE]	3 / 81 (3.7)	NE [NE, NE]	NE [NE, NE] NE NE	
≥1	0 / 148	NE [NE, NE]	7 / 152 (4.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Primary tumor location						NE
Gastric	0 / 152	NE [NE, NE]	8 / 139 (5.8)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	0 / 92	NE [NE, NE]	2 / 94 (2.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Histological subtype						NE
Intestinal	0 / 68	NE [NE, NE]	1 / 63 (1.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	2 / 18 (11.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Others	0 / 151	NE [NE, NE]	7 / 152 (4.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Number of metastatic sites						NE
<2	0 / 72	NE [NE, NE]	4 / 72 (5.6)	NE [NE, NE]	NE [NE, NE] NE NE	
≥2	0 / 172	NE [NE, NE]	6 / 161 (3.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Prior adjuvant/neoadjuvant therapy						NE
Yes	0 / 31	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 213	NE [NE, NE]	9 / 205 (4.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Prior nivolumab or pembrolizumab treatment						NE
Yes	0 / 20	NE [NE, NE]	2 / 16 (12.5)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 224	NE [NE, NE]	8 / 217 (3.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						NE
Yes	0 / 39	NE [NE, NE]	4 / 36 (11.1)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 205	NE [NE, NE]	6 / 197 (3.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Presence of liver metastasis at baseline						NE
Yes	0 / 145	NE [NE, NE]	5 / 149 (3.4)	NE [NE, NE]	NE [NE, NE] NE NE	
No	0 / 99	NE [NE, NE]	5 / 84 (6.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Renal function at baseline						NE
Normal renal function	0 / 116	NE [NE, NE]	7 / 114 (6.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	0 / 87	NE [NE, NE]	1 / 81 (1.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	0 / 41	NE [NE, NE]	2 / 38 (5.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Injury, poisoning and procedural complications; PT: Infusion related reaction						
Hepatic function at baseline						NE
Normal hepatic function	0 / 185	NE [NE, NE]	9 / 177 (5.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	0 / 59	NE [NE, NE]	1 / 55 (1.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.9270
IHC 3+	3 / 205 (1.5)	NE [NE, NE]	9 / 196 (4.6)	NE [NE, NE]	0.2944 [0.0797, 1.0881] 0.0667 0.0512	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	3 / 37 (8.1)	NE [NE, NE]	0.3080 [0.0320, 2.9623] 0.3079 0.2803	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						NE
Geography stratification factor						
Asia [excluding mainland China]	3 / 57 (5.3)	NE [NE, NE]	5 / 59 (8.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	1 / 138 (0.7)	NE [NE, NE]	3 / 129 (2.3)	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	4 / 45 (8.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						
Time to progression on first-line therapy from IRT						0.5970
<6 Months	2 / 61 (3.3)	NE [NE, NE]	4 / 57 (7.0)	NE [NE, NE]	0.4391 [0.0804, 2.3991] 0.3421 0.3286	
≥6 Months	2 / 183 (1.1)	NE [NE, NE]	8 / 176 (4.5)	NE [NE, NE]	0.2225 [0.0472, 1.0486] 0.0574 0.0372	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						0.8783
Age at randomization						
<65	3 / 139 (2.2)	NE [NE, NE]	8 / 123 (6.5)	NE [NE, NE]	0.3000 [0.0795, 1.1318] 0.0755 0.0593	
≥65	1 / 105 (1.0)	NE [NE, NE]	4 / 110 (3.6)	NE [NE, NE]	0.2408 [0.0268, 2.1600] 0.2034 0.1668	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						0.5485
Age at randomization						
<75	4 / 220 (1.8)	NE [NE, NE]	11 / 198 (5.6)	NE [NE, NE]	0.2956 [0.0940, 0.9293] 0.0370 0.0267	
≥75	0 / 24	NE [NE, NE]	1 / 35 (2.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any Sex						0.3766
Male	4 / 186 (2.2)	NE [NE, NE]	11 / 194 (5.7)	NE [NE, NE]	0.3396 [0.1080, 1.0681] 0.0647 0.0527	
Female	0 / 58	NE [NE, NE]	1 / 39 (2.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any Race						NE
White	1 / 115 (0.9)	NE [NE, NE]	6 / 120 (5.0)	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	3 / 101 (3.0)	NE [NE, NE]	6 / 93 (6.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						
ECOG						NE
0	2 / 96 (2.1)	NE [NE, NE]	6 / 81 (7.4)	NE [NE, NE]	NE [NE, NE] NE NE	
≥1	2 / 148 (1.4)	NE [NE, NE]	6 / 152 (3.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any Primary tumor location						NE
Gastric	3 / 152 (2.0)	NE [NE, NE]	4 / 139 (2.9)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	1 / 92 (1.1)	NE [NE, NE]	8 / 94 (8.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						NE
Histological subtype						
Intestinal	1 / 68 (1.5)	NE [NE, NE]	4 / 63 (6.3)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	1 / 25 (4.0)	NE [NE, NE]	1 / 18 (5.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Others	2 / 151 (1.3)	NE [NE, NE]	7 / 152 (4.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						0.1285
Number of metastatic sites						
<2	0 / 72	NE [NE, NE]	4 / 72 (5.6)	NE [NE, NE]	NE [NE, NE] NE NE	
≥2	4 / 172 (2.3)	NE [NE, NE]	8 / 161 (5.0)	NE [NE, NE]	0.4069 [0.1220, 1.3565] 0.1433 0.1304	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						0.0880
Prior adjuvant/neoadjuvant therapy						
Yes	2 / 31 (6.5)	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	1.6570 [0.1501, 18.2920] 0.6802 0.6770	
No	2 / 213 (0.9)	NE [NE, NE]	11 / 205 (5.4)	NE [NE, NE]	0.1608 [0.0356, 0.7259] 0.0175 0.0065	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						0.2260
Prior nivolumab or pembrolizumab treatment						
Yes	0 / 20	NE [NE, NE]	2 / 16 (12.5)	NE [4.0, NE]	NE [NE, NE] NE NE	
No	4 / 224 (1.8)	NE [NE, NE]	10 / 217 (4.6)	NE [NE, NE]	0.3600 [0.1128, 1.1485] 0.0843 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.1610
Yes	0 / 39	NE [NE, NE]	3 / 36 (8.3)	NE [NE, NE]	NE [NE, NE] NE NE	
No	4 / 205 (2.0)	NE [NE, NE]	9 / 197 (4.6)	NE [NE, NE]	0.3946 [0.1214, 1.2826] 0.1221 0.1091	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						
Presence of liver metastasis at baseline						NE
Yes	2 / 145 (1.4)	NE [NE, NE]	7 / 149 (4.7)	NE [NE, NE]	NE [NE, NE] NE NE	
No	2 / 99 (2.0)	NE [NE, NE]	5 / 84 (6.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						NE
Renal function at baseline						
Normal renal function	2 / 116 (1.7)	NE [NE, NE]	7 / 114 (6.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	1 / 87 (1.1)	NE [NE, NE]	3 / 81 (3.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	1 / 41 (2.4)	NE [NE, NE]	2 / 38 (5.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps); PT: Any						0.0842
Hepatic function at baseline						
Normal hepatic function	2 / 185 (1.1)	NE [NE, NE]	11 / 177 (6.2)	NE [NE, NE]	0.1636 [0.0363, 0.7383] 0.0185 0.0072	
Mild, Moderate or Severe dysfunction	2 / 59 (3.4)	NE [NE, NE]	1 / 55 (1.8)	NE [8.0, NE]	1.5465 [0.1402, 17.0568] 0.7219 0.7197	

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

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Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.4968
IHC 3+	2 / 205 (1.0)	NE [NE, NE]	8 / 196 (4.1)	NE [NE, NE]	0.2216 [0.0470, 1.0437] 0.0567 0.0365	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	1 / 37 (2.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						
Geography stratification factor						NE
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	2 / 59 (3.4)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	2 / 138 (1.4)	NE [NE, NE]	6 / 129 (4.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	1 / 45 (2.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						
Time to progression on first-line therapy from IRT						NE
<6 Months	1 / 61 (1.6)	NE [NE, NE]	4 / 57 (7.0)	NE [NE, NE]	NE [NE, NE] NE NE	
≥6 Months	1 / 183 (0.5)	NE [NE, NE]	5 / 176 (2.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						NE
Age at randomization						
<65	0 / 139	NE [NE, NE]	3 / 123 (2.4)	NE [NE, NE]	NE [NE, NE] NE NE	
≥65	2 / 105 (1.9)	NE [NE, NE]	6 / 110 (5.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						
Age at randomization						0.6200
<75	2 / 220 (0.9)	NE [NE, NE]	8 / 198 (4.0)	NE [NE, NE]	0.2019 [0.0429, 0.9513] 0.0431 0.0248	
≥75	0 / 24	NE [NE, NE]	1 / 35 (2.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						
Sex						0.4538
Male	2 / 186 (1.1)	NE [NE, NE]	8 / 194 (4.1)	NE [NE, NE]	0.2324 [0.0493, 1.0954] 0.0651 0.0442	
Female	0 / 58	NE [NE, NE]	1 / 39 (2.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						
Race						NE
White	2 / 115 (1.7)	NE [NE, NE]	5 / 120 (4.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	0 / 101	NE [NE, NE]	3 / 93 (3.2)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	1 / 20 (5.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						NE
ECOG						
0	2 / 96 (2.1)	NE [NE, NE]	5 / 81 (6.2)	NE [NE, NE]	NE [NE, NE] NE NE	
≥1	0 / 148	NE [NE, NE]	4 / 152 (2.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						NE
Primary tumor location						
Gastric	1 / 152 (0.7)	NE [NE, NE]	5 / 139 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	1 / 92 (1.1)	NE [NE, NE]	4 / 94 (4.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						NE
Histological subtype						
Intestinal	0 / 68	NE [NE, NE]	3 / 63 (4.8)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	2 / 151 (1.3)	NE [NE, NE]	6 / 152 (3.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						
Number of metastatic sites						NE
<2	0 / 72	NE [NE, NE]	2 / 72 (2.8)	NE [NE, NE]	NE [NE, NE] NE NE	
≥2	2 / 172 (1.2)	NE [NE, NE]	7 / 161 (4.3)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						0.0500
Prior adjuvant/neoadjuvant therapy						
Yes	1 / 31 (3.2)	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 213 (0.5)	NE [NE, NE]	9 / 205 (4.4)	NE [NE, NE]	0.0986 [0.0125, 0.7782] 0.0280 0.0065	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						NE
Prior nivolumab or pembrolizumab treatment						
Yes	0 / 20	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	2 / 224 (0.9)	NE [NE, NE]	9 / 217 (4.1)	NE [NE, NE]	0.1962 [0.0424, 0.9082] 0.0372 0.0203	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						0.9996
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						
Yes	0 / 39	NE [NE, NE]	0 / 36	NE [NE, NE]	NE [NE, NE] NE NE	
No	2 / 205 (1.0)	NE [NE, NE]	9 / 197 (4.6)	NE [NE, NE]	0.1919 [0.0414, 0.8889] 0.0348 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						
Presence of liver metastasis at baseline						NE
Yes	1 / 145 (0.7)	NE [NE, NE]	5 / 149 (3.4)	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 99 (1.0)	NE [NE, NE]	4 / 84 (4.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						
Renal function at baseline						NE
Normal renal function	0 / 116	NE [NE, NE]	2 / 114 (1.8)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	0 / 87	NE [NE, NE]	7 / 81 (8.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	2 / 41 (4.9)	NE [NE, NE]	0 / 38	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Table 9.16.2 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Ear and labyrinth disorders; PT: Any						
Hepatic function at baseline						NE
Normal hepatic function	1 / 185 (0.5)	NE [NE, NE]	7 / 177 (4.0)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	1 / 59 (1.7)	NE [NE, NE]	2 / 55 (3.6)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:16 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.16.2_10TEAE_SAF_SUB.rtf

Anhang 4-G 4.3.3 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT – SAF

Table 9.18.1 Serious Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	39 (16.0)	NE [19.0, NE]	41 (17.6)	22.5 [13.8, NE]	0.7925 [0.5101, 1.2312] 0.3009	0.2997
PT: Vomiting	9 (3.7)	NE [NE, NE]	2 (0.9)	NE [NE, NE]	3.9346 [0.8482, 18.2520] 0.0802	0.0590
PT: Dysphagia	7 (2.9)	NE [NE, NE]	4 (1.7)	NE [NE, NE]	1.3957 [0.4056, 4.8027] 0.5969	0.5953
PT: Upper gastrointestinal haemorrhage	4 (1.6)	NE [19.0, NE]	6 (2.6)	NE [NE, NE]	0.5332 [0.1493, 1.9042] 0.3329	0.3258
PT: Ascites	3 (1.2)	NE [NE, NE]	8 (3.4)	NE [NE, NE]	0.3150 [0.0835, 1.1887] 0.0882	0.0718

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.18.1_10SAE_SAF.rtf

Table 9.18.1 Serious Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	23 (9.4)	NE [NE, NE]	26 (11.2)	NE [NE, NE]	0.7034 [0.4002, 1.2365] 0.2216	0.2191
PT: Pneumonia	10 (4.1)	NE [NE, NE]	8 (3.4)	NE [NE, NE]	0.9880 [0.3879, 2.5164] 0.9798	0.9798

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.18.1_10SAE_SAF.rtf

Table 9.18.1 Serious Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	21 (8.6)	NE [NE, NE]	14 (6.0)	NE [NE, NE]	1.3836 [0.7031, 2.7225] 0.3472	0.3455
PT: Anaemia	12 (4.9)	NE [NE, NE]	8 (3.4)	NE [NE, NE]	1.3338 [0.5445, 3.2673] 0.5287	0.5272
PT: Febrile neutropenia	6 (2.5)	NE [NE, NE]	6 (2.6)	NE [NE, NE]	0.9231 [0.2976, 2.8631] 0.8898	0.8894

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.18.1_10SAE_SAF.rtf

Table 9.18.1 Serious Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: General disorders and administration site conditions						
PT: Any	20 (8.2)	NE [NE, NE]	22 (9.4)	NE [NE, NE]	0.7717 [0.4207, 1.4157] 0.4025	0.4013
PT: Disease progression	8 (3.3)	NE [NE, NE]	18 (7.7)	NE [NE, NE]	0.3710 [0.1611, 0.8541] 0.0198	0.0152

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.18.1_10SAE_SAF.rtf

Table 9.18.1 Serious Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	18 (7.4)	NE [NE, NE]	12 (5.2)	NE [NE, NE]	1.3333 [0.6421, 2.7684] 0.4403	0.4387

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.18.1_10SAE_SAF.rtf

Table 9.18.1 Serious Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	12 (4.9)	NE [NE, NE]	10 (4.3)	NE [NE, NE]	1.1018 [0.4759, 2.5509] 0.8210	0.8206

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.18.1_10SAE_SAF.rtf

Table 9.18.1 Serious Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	7 (2.9)	NE [NE, NE]	4 (1.7)	NE [NE, NE]	1.3982 [0.4074, 4.7984] 0.5941	0.5924

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.18.1_10SAE_SAF.rtf

Anhang 4-G 4.3.4 Schwerwiegende Unerwünschte Ereignisse nach SOC und PT mit statistisch signifikantem Ergebnis auf Endpunktebene – Subgruppenanalyse – SAF

Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.4475
IHC 3+	7 / 205 (3.4)	NE [NE, NE]	14 / 196 (7.1)	NE [NE, NE]	0.4254 [0.1716, 1.0550] 0.0651 0.0573	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	4 / 37 (10.8)	NE [NE, NE]	0.2009 [0.0224, 1.8034] 0.1517 0.1118	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:17 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.18.2_10SAE_SAF_SUB.rtf

Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Geography stratification factor						0.4363
Asia [excluding mainland China]	2 / 57 (3.5)	NE [NE, NE]	2 / 59 (3.4)	NE [NE, NE]	0.9666 [0.1360, 6.8699] 0.9729 0.9729	
Western Europe	5 / 138 (3.6)	NE [NE, NE]	10 / 129 (7.8)	NE [NE, NE]	0.3994 [0.1363, 1.1703] 0.0943 0.0832	
Mainland China/Rest of World (ROW)	1 / 49 (2.0)	NE [NE, NE]	6 / 45 (13.3)	NE [NE, NE]	0.1476 [0.0177, 1.2287] 0.0768 0.0404	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Time to progression on first-line therapy from IRT						0.7923
<6 Months	2 / 61 (3.3)	NE [NE, NE]	5 / 57 (8.8)	NE [7.3, NE]	0.3159 [0.0607, 1.6437] 0.1709 0.1488	
≥6 Months	6 / 183 (3.3)	NE [NE, NE]	13 / 176 (7.4)	NE [NE, NE]	0.3910 [0.1485, 1.0297] 0.0573 0.0487	

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

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Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Age at randomization						0.0214
<65	2 / 139 (1.4)	NE [NE, NE]	12 / 123 (9.8)	NE [NE, NE]	0.1245 [0.0278, 0.5568] 0.0064 0.0012	
≥65	6 / 105 (5.7)	NE [NE, NE]	6 / 110 (5.5)	NE [NE, NE]	0.9654 [0.3110, 2.9966] 0.9515 0.9515	

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

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Run date: 23JUN2025 11:17 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.18.2_10SAE_SAF_SUB.rtf

Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Age at randomization						0.3270
<75	7 / 220 (3.2)	NE [NE, NE]	17 / 198 (8.6)	NE [NE, NE]	0.3206 [0.1328, 0.7739] 0.0114 0.0076	
≥75	1 / 24 (4.2)	NE [NE, NE]	1 / 35 (2.9)	NE [NE, NE]	1.3647 [0.0850, 21.9105] 0.8262 0.8255	

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

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Run date: 23JUN2025 11:17 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.18.2_10SAE_SAF_SUB.rtf

Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Sex						0.4225
Male	5 / 186 (2.7)	NE [NE, NE]	15 / 194 (7.7)	NE [NE, NE]	0.2997 [0.1088, 0.8257] 0.0198 0.0134	
Female	3 / 58 (5.2)	NE [NE, NE]	3 / 39 (7.7)	NE [NE, NE]	0.6331 [0.1274, 3.1463] 0.5763 0.5730	

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

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Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Race						0.5714
White	5 / 115 (4.3)	NE [NE, NE]	11 / 120 (9.2)	NE [NE, NE]	0.4080 [0.1417, 1.1749] 0.0967 0.0859	
Asian	3 / 101 (3.0)	NE [NE, NE]	6 / 93 (6.5)	NE [NE, NE]	0.4145 [0.1035, 1.6599] 0.2135 0.1990	
Other	0 / 28	NE [NE, NE]	1 / 20 (5.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
ECOG						0.2311
0	1 / 96 (1.0)	NE [NE, NE]	5 / 81 (6.2)	NE [NE, NE]	0.1323 [0.0154, 1.1360] 0.0652 0.0300	
≥1	7 / 148 (4.7)	NE [NE, NE]	13 / 152 (8.6)	NE [NE, NE]	0.5082 [0.2027, 1.2743] 0.1490 0.1413	

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

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Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Primary tumor location						0.4727
Gastric	6 / 152 (3.9)	NE [NE, NE]	11 / 139 (7.9)	NE [NE, NE]	0.4514 [0.1667, 1.2224] 0.1176 0.1083	
GEJ	2 / 92 (2.2)	NE [NE, NE]	7 / 94 (7.4)	NE [NE, NE]	0.2460 [0.0510, 1.1855] 0.0805 0.0582	

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

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Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Histological subtype						0.9394
Intestinal	0 / 68	NE [NE, NE]	0 / 63	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	1 / 25 (4.0)	NE [NE, NE]	1 / 18 (5.6)	NE [NE, NE]	0.6574 [0.0411, 10.5155] 0.7668 0.7651	
Others	7 / 151 (4.6)	NE [NE, NE]	17 / 152 (11.2)	NE [NE, NE]	0.3710 [0.1538, 0.8950] 0.0273 0.0216	

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

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Number of metastatic sites						0.9368
<2	2 / 72 (2.8)	NE [NE, NE]	6 / 72 (8.3)	NE [NE, NE]	0.3465 [0.0699, 1.7172] 0.1944 0.1740	
≥2	6 / 172 (3.5)	NE [NE, NE]	12 / 161 (7.5)	NE [NE, NE]	0.3611 [0.1347, 0.9682] 0.0430 0.0349	

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

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Prior adjuvant/neoadjuvant therapy						0.3722
Yes	0 / 31	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	8 / 213 (3.8)	NE [NE, NE]	17 / 205 (8.3)	NE [NE, NE]	0.3953 [0.1704, 0.9171] 0.0307 0.0251	

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

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DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Prior nivolumab or pembrolizumab treatment						0.1658
Yes	0 / 20	NE [NE, NE]	2 / 16 (12.5)	NE [6.8, NE]	NE [NE, NE] NE NE	
No	8 / 224 (3.6)	NE [NE, NE]	16 / 217 (7.4)	NE [NE, NE]	0.4282 [0.1831, 1.0015] 0.0504 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:17 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.18.2_10SAE_SAF_SUB.rtf

Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						0.0727
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						
Yes	0 / 39	NE [NE, NE]	4 / 36 (11.1)	NE [NE, NE]	NE [NE, NE] NE NE	
No	8 / 205 (3.9)	NE [NE, NE]	14 / 197 (7.1)	NE [NE, NE]	0.4776 [0.2001, 1.1397] 0.0959 0.0885	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:17 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.18.2_10SAE_SAF_SUB.rtf

Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Presence of liver metastasis at baseline						0.3207
Yes	2 / 145 (1.4)	NE [NE, NE]	9 / 149 (6.0)	NE [NE, NE]	0.2066 [0.0446, 0.9570] 0.0438 0.0257	
No	6 / 99 (6.1)	NE [NE, NE]	9 / 84 (10.7)	NE [NE, NE]	0.4866 [0.1728, 1.3702] 0.1727 0.1636	

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

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Run date: 23JUN2025 11:17 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.18.2_10SAE_SAF_SUB.rtf

Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Renal function at baseline						0.8231
Normal renal function	4 / 116 (3.4)	NE [NE, NE]	9 / 114 (7.9)	NE [NE, NE]	0.3944 [0.1213, 1.2829] 0.1221 0.1091	
Mild impairment	2 / 87 (2.3)	NE [NE, NE]	6 / 81 (7.4)	NE [NE, NE]	0.2625 [0.0529, 1.3026] 0.1017 0.0783	
Moderate impairment	2 / 41 (4.9)	NE [NE, NE]	3 / 38 (7.9)	NE [NE, NE]	0.5387 [0.0893, 3.2491] 0.4999 0.4933	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:17 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.18.2_10SAE_SAF_SUB.rtf

Table 9.18.2 Serious Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Hepatic function at baseline						0.8921
Normal hepatic function	5 / 185 (2.7)	NE [NE, NE]	12 / 177 (6.8)	NE [NE, NE]	0.3467 [0.1220, 0.9850] 0.0468 0.0373	
Mild, Moderate or Severe dysfunction	3 / 59 (5.1)	NE [NE, NE]	6 / 55 (10.9)	NE [NE, NE]	0.3951 [0.0985, 1.5844] 0.1900 0.1746	

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

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Anhang 4-G 4.3.5 Schwere Unerwünschte Ereignisse (CTCAE-Grad ≥3) nach SOC und PT – SAF

Daiichi Sankyo Europe GmbH
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Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	76 (31.1)	NE [NE, NE]	80 (34.3)	12.4 [7.9, NE]	0.8542 [0.6238, 1.1698] 0.3260	0.3216
PT: Anaemia	56 (23.0)	NE [NE, NE]	48 (20.6)	NE [12.4, NE]	1.0719 [0.7287, 1.5769] 0.7243	0.7257
PT: Neutropenia	23 (9.4)	NE [NE, NE]	31 (13.3)	NE [NE, NE]	0.6524 [0.3800, 1.1199] 0.1214	0.1172
PT: Febrile neutropenia	7 (2.9)	NE [NE, NE]	11 (4.7)	NE [NE, NE]	0.5813 [0.2253, 1.5000] 0.2620	0.2562

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.20.1_10SEVAE_SAF.rtf

Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	70 (28.7)	NE [20.3, NE]	69 (29.6)	NE [8.8, NE]	0.8882 [0.6361, 1.2402] 0.4863	0.4844
PT: Neutrophil count decreased	50 (20.5)	NE [NE, NE]	53 (22.7)	NE [NE, NE]	0.8288 [0.5628, 1.2205] 0.3416	0.3368
PT: Platelet count decreased	17 (7.0)	NE [23.1, NE]	8 (3.4)	NE [NE, NE]	1.8801 [0.8097, 4.3655] 0.1419	0.1388
PT: White blood cell count decreased	17 (7.0)	NE [NE, NE]	25 (10.7)	NE [NE, NE]	0.5967 [0.3220, 1.1058] 0.1009	0.0970
PT: Lymphocyte count decreased	7 (2.9)	NE [20.3, NE]	4 (1.7)	NE [NE, NE]	1.4424 [0.4201, 4.9517] 0.5606	0.5576

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Weight decreased	6 (2.5)	NE [NE, NE]	4 (1.7)	NE [NE, NE]	0.9169 [0.2551, 3.2957] 0.8943	0.8943

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.20.1_10SEVAE_SAF.rtf

Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	53 (21.7)	NE [19.0, NE]	50 (21.5)	22.5 [13.8, NE]	0.9240 [0.6272, 1.3614] 0.6895	0.6897
PT: Nausea	13 (5.3)	NE [NE, NE]	0	NE [NE, NE]	NE [NE, NE] NE	0.0005
PT: Vomiting	10 (4.1)	NE [NE, NE]	3 (1.3)	NE [NE, NE]	2.9226 [0.8035, 10.6303] 0.1035	0.0879
PT: Dysphagia	7 (2.9)	NE [NE, NE]	6 (2.6)	NE [NE, NE]	0.9302 [0.3108, 2.7840] 0.8971	0.8975
PT: Abdominal pain	6 (2.5)	NE [NE, NE]	4 (1.7)	NE [NE, NE]	1.2748 [0.3592, 4.5250] 0.7072	0.7065

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.20.1_10SEVAE_SAF.rtf

Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
PT: Ascites	5 (2.0)	NE [NE, NE]	9 (3.9)	NE [NE, NE]	0.4766 [0.1596, 1.4230] 0.1842	0.1743
PT: Upper gastrointestinal haemorrhage	5 (2.0)	NE [19.0, NE]	6 (2.6)	NE [NE, NE]	0.6567 [0.1990, 2.1667] 0.4899	0.4871
PT: Diarrhoea	4 (1.6)	NE [NE, NE]	6 (2.6)	NE [NE, NE]	0.5166 [0.1440, 1.8535] 0.3109	0.3026

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.20.1_10SEVAE_SAF.rtf

Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: General disorders and administration site conditions						
PT: Any	34 (13.9)	NE [NE, NE]	34 (14.6)	NE [NE, NE]	0.8459 [0.5252, 1.3624] 0.4913	0.4913
PT: Fatigue	10 (4.1)	NE [NE, NE]	3 (1.3)	NE [NE, NE]	2.7846 [0.7637, 10.1522] 0.1208	0.1054
PT: Asthenia	9 (3.7)	NE [NE, NE]	8 (3.4)	NE [NE, NE]	0.9019 [0.3465, 2.3477] 0.8325	0.8324
PT: Disease progression	8 (3.3)	NE [NE, NE]	18 (7.7)	NE [NE, NE]	0.3710 [0.1611, 0.8541] 0.0198	0.0152

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.20.1_10SEVAE_SAF.rtf

Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	32 (13.1)	NE [23.4, NE]	23 (9.9)	NE [16.8, NE]	1.1215 [0.6546, 1.9215] 0.6764	0.6766
PT: Hypokalaemia	20 (8.2)	NE [23.4, NE]	8 (3.4)	NE [NE, NE]	1.9611 [0.8611, 4.4666] 0.1088	0.1022
PT: Decreased appetite	8 (3.3)	NE [NE, NE]	5 (2.1)	NE [NE, NE]	1.3093 [0.4264, 4.0202] 0.6378	0.6363

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	26 (10.7)	NE [NE, NE]	25 (10.7)	NE [NE, NE]	0.8677 [0.5008, 1.5034] 0.6129	0.6126
PT: Pneumonia	12 (4.9)	NE [NE, NE]	7 (3.0)	NE [NE, NE]	1.3967 [0.5482, 3.5588] 0.4838	0.4818

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.20.1_10SEVAE_SAF.rtf

Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	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						
PT: Any	19 (7.8)	NE [NE, NE]	12 (5.2)	NE [NE, NE]	1.3735 [0.6663, 2.8312] 0.3898	0.3878

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.20.1_10SEVAE_SAF.rtf

Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Nervous system disorders						
PT: Any	8 (3.3)	NE [NE, NE]	16 (6.9)	NE [NE, NE]	0.4104 [0.1754, 0.9604] 0.0401	0.0339

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.20.1_10SEVAE_SAF.rtf

Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Hepatobiliary disorders						
PT: Any	5 (2.0)	NE [NE, NE]	10 (4.3)	NE [14.7, NE]	0.3940 [0.1338, 1.1602] 0.0910	0.0801

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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:08 (CET); Program name: t_tte_socpt.sas; Output name: T.9.20.1_10SEVAE_SAF.rtf

Table 9.20.1 Severe (CTCAE grade ≥3) Treatment-Emergent 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 Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	
	n (%)	Median [95% CI] in months [a]	n (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b]	p-value [c]
SOC: Vascular disorders						
PT: Any	2 (0.8)	NE [NE, NE]	26 (11.2)	NE [NE, NE]	0.0622 [0.0147, 0.2628] 0.0002	<0.0001
PT: Hypertension	1 (0.4)	NE [NE, NE]	25 (10.7)	NE [NE, NE]	0.0324 [0.0044, 0.2393] 0.0008	<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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Anhang 4-G 4.3.6 Schwere Unerwünschte Ereignisse (CTCAE-Grad ≥3) nach SOC und PT mit statistisch signifikantem Ergebnis auf Endpunktebene – Subgruppenanalyse – SAF

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.9997
IHC 3+	10 / 205 (4.9)	NE [NE, NE]	0 / 196	NE [NE, NE]	NE [NE, NE] NE NE	
IHC 2+/ISH+	3 / 39 (7.7)	NE [NE, NE]	0 / 37	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Geography stratification factor						1.0000
Asia [excluding mainland China]	1 / 57 (1.8)	NE [NE, NE]	0 / 59	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	11 / 138 (8.0)	NE [NE, NE]	0 / 129	NE [NE, NE]	NE [NE, NE] NE NE	
Mainland China/Rest of World (ROW)	1 / 49 (2.0)	NE [NE, NE]	0 / 45	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Time to progression on first-line therapy from IRT						0.9998
<6 Months	2 / 61 (3.3)	NE [NE, NE]	0 / 57	NE [NE, NE]	NE [NE, NE] NE NE	
≥6 Months	11 / 183 (6.0)	NE [NE, NE]	0 / 176	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Age at randomization						NE
<65	6 / 139 (4.3)	NE [NE, NE]	0 / 123	NE [NE, NE]	NE [NE, NE] NE NE	
≥65	7 / 105 (6.7)	NE [NE, NE]	0 / 110	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Age at randomization						0.9999
<75	12 / 220 (5.5)	NE [NE, NE]	0 / 198	NE [NE, NE]	NE [NE, NE] NE NE	
≥75	1 / 24 (4.2)	NE [NE, NE]	0 / 35	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Sex						NE
Male	9 / 186 (4.8)	NE [NE, NE]	0 / 194	NE [NE, NE]	NE [NE, NE] NE NE	
Female	4 / 58 (6.9)	NE [NE, NE]	0 / 39	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Race						NE
White	6 / 115 (5.2)	NE [NE, NE]	0 / 120	NE [NE, NE]	NE [NE, NE] NE NE	
Asian	3 / 101 (3.0)	NE [NE, NE]	0 / 93	NE [NE, NE]	NE [NE, NE] NE NE	
Other	4 / 28 (14.3)	NE [NE, NE]	0 / 20	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
ECOG						NE
0	5 / 96 (5.2)	NE [NE, NE]	0 / 81	NE [NE, NE]	NE [NE, NE] NE NE	
≥1	8 / 148 (5.4)	NE [NE, NE]	0 / 152	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Primary tumor location						0.9996
Gastric	3 / 152 (2.0)	NE [NE, NE]	0 / 139	NE [NE, NE]	NE [NE, NE] NE NE	
GEJ	10 / 92 (10.9)	NE [NE, NE]	0 / 94	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Histological subtype						NE
Intestinal	6 / 68 (8.8)	NE [NE, NE]	0 / 63	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	1 / 25 (4.0)	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	6 / 151 (4.0)	NE [NE, NE]	0 / 152	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Number of metastatic sites						0.9997
<2	2 / 72 (2.8)	NE [NE, NE]	0 / 72	NE [NE, NE]	NE [NE, NE] NE NE	
≥2	11 / 172 (6.4)	NE [NE, NE]	0 / 161	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Prior adjuvant/neoadjuvant therapy						0.9999
Yes	2 / 31 (6.5)	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	11 / 213 (5.2)	NE [NE, NE]	0 / 205	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Prior nivolumab or pembrolizumab treatment						0.9996
Yes	0 / 20	NE [NE, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	13 / 224 (5.8)	NE [NE, NE]	0 / 217	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.9995
Yes	0 / 39	NE [NE, NE]	0 / 36	NE [NE, NE]	NE [NE, NE] NE NE	
No	13 / 205 (6.3)	NE [NE, NE]	0 / 197	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Presence of liver metastasis at baseline						0.9997
Yes	10 / 145 (6.9)	NE [NE, NE]	0 / 149	NE [NE, NE]	NE [NE, NE] NE NE	
No	3 / 99 (3.0)	NE [NE, NE]	0 / 84	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Renal function at baseline						NE
Normal renal function	8 / 116 (6.9)	NE [NE, NE]	0 / 114	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	3 / 87 (3.4)	NE [NE, NE]	0 / 81	NE [NE, NE]	NE [NE, NE] NE NE	
Moderate impairment	2 / 41 (4.9)	NE [NE, NE]	0 / 38	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Gastrointestinal disorders; PT: Nausea						
Hepatic function at baseline						NE
Normal hepatic function	9 / 185 (4.9)	NE [NE, NE]	0 / 177	NE [NE, NE]	NE [NE, NE] NE NE	
Mild, Moderate or Severe dysfunction	4 / 59 (6.8)	NE [NE, NE]	0 / 55	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.4475
IHC 3+	7 / 205 (3.4)	NE [NE, NE]	14 / 196 (7.1)	NE [NE, NE]	0.4254 [0.1716, 1.0550] 0.0651 0.0573	
IHC 2+/ISH+	1 / 39 (2.6)	NE [NE, NE]	4 / 37 (10.8)	NE [NE, NE]	0.2009 [0.0224, 1.8034] 0.1517 0.1118	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Geography stratification factor						0.4363
Asia [excluding mainland China]	2 / 57 (3.5)	NE [NE, NE]	2 / 59 (3.4)	NE [NE, NE]	0.9666 [0.1360, 6.8699] 0.9729 0.9729	
Western Europe	5 / 138 (3.6)	NE [NE, NE]	10 / 129 (7.8)	NE [NE, NE]	0.3994 [0.1363, 1.1703] 0.0943 0.0832	
Mainland China/Rest of World (ROW)	1 / 49 (2.0)	NE [NE, NE]	6 / 45 (13.3)	NE [NE, NE]	0.1476 [0.0177, 1.2287] 0.0768 0.0404	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Time to progression on first-line therapy from IRT						0.7923
<6 Months	2 / 61 (3.3)	NE [NE, NE]	5 / 57 (8.8)	NE [7.3, NE]	0.3159 [0.0607, 1.6437] 0.1709 0.1488	
≥6 Months	6 / 183 (3.3)	NE [NE, NE]	13 / 176 (7.4)	NE [NE, NE]	0.3910 [0.1485, 1.0297] 0.0573 0.0487	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Age at randomization						0.0214
<65	2 / 139 (1.4)	NE [NE, NE]	12 / 123 (9.8)	NE [NE, NE]	0.1245 [0.0278, 0.5568] 0.0064 0.0012	
≥65	6 / 105 (5.7)	NE [NE, NE]	6 / 110 (5.5)	NE [NE, NE]	0.9654 [0.3110, 2.9966] 0.9515 0.9515	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Age at randomization						0.3270
<75	7 / 220 (3.2)	NE [NE, NE]	17 / 198 (8.6)	NE [NE, NE]	0.3206 [0.1328, 0.7739] 0.0114 0.0076	
≥75	1 / 24 (4.2)	NE [NE, NE]	1 / 35 (2.9)	NE [NE, NE]	1.3647 [0.0850, 21.9105] 0.8262 0.8255	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Sex						0.4225
Male	5 / 186 (2.7)	NE [NE, NE]	15 / 194 (7.7)	NE [NE, NE]	0.2997 [0.1088, 0.8257] 0.0198 0.0134	
Female	3 / 58 (5.2)	NE [NE, NE]	3 / 39 (7.7)	NE [NE, NE]	0.6331 [0.1274, 3.1463] 0.5763 0.5730	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Race						0.5714
White	5 / 115 (4.3)	NE [NE, NE]	11 / 120 (9.2)	NE [NE, NE]	0.4080 [0.1417, 1.1749] 0.0967 0.0859	
Asian	3 / 101 (3.0)	NE [NE, NE]	6 / 93 (6.5)	NE [NE, NE]	0.4145 [0.1035, 1.6599] 0.2135 0.1990	
Other	0 / 28	NE [NE, NE]	1 / 20 (5.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
ECOG						0.2311
0	1 / 96 (1.0)	NE [NE, NE]	5 / 81 (6.2)	NE [NE, NE]	0.1323 [0.0154, 1.1360] 0.0652 0.0300	
≥1	7 / 148 (4.7)	NE [NE, NE]	13 / 152 (8.6)	NE [NE, NE]	0.5082 [0.2027, 1.2743] 0.1490 0.1413	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Primary tumor location						0.4727
Gastric	6 / 152 (3.9)	NE [NE, NE]	11 / 139 (7.9)	NE [NE, NE]	0.4514 [0.1667, 1.2224] 0.1176 0.1083	
GEJ	2 / 92 (2.2)	NE [NE, NE]	7 / 94 (7.4)	NE [NE, NE]	0.2460 [0.0510, 1.1855] 0.0805 0.0582	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Histological subtype						0.9394
Intestinal	0 / 68	NE [NE, NE]	0 / 63	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	1 / 25 (4.0)	NE [NE, NE]	1 / 18 (5.6)	NE [NE, NE]	0.6574 [0.0411, 10.5155] 0.7668 0.7651	
Others	7 / 151 (4.6)	NE [NE, NE]	17 / 152 (11.2)	NE [NE, NE]	0.3710 [0.1538, 0.8950] 0.0273 0.0216	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Number of metastatic sites						0.9368
<2	2 / 72 (2.8)	NE [NE, NE]	6 / 72 (8.3)	NE [NE, NE]	0.3465 [0.0699, 1.7172] 0.1944 0.1740	
≥2	6 / 172 (3.5)	NE [NE, NE]	12 / 161 (7.5)	NE [NE, NE]	0.3611 [0.1347, 0.9682] 0.0430 0.0349	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Prior adjuvant/neoadjuvant therapy						0.3722
Yes	0 / 31	NE [NE, NE]	1 / 28 (3.6)	NE [NE, NE]	NE [NE, NE] NE NE	
No	8 / 213 (3.8)	NE [NE, NE]	17 / 205 (8.3)	NE [NE, NE]	0.3953 [0.1704, 0.9171] 0.0307 0.0251	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Prior nivolumab or pembrolizumab treatment						0.1658
Yes	0 / 20	NE [NE, NE]	2 / 16 (12.5)	NE [6.8, NE]	NE [NE, NE] NE NE	
No	8 / 224 (3.6)	NE [NE, NE]	16 / 217 (7.4)	NE [NE, NE]	0.4282 [0.1831, 1.0015] 0.0504 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.0727
Yes	0 / 39	NE [NE, NE]	4 / 36 (11.1)	NE [NE, NE]	NE [NE, NE] NE NE	
No	8 / 205 (3.9)	NE [NE, NE]	14 / 197 (7.1)	NE [NE, NE]	0.4776 [0.2001, 1.1397] 0.0959 0.0885	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Presence of liver metastasis at baseline						0.3207
Yes	2 / 145 (1.4)	NE [NE, NE]	9 / 149 (6.0)	NE [NE, NE]	0.2066 [0.0446, 0.9570] 0.0438 0.0257	
No	6 / 99 (6.1)	NE [NE, NE]	9 / 84 (10.7)	NE [NE, NE]	0.4866 [0.1728, 1.3702] 0.1727 0.1636	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Renal function at baseline						0.8231
Normal renal function	4 / 116 (3.4)	NE [NE, NE]	9 / 114 (7.9)	NE [NE, NE]	0.3944 [0.1213, 1.2829] 0.1221 0.1091	
Mild impairment	2 / 87 (2.3)	NE [NE, NE]	6 / 81 (7.4)	NE [NE, NE]	0.2625 [0.0529, 1.3026] 0.1017 0.0783	
Moderate impairment	2 / 41 (4.9)	NE [NE, NE]	3 / 38 (7.9)	NE [NE, NE]	0.5387 [0.0893, 3.2491] 0.4999 0.4933	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: General disorders and administration site conditions; PT: Disease progression						
Hepatic function at baseline						0.8921
Normal hepatic function	5 / 185 (2.7)	NE [NE, NE]	12 / 177 (6.8)	NE [NE, NE]	0.3467 [0.1220, 0.9850] 0.0468 0.0373	
Mild, Moderate or Severe dysfunction	3 / 59 (5.1)	NE [NE, NE]	6 / 55 (10.9)	NE [NE, NE]	0.3951 [0.0985, 1.5844] 0.1900 0.1746	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.0395
IHC 3+	8 / 205 (3.9)	NE [NE, NE]	12 / 196 (6.1)	NE [NE, NE]	0.5681 [0.2320, 1.3911] 0.2159 0.2098	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	4 / 37 (10.8)	NE [7.1, 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Geography stratification factor						0.1121
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	5 / 59 (8.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	7 / 138 (5.1)	NE [NE, NE]	9 / 129 (7.0)	NE [NE, NE]	0.6094 [0.2265, 1.6397] 0.3267 0.3219	
Mainland China/Rest of World (ROW)	1 / 49 (2.0)	NE [NE, NE]	2 / 45 (4.4)	NE [NE, NE]	0.3985 [0.0361, 4.4044] 0.4529 0.4371	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Time to progression on first-line therapy from IRT						0.5969
<6 Months	1 / 61 (1.6)	NE [NE, NE]	3 / 57 (5.3)	NE [NE, NE]	0.2764 [0.0287, 2.6582] 0.2655 0.2334	
≥6 Months	7 / 183 (3.8)	NE [NE, NE]	13 / 176 (7.4)	NE [NE, NE]	0.4586 [0.1828, 1.1507] 0.0968 0.0886	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Age at randomization						0.1213
<65	6 / 139 (4.3)	NE [NE, NE]	6 / 123 (4.9)	NE [NE, NE]	0.7125 [0.2294, 2.2132] 0.5578 0.5559	
≥65	2 / 105 (1.9)	NE [NE, NE]	10 / 110 (9.1)	NE [NE, NE]	0.1972 [0.0432, 0.8999] 0.0361 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Age at randomization						0.8212
<75	7 / 220 (3.2)	NE [NE, NE]	12 / 198 (6.1)	NE [NE, NE]	0.4418 [0.1736, 1.1242] 0.0865 0.0781	
≥75	1 / 24 (4.2)	NE [NE, NE]	4 / 35 (11.4)	NE [NE, NE]	0.3561 [0.0397, 3.1966] 0.3565 0.3355	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Sex						0.2854
Male	6 / 186 (3.2)	NE [NE, NE]	15 / 194 (7.7)	NE [NE, NE]	0.3499 [0.1355, 0.9037] 0.0301 0.0233	
Female	2 / 58 (3.4)	NE [NE, NE]	1 / 39 (2.6)	NE [NE, NE]	1.2326 [0.1114, 13.6406] 0.8646 0.8644	

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

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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Race						0.0506
White	6 / 115 (5.2)	NE [NE, NE]	6 / 120 (5.0)	NE [NE, NE]	0.8751 [0.2818, 2.7180] 0.8176 0.8180	
Asian	2 / 101 (2.0)	NE [NE, NE]	7 / 93 (7.5)	NE [NE, NE]	0.2287 [0.0474, 1.1027] 0.0660 0.0446	
Other	0 / 28	NE [NE, NE]	3 / 20 (15.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
ECOG						0.0208
0	1 / 96 (1.0)	NE [NE, NE]	8 / 81 (9.9)	NE [NE, NE]	0.0827 [0.0103, 0.6642] 0.0190 0.0028	
≥1	7 / 148 (4.7)	NE [NE, NE]	8 / 152 (5.3)	NE [NE, NE]	0.8223 [0.2978, 2.2705] 0.7058 0.7053	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Primary tumor location						0.5637
Gastric	3 / 152 (2.0)	NE [NE, NE]	8 / 139 (5.8)	NE [NE, NE]	0.2965 [0.0785, 1.1206] 0.0731 0.0570	
GEJ	5 / 92 (5.4)	NE [NE, NE]	8 / 94 (8.5)	NE [NE, NE]	0.5398 [0.1763, 1.6527] 0.2802 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Histological subtype						0.9830
Intestinal	2 / 68 (2.9)	NE [NE, NE]	4 / 63 (6.3)	NE [NE, NE]	0.4349 [0.0796, 2.3760] 0.3365 0.3226	
Diffuse	0 / 25	NE [NE, NE]	0 / 18	NE [NE, NE]	NE [NE, NE] NE NE	
Others	6 / 151 (4.0)	NE [NE, NE]	12 / 152 (7.9)	NE [NE, NE]	0.4372 [0.1639, 1.1657] 0.0982 0.0889	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Number of metastatic sites						0.9527
<2	3 / 72 (4.2)	NE [NE, NE]	7 / 72 (9.7)	NE [NE, NE]	0.4304 [0.1113, 1.6651] 0.2220 0.2083	
≥2	5 / 172 (2.9)	NE [NE, NE]	9 / 161 (5.6)	NE [NE, NE]	0.4284 [0.1431, 1.2827] 0.1298 0.1188	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Prior adjuvant/neoadjuvant therapy						0.1631
Yes	0 / 31	NE [NE, NE]	2 / 28 (7.1)	NE [NE, NE]	NE [NE, NE] NE NE	
No	8 / 213 (3.8)	NE [NE, NE]	14 / 205 (6.8)	NE [NE, NE]	0.4774 [0.2000, 1.1395] 0.0958 0.0884	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						0.1589
Prior nivolumab or pembrolizumab treatment						
Yes	1 / 20 (5.0)	NE [6.4, NE]	0 / 16	NE [NE, NE]	NE [NE, NE] NE NE	
No	7 / 224 (3.1)	NE [NE, NE]	16 / 217 (7.4)	NE [NE, NE]	0.3675 [0.1510, 0.8944] 0.0274 0.0215	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						0.9832
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						
Yes	1 / 39 (2.6)	NE [NE, NE]	2 / 36 (5.6)	NE [NE, NE]	0.3759 [0.0341, 4.1490] 0.4245 0.4061	
No	7 / 205 (3.4)	NE [NE, NE]	14 / 197 (7.1)	NE [NE, NE]	0.4112 [0.1657, 1.0205] 0.0553 0.0478	

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

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Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Presence of liver metastasis at baseline						0.8008
Yes	5 / 145 (3.4)	NE [NE, NE]	10 / 149 (6.7)	NE [NE, NE]	0.4587 [0.1567, 1.3427] 0.1549 0.1447	
No	3 / 99 (3.0)	NE [NE, NE]	6 / 84 (7.1)	NE [NE, NE]	0.3438 [0.0855, 1.3822] 0.1326 0.1153	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Renal function at baseline						0.5161
Normal renal function	4 / 116 (3.4)	NE [NE, NE]	5 / 114 (4.4)	NE [NE, NE]	0.7157 [0.1920, 2.6683] 0.6184 0.6167	
Mild impairment	3 / 87 (3.4)	NE [NE, NE]	7 / 81 (8.6)	NE [NE, NE]	0.3224 [0.0830, 1.2521] 0.1020 0.0850	
Moderate impairment	1 / 41 (2.4)	NE [NE, NE]	4 / 38 (10.5)	NE [NE, NE]	0.1833 [0.0201, 1.6694] 0.1323 0.0927	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Nervous system disorders; PT: Any						
Hepatic function at baseline						0.4547
Normal hepatic function	6 / 185 (3.2)	NE [NE, NE]	14 / 177 (7.9)	NE [NE, NE]	0.3479 [0.1334, 0.9072] 0.0308 0.0238	
Mild, Moderate or Severe dysfunction	2 / 59 (3.4)	NE [NE, NE]	2 / 55 (3.6)	NE [NE, NE]	0.8256 [0.1161, 5.8727] 0.8482 0.8480	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.4574
IHC 3+	2 / 205 (1.0)	NE [NE, NE]	23 / 196 (11.7)	NE [NE, NE]	0.0721 [0.0170, 0.3062] 0.0004 <.0001	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	3 / 37 (8.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Geography stratification factor						0.2288
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	11 / 59 (18.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	2 / 138 (1.4)	NE [NE, NE]	11 / 129 (8.5)	NE [13.3, NE]	0.1262 [0.0274, 0.5803] 0.0078 0.0018	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	4 / 45 (8.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Time to progression on first-line therapy from IRT						0.4964
<6 Months	0 / 61	NE [NE, NE]	3 / 57 (5.3)	13.3 [NE, NE]	NE [NE, NE] NE NE	
≥6 Months	2 / 183 (1.1)	NE [NE, NE]	23 / 176 (13.1)	NE [NE, NE]	0.0727 [0.0171, 0.3083] 0.0004 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Age at randomization						0.1252
<65	0 / 139	NE [NE, NE]	11 / 123 (8.9)	NE [NE, NE]	NE [NE, NE] NE NE	
≥65	2 / 105 (1.9)	NE [NE, NE]	15 / 110 (13.6)	NE [13.3, NE]	0.1092 [0.0244, 0.4883] 0.0038 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] Median time to first event is from Kaplan-Meier estimate. Confidence interval for median was computed using the Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Age at randomization						0.1372
<75	1 / 220 (0.5)	NE [NE, NE]	22 / 198 (11.1)	NE [NE, NE]	0.0353 [0.0048, 0.2623] 0.0011 <.0001	
≥75	1 / 24 (4.2)	NE [NE, NE]	4 / 35 (11.4)	NE [13.3, NE]	0.3743 [0.0418, 3.3491] 0.3794 0.3603	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Sex						0.2579
Male	2 / 186 (1.1)	NE [NE, NE]	20 / 194 (10.3)	NE [13.3, NE]	0.0831 [0.0192, 0.3586] 0.0009 <.0001	
Female	0 / 58	NE [NE, NE]	6 / 39 (15.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Race						0.1453
White	2 / 115 (1.7)	NE [NE, NE]	10 / 120 (8.3)	NE [13.3, NE]	0.1615 [0.0349, 0.7470] 0.0196 0.0080	
Asian	0 / 101	NE [NE, NE]	15 / 93 (16.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	1 / 20 (5.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						0.0491
ECOG						
0	2 / 96 (2.1)	NE [NE, NE]	8 / 81 (9.9)	NE [13.3, NE]	0.1707 [0.0359, 0.8113] 0.0262 0.0120	
≥1	0 / 148	NE [NE, NE]	18 / 152 (11.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						0.0180
Primary tumor location						
Gastric	0 / 152	NE [NE, NE]	20 / 139 (14.4)	NE [13.3, NE]	NE [NE, NE] NE NE	
GEJ	2 / 92 (2.2)	NE [NE, NE]	6 / 94 (6.4)	NE [NE, NE]	0.2866 [0.0578, 1.4208] 0.1260 0.1028	

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

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Histological subtype						0.3928
Intestinal	0 / 68	NE [NE, NE]	6 / 63 (9.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	3 / 18 (16.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Others	2 / 151 (1.3)	NE [NE, NE]	17 / 152 (11.2)	NE [13.3, NE]	0.0983 [0.0226, 0.4269] 0.0020 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Number of metastatic sites						0.7376
<2	1 / 72 (1.4)	NE [NE, NE]	11 / 72 (15.3)	NE [NE, NE]	0.0870 [0.0112, 0.6737] 0.0194 0.0030	
≥2	1 / 172 (0.6)	NE [NE, NE]	15 / 161 (9.3)	NE [13.3, NE]	0.0503 [0.0066, 0.3826] 0.0039 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						0.9993
Prior adjuvant/neoadjuvant therapy						
Yes	0 / 31	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	2 / 213 (0.9)	NE [NE, NE]	26 / 205 (12.7)	NE [NE, NE]	0.0625 [0.0148, 0.2640] 0.0002 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						0.0797
Prior nivolumab or pembrolizumab treatment						
Yes	1 / 20 (5.0)	NE [NE, NE]	1 / 16 (6.3)	NE [NE, NE]	0.8009 [0.0501, 12.8054] 0.8753 0.8750	
No	1 / 224 (0.4)	NE [NE, NE]	25 / 217 (11.5)	NE [NE, NE]	0.0326 [0.0044, 0.2413] 0.0008 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						0.1869
Yes	1 / 39 (2.6)	NE [NE, NE]	3 / 36 (8.3)	NE [NE, NE]	0.2965 [0.0308, 2.8512] 0.2925 0.2633	
No	1 / 205 (0.5)	NE [NE, NE]	23 / 197 (11.7)	NE [NE, NE]	0.0345 [0.0046, 0.2563] 0.0010 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Presence of liver metastasis at baseline						0.8966
Yes	1 / 145 (0.7)	NE [NE, NE]	13 / 149 (8.7)	NE [13.3, NE]	0.0639 [0.0083, 0.4923] 0.0083 0.0004	
No	1 / 99 (1.0)	NE [NE, NE]	13 / 84 (15.5)	NE [NE, NE]	0.0570 [0.0075, 0.4361] 0.0058 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Renal function at baseline						0.0930
Normal renal function	0 / 116	NE [NE, NE]	11 / 114 (9.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	2 / 87 (2.3)	NE [NE, NE]	7 / 81 (8.6)	NE [13.3, NE]	0.2035 [0.0419, 0.9879] 0.0483 0.0291	
Moderate impairment	0 / 41	NE [NE, NE]	8 / 38 (21.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Any						
Hepatic function at baseline						0.2113
Normal hepatic function	2 / 185 (1.1)	NE [NE, NE]	18 / 177 (10.2)	NE [NE, NE]	0.0908 [0.0210, 0.3928] 0.0013 <.0001	
Mild, Moderate or Severe dysfunction	0 / 59	NE [NE, NE]	8 / 55 (14.5)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
HER2 Status (IHC 3+ vs. IHC 2+/ISH+) from IRT						0.5856
IHC 3+	1 / 205 (0.5)	NE [NE, NE]	22 / 196 (11.2)	NE [NE, NE]	0.0377 [0.0051, 0.2803] 0.0014 <.0001	
IHC 2+/ISH+	0 / 39	NE [NE, NE]	3 / 37 (8.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Geography stratification factor						0.4887
Asia [excluding mainland China]	0 / 57	NE [NE, NE]	10 / 59 (16.9)	NE [NE, NE]	NE [NE, NE] NE NE	
Western Europe	1 / 138 (0.7)	NE [NE, NE]	11 / 129 (8.5)	NE [13.3, NE]	0.0621 [0.0079, 0.4907] 0.0084 0.0005	
Mainland China/Rest of World (ROW)	0 / 49	NE [NE, NE]	4 / 45 (8.9)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Time to progression on first-line therapy from IRT						0.6189
<6 Months	0 / 61	NE [NE, NE]	3 / 57 (5.3)	13.3 [NE, NE]	NE [NE, NE] NE NE	
≥6 Months	1 / 183 (0.5)	NE [NE, NE]	22 / 176 (12.5)	NE [NE, NE]	0.0382 [0.0052, 0.2837] 0.0014 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Age at randomization						0.2602
<65	0 / 139	NE [NE, NE]	11 / 123 (8.9)	NE [NE, NE]	NE [NE, NE] NE NE	
≥65	1 / 105 (1.0)	NE [NE, NE]	14 / 110 (12.7)	NE [13.3, NE]	0.0569 [0.0073, 0.4436] 0.0062 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Age at randomization						0.6725
<75	1 / 220 (0.5)	NE [NE, NE]	21 / 198 (10.6)	NE [NE, NE]	0.0371 [0.0050, 0.2759] 0.0013 <.0001	
≥75	0 / 24	NE [NE, NE]	4 / 35 (11.4)	NE [13.3, 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Sex						0.4099
Male	1 / 186 (0.5)	NE [NE, NE]	19 / 194 (9.8)	NE [13.3, NE]	0.0432 [0.0057, 0.3258] 0.0023 <.0001	
Female	0 / 58	NE [NE, NE]	6 / 39 (15.4)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Race						0.3868
White	1 / 115 (0.9)	NE [NE, NE]	10 / 120 (8.3)	NE [13.3, NE]	0.0799 [0.0101, 0.6329] 0.0167 0.0024	
Asian	0 / 101	NE [NE, NE]	14 / 93 (15.1)	NE [NE, NE]	NE [NE, NE] NE NE	
Other	0 / 28	NE [NE, NE]	1 / 20 (5.0)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
ECOG						0.1410
0	1 / 96 (1.0)	NE [NE, NE]	7 / 81 (8.6)	NE [13.3, NE]	0.0956 [0.0116, 0.7861] 0.0290 0.0070	
≥1	0 / 148	NE [NE, NE]	18 / 152 (11.8)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Primary tumor location						0.0935
Gastric	0 / 152	NE [NE, NE]	19 / 139 (13.7)	NE [13.3, NE]	NE [NE, NE] NE NE	
GEJ	1 / 92 (1.1)	NE [NE, NE]	6 / 94 (6.4)	NE [NE, NE]	0.1444 [0.0174, 1.1996] 0.0732 0.0371	

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

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Histological subtype						0.6040
Intestinal	0 / 68	NE [NE, NE]	6 / 63 (9.5)	NE [NE, NE]	NE [NE, NE] NE NE	
Diffuse	0 / 25	NE [NE, NE]	3 / 18 (16.7)	NE [NE, NE]	NE [NE, NE] NE NE	
Others	1 / 151 (0.7)	NE [NE, NE]	16 / 152 (10.5)	NE [13.3, NE]	0.0521 [0.0069, 0.3940] 0.0042 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Number of metastatic sites						0.1806
<2	1 / 72 (1.4)	NE [NE, NE]	11 / 72 (15.3)	NE [NE, NE]	0.0870 [0.0112, 0.6737] 0.0194 0.0030	
≥2	0 / 172	NE [NE, NE]	14 / 161 (8.7)	NE [13.3, 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Prior adjuvant/neoadjuvant therapy						0.9993
Yes	0 / 31	NE [NE, NE]	0 / 28	NE [NE, NE]	NE [NE, NE] NE NE	
No	1 / 213 (0.5)	NE [NE, NE]	25 / 205 (12.2)	NE [NE, NE]	0.0325 [0.0044, 0.2406] 0.0008 <.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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Prior nivolumab or pembrolizumab treatment						0.0181
Yes	1 / 20 (5.0)	NE [NE, NE]	1 / 16 (6.3)	NE [NE, NE]	0.8009 [0.0501, 12.8054] 0.8753	
No	0 / 224	NE [NE, NE]	24 / 217 (11.1)	NE [NE, NE]	0.8750 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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						0.0419
Prior treatment with immune-checkpoint inhibitor or other immuno-oncology therapy						
Yes	1 / 39 (2.6)	NE [NE, NE]	3 / 36 (8.3)	NE [NE, NE]	0.2965 [0.0308, 2.8512] 0.2925 0.2633	
No	0 / 205	NE [NE, NE]	22 / 197 (11.2)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Presence of liver metastasis at baseline						0.2012
Yes	1 / 145	NE	12 / 149	NE	0.0689 [0.0089, 0.5344]	
	(0.7)	[NE, NE]	(8.1)	[13.3, NE]	0.0105	
					0.0008	
No	0 / 99	NE	13 / 84	NE	NE [NE, NE]	
		[NE, NE]	(15.5)	[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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Renal function at baseline						0.2611
Normal renal function	0 / 116	NE [NE, NE]	11 / 114 (9.6)	NE [NE, NE]	NE [NE, NE] NE NE	
Mild impairment	1 / 87 (1.1)	NE [NE, NE]	6 / 81 (7.4)	NE [13.3, NE]	0.1169 [0.0139, 0.9808] 0.0479 0.0181	
Moderate impairment	0 / 41	NE [NE, NE]	8 / 38 (21.1)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
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Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Table 9.20.2 Severe (CTCAE grade ≥3) Treatment-Emergent Adverse Events by SOC and PT observed for ≥ 10 patients (in total) and ≥ 1% of the patients in at least one arm - Subgroup Analysis - Safety Analysis Set

DESTINY Gastric-04	T-DXd N = 244		Ram + PTX N = 233		T-DXd vs. Ram + PTX	Interaction
	n / Nsub (%)	Median [95% CI] in months [a]	n / Nsub (%)	Median [95% CI] in months [a]	HR [95% CI] p-value [b] p-value [c]	p-value [d]
SOC: Vascular disorders; PT: Hypertension						
Hepatic function at baseline						0.4020
Normal hepatic function	1 / 185 (0.5)	NE [NE, NE]	18 / 177 (10.2)	NE [NE, NE]	0.0453 [0.0060, 0.3402] 0.0026 <.0001	
Mild, Moderate or Severe dysfunction	0 / 59	NE [NE, NE]	7 / 55 (12.7)	NE [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 Brookmeyer-Crowley method.
[b] Hazard ratio is from unstratified Cox proportional hazards model with treatment as the only categorical variable in the model. CI and p-value are based on the Wald test.
[c] Two-sided p-value from unstratified log-rank test.
[d] Two-sided interaction p-value is for the interaction term from unstratified Cox proportional hazards model with treatment, subgroup, and treatment -by-subgroup interaction as categorical variables in the model.
CI: confidence interval; HR: hazard ratio; NE: not estimable; PT: preferred term; SOC: system organ class

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:18 (CET); Program name: t_tte_socpt_subgrp.sas; Output name: T.9.20.2_10SEVAE_SAF_SUB.rtf

Anhang 4-G 4.3.7 Unerwünschte Ereignisse, die zum Therapieabbruch führten, nach SOC und PT – SAF

Table 9.22.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT associated with study drug discontinuation by SOC and PT - Descriptive Summary - Safety Analysis Set

DESTINY Gastric-04 System Organ Class (SOC) Preferred Term (PT)	T-DXd N = 244 n (%)	Ram + PTX N = 233 n (%)
Subjects with any treatment-emergent adverse events associated with study drug discontinuation	35 (14.3)	40 (17.2)
Respiratory, thoracic and mediastinal disorders	20 (8.2)	5 (2.1)
Interstitial lung disease	10 (4.1)	2 (0.9)
Pneumonitis	9 (3.7)	1 (0.4)
Respiratory failure	1 (0.4)	0
Epistaxis	0	1 (0.4)
Pulmonary embolism	0	1 (0.4)
Gastrointestinal disorders	4 (1.6)	11 (4.7)
Abdominal pain	1 (0.4)	1 (0.4)
Ascites	1 (0.4)	1 (0.4)
Intestinal obstruction	1 (0.4)	0
Upper gastrointestinal haemorrhage	1 (0.4)	3 (1.3)
Dysphagia	0	1 (0.4)
Gastric haemorrhage	0	2 (0.9)
Gastric perforation	0	2 (0.9)
Gastrointestinal haemorrhage	0	1 (0.4)
General disorders and administration site conditions	3 (1.2)	3 (1.3)
Asthenia	1 (0.4)	1 (0.4)

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:28 (CET); Program name: t_socptdesc.sas; Output name: T.9.22.1_TEAEDISC_SAF.rtf

Table 9.22.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT associated with study drug discontinuation by SOC and PT - Descriptive Summary - Safety Analysis Set

DESTINY Gastric-04 System Organ Class (SOC) Preferred Term (PT)	T-DXd N = 244 n (%)	Ram + PTX N = 233 n (%)
Death	1 (0.4)	0
Sudden death	1 (0.4)	0
Disease progression	0	2 (0.9)
Infections and infestations	2 (0.8)	2 (0.9)
Pneumonia	2 (0.8)	1 (0.4)
Infection	0	1 (0.4)
Blood and lymphatic system disorders	1 (0.4)	2 (0.9)
Thrombocytopenia	1 (0.4)	0
Febrile neutropenia	0	2 (0.9)
Hepatobiliary disorders	1 (0.4)	0
Drug-induced liver injury	1 (0.4)	0
Investigations	1 (0.4)	4 (1.7)
Ejection fraction decreased	1 (0.4)	0
Neutrophil count decreased	0	3 (1.3)
Platelet count decreased	0	1 (0.4)
Metabolism and nutrition disorders	1 (0.4)	1 (0.4)

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:28 (CET); Program name: t_socptdesc.sas; Output name: T.9.22.1_TEAEDISC_SAF.rtf

Table 9.22.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT associated with study drug discontinuation by SOC and PT - Descriptive Summary - Safety Analysis Set

DESTINY Gastric-04 System Organ Class (SOC) Preferred Term (PT)	T-DXd N = 244 n (%)	Ram + PTX N = 233 n (%)
Decreased appetite	1 (0.4)	1 (0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (0.4)	3 (1.3)
Lymphangiosis carcinomatosa	1 (0.4)	0
Gastric neoplasm	0	1 (0.4)
Tumour haemorrhage	0	2 (0.9)
Renal and urinary disorders	1 (0.4)	0
Pyelocaliectasis	1 (0.4)	0
Immune system disorders	0	1 (0.4)
Drug hypersensitivity	0	1 (0.4)
Injury, poisoning and procedural complications	0	2 (0.9)
Infusion related reaction	0	1 (0.4)
Limb injury	0	1 (0.4)
Nervous system disorders	0	7 (3.0)
Neuropathy peripheral	0	5 (2.1)
Neurotoxicity	0	1 (0.4)
Peripheral sensory neuropathy	0	1 (0.4)

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:28 (CET); Program name: t_socptdesc.sas; Output name: T.9.22.1_TEAEDISC_SAF.rtf

Table 9.22.1 Treatment-Emergent Adverse Events (TEAEs) by SOC and PT associated with study drug discontinuation by SOC and PT - Descriptive Summary - Safety Analysis Set

DESTINY Gastric-04 System Organ Class (SOC) Preferred Term (PT)	T-DXd N = 244 n (%)	Ram + PTX N = 233 n (%)
Skin and subcutaneous tissue disorders	0	1 (0.4)
Nail toxicity	0	1 (0.4)

N: number of subjects in analysis set; n: number of subjects with event; %: proportion of number of subjects in analysis set

Data source: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_adam/ADAE
Program Location: DS8201-A-U306/prod/restricted/rstrct_eg/rstrct_DCO20241024_eg/rstrct_eg_valos/20250414_AMNOG_ID009/rstrct_programs/tlfs
Run date: 23JUN2025 11:28 (CET); Program name: t_socptdesc.sas; Output name: T.9.22.1_TEAEDISC_SAF.rtf