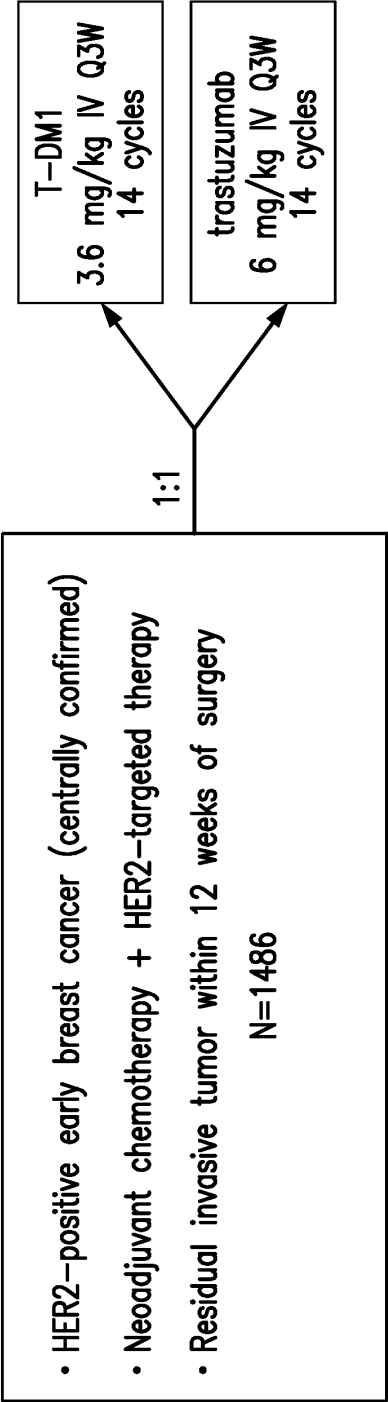




Radiation and endocrine therapy
in accordance with protocol and
local recommendations

FIG. 1

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Characteristic	Trastuzumab (n=743)	T-DM1 (n=743)
Age – yr		
Median	49	49
Age groups – no. of patients (%)		
<40 years	153 (20.6)	143 (19.2)
40–64 years	522 (70.3)	542 (72.9)
≥65 years	68 (9.2)	58 (7.8)
Race – no. of patients (%)		
White	531 (71.5)	551 (74.2)
Asian	64 (8.6)	65 (8.7)
Black or African American	19 (2.6)	21 (2.8)
American Indian* or Alaska Native	50 (6.7)	36 (4.8)
Multiple/unknown	76 (10.6)	70 (9.4)
Region – no. of patients (%)		
North America	164 (22.1)	170 (22.9)
Western Europe	403 (54.2)	403 (54.2)
Rest of world	176 (23.7)	170 (22.9)

FIG. 2A

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Characteristic	Trastuzumab (n=743)	T-DM1 (n=743)
Primary tumor stage (at definitive surgery) – no. of patients (%)		
ypT0, ypT1a, ypT1b, ypT1mic, ypTis	306 (41.2)	331 (44.5)
ypT1/ypT1c	184 (24.8)	175 (23.6)
ypT2	185 (24.9)	174 (23.4)
ypT3	57 (7.7)	51 (6.9)
ypT4, ypT4a, ypT4b, ypT4c	9 (1.2)	7 (0.9)
ypT4d	1 (0.1)	5 (0.7)
ypTX	1 (0.1)	0
Regional lymph node stage (at definitive surgery) – no. of patients (%)		
ypN0	335 (45.1)	344 (46.3)
ypN1	213 (28.7)	220 (29.6)
ypN2	103 (13.9)	86 (11.6)
ypN3	30 (4.0)	37 (5.0)
ypNX	62 (8.3)	56 (7.5)

FIG. 2B

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Characteristic	Trastuzumab (n=743)	T-DM1 (n=743)
Clinical stage at presentation – no. of patients (%)		
Inoperable (stage T4NxM0 or TxN2–3M0)	190 (25.6)	185 (24.9)
Operable (stages T1–3N0–1M0)	553 (74.4)	558 (75.1)
Hormone–receptor status – no. of patients (%)		
Positive (estrogen receptor and/or progesterone receptor)	540 (72.7)	534 (71.9)
Negative/unknown	203 (27.3)	209 (28.1)
Prior anthracycline – no. of patients (%)	564 (75.9)	579 (77.9)
Neoadjuvant HER2–targeted therapy – no. of patients (%)		
Trastuzumab alone	596 (80.2)	600 (80.8)
Trastuzumab plus pertuzumab	139 (18.7)	133 (17.9)
Trastuzumab plus other HER2–targeted therapy†	8 (1.1)	10 (1.3)
Pathologic nodal status evaluated after neoadjuvant therapy – no. of patients (%)		
Node positive	346 (46.6)	343 (46.2)
Node negative/not done	397 (53.4)	400 (53.8)

FIG. 2C

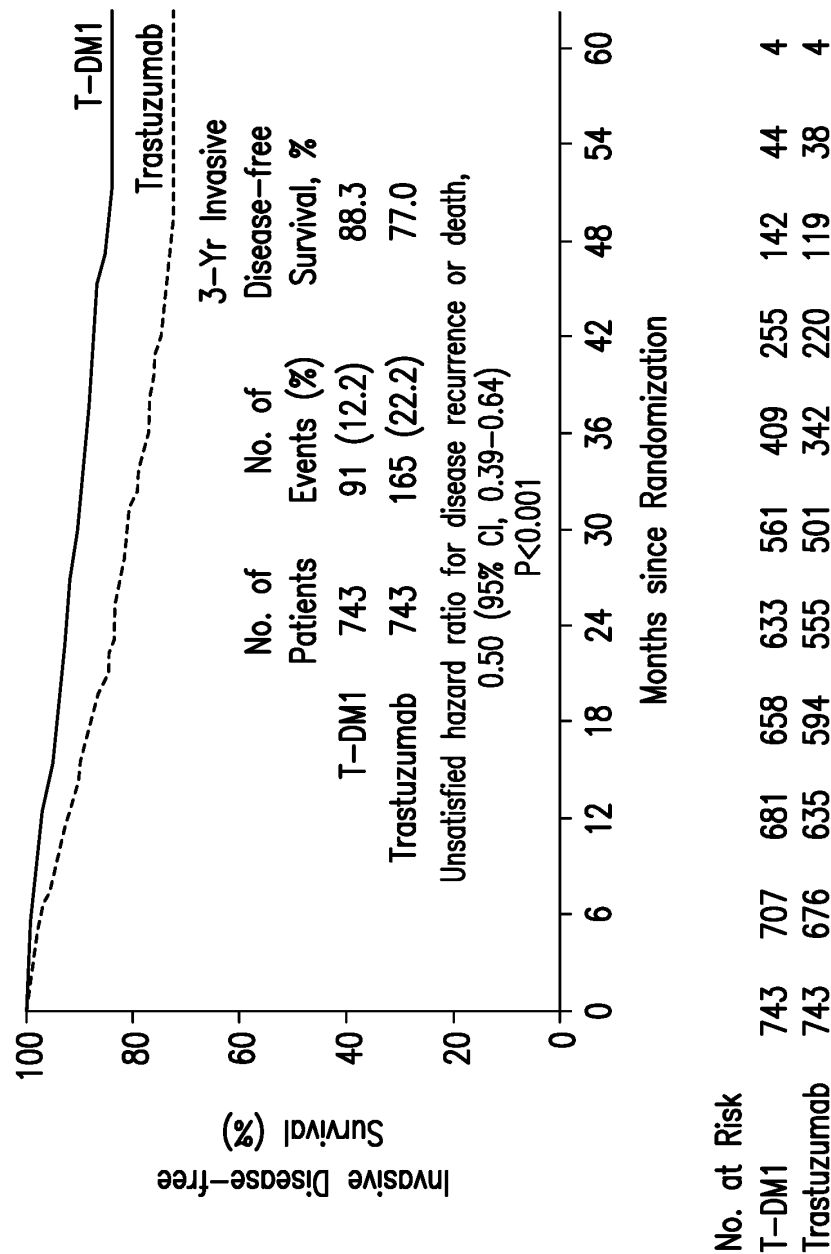


FIG. 3

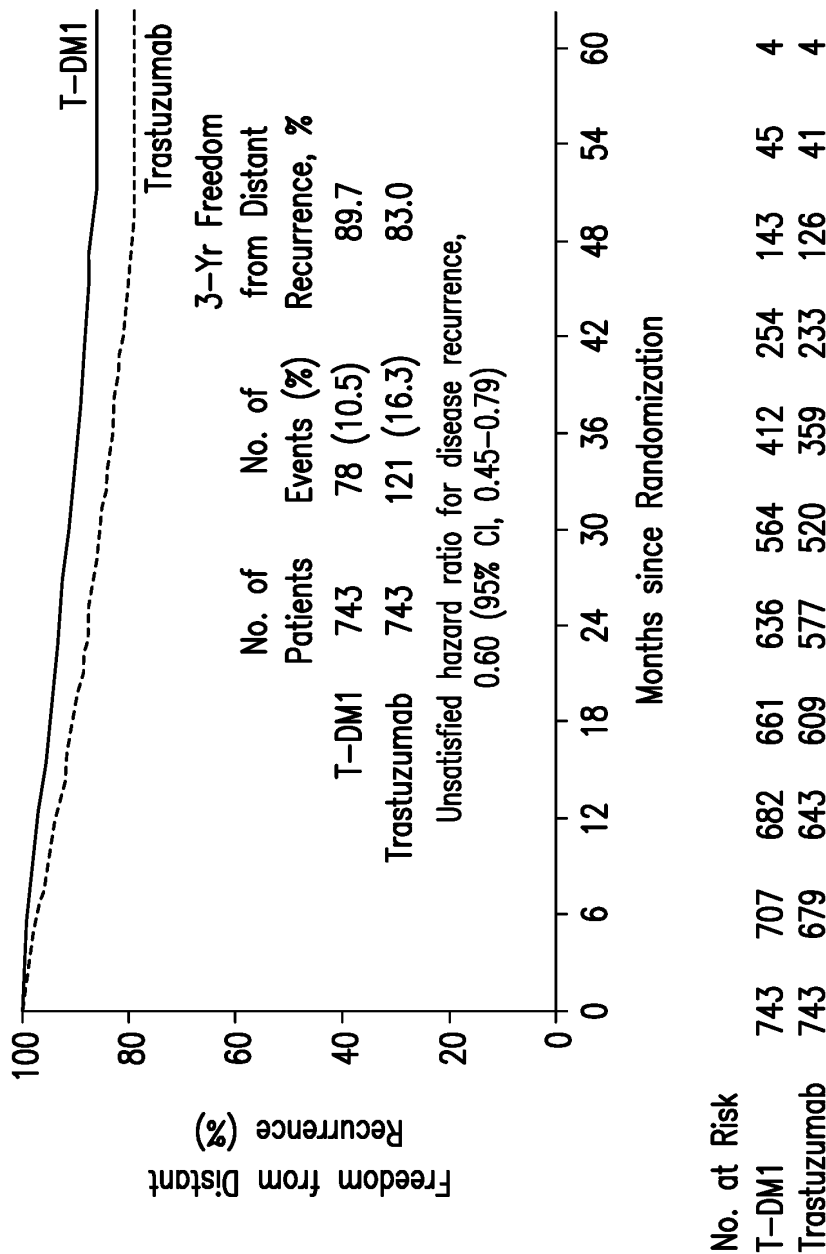


FIG. 4A

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Event	Trastuzumab (n=743)	T-DM1 (n=743)
	<i>no. of patients (%)</i>	
Any invasive–disease event†	165 (22.2)	91 (12.2)
Category of first invasive–disease event		
Distant recurrence	118 (15.9)	78 (10.5)
Central nervous system recurrence	32 (4.3)	44 (5.9)
Locoregional recurrence	34 (4.6)	8 (1.1)
Contralateral breast cancer	10 (1.3)	3 (0.4)
Death without previous event	3 (0.4)	2 (0.3)

FIG. 4B

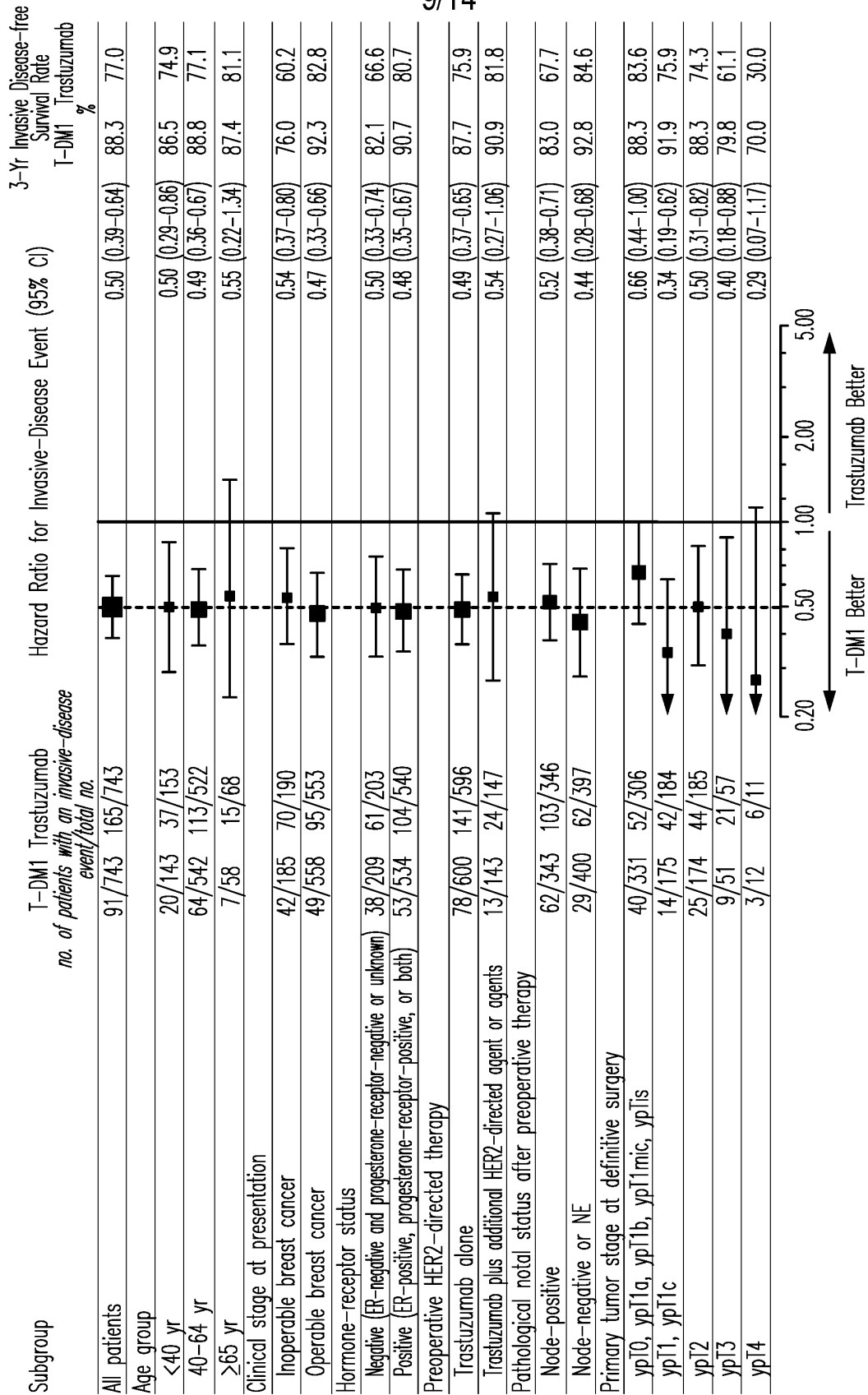
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End Point	Trastuzumab (n=743)	T-DM1 (n=743)
Invasive-disease-free-survival (STEEP definition)		
Patients with an event- no. of patients (%)	167 (22.5)	95 (12.8)
3-year event-free rate-% (95% CI)	76.9 (73.7-80.1)	87.7 (85.2-90.2)
Hazard ratio (95% CI)	0.51 (0.40-0.66)	
Disease-free survival		
Patients with an event- no. of patients (%)	167 (22.5)	98 (13.2)
3-year event-free rate-% (95% CI)	76.9 (73.6-80.1)	87.4 (84.9-89.9)
Hazard ratio (95% CI)	0.53 (0.41-0.68)	
Distant recurrence-free interval		
Patients with an event- no. of patients (%)	121 (16.3)	78 (10.5)
3-year event-free rate-% (95% CI)	83.0 (80.1-85.9)	89.7 (87.4-92.0)
Hazard ratio (95% CI)	0.60 (0.45-0.79)	
Overall survival		
Patients with an event- no. of patients (%)	56 (7.5)	42 (5.7)
Hazard ratio (95% CI)	0.70 (0.47-1.05)	
P-value (log-rank) ‡	0.0848	

CI denotes confidence interval, STEEP denotes standardized efficacy end points, T-DM1 denotes trastuzumab emtansine.

FIG. 5

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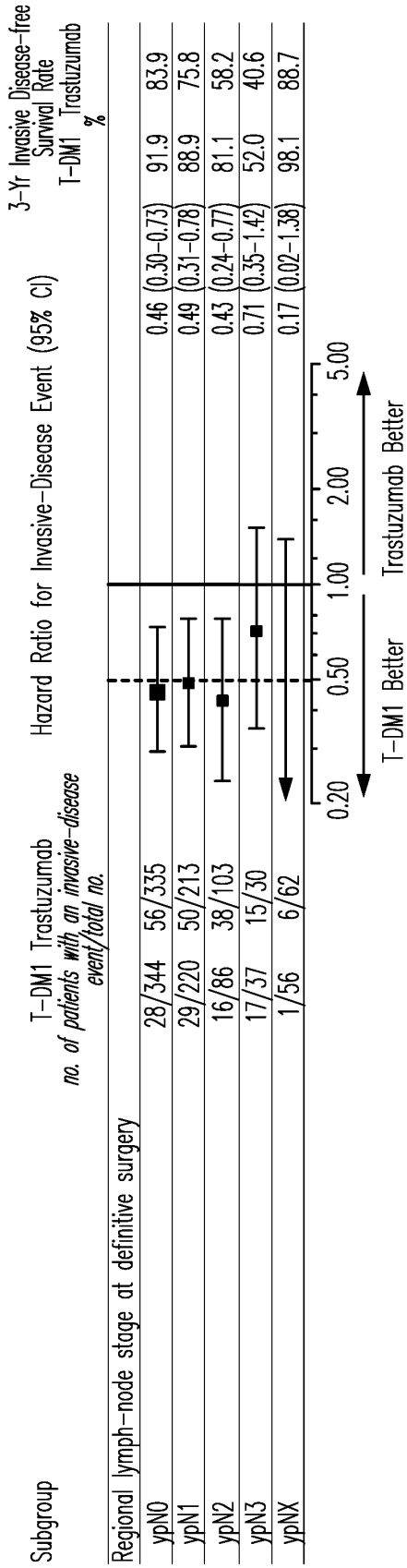


FIG. 6A continued

No. of Patients with an
Invasive-Disease Event/Total No.

3-Yr Invasive Disease-free
Survival Rate

Group	Trastuzumab (n=743)	T-DM1 (n=743)	Hazard Ratio (95% CI)	Trastuzumab (n=743)	T-DM1 (n=743)
Race					
White	107/531	62/551	0.51 (0.37-0.69)	79.1	88.8
Black or African American	6/19	1/21	0.13 (0.02-1.10)	66.0	94.7
Asian	18/64	13/65	0.65 (0.32-1.32)	71.9	82.5
American Indian or Alaska Native	20/50	7/36	0.44 (0.18-1.03)	60.3	81.8
Native Hawaiian or Other Pacific Islander	0/1		NE (NE-NE)	100.0	
Multiple	0/1	0/1	NE (NE-NE)	100.0	100.0
Unknown	14/77	8/69	0.58 (0.24-1.38)	80.3	90.7
Region					
North America	29/164	14/170	0.40 (0.21-0.76)	79.7	93.4
Western Europe	74/403	48/403	0.61 (0.43-0.88)	64.6	83.8
Rest of the World	62/176	29/170	0.41 (0.27-0.64)	81.5	88.1
Primary tumor stage (at initial diagnosis)					
cT1	13/81	6/99	0.33 (0.13-0.88)	83.4	94.8
cT2	70/389	36/365	0.52 (0.35-0.78)	82.0	90.4
cT3	49/185	21/177	0.38 (0.23-0.63)	71.0	89.8
cT4, cT4a, cT4b, cT4c	20/54	19/59	0.74 (0.39-1.38)	57.2	65.8
cT4d	13/34	9/43	0.50 (0.21-1.17)	65.3	78.6

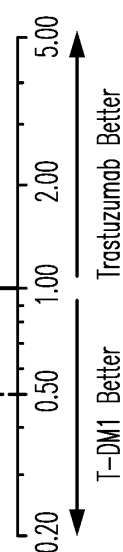


FIG. 6B

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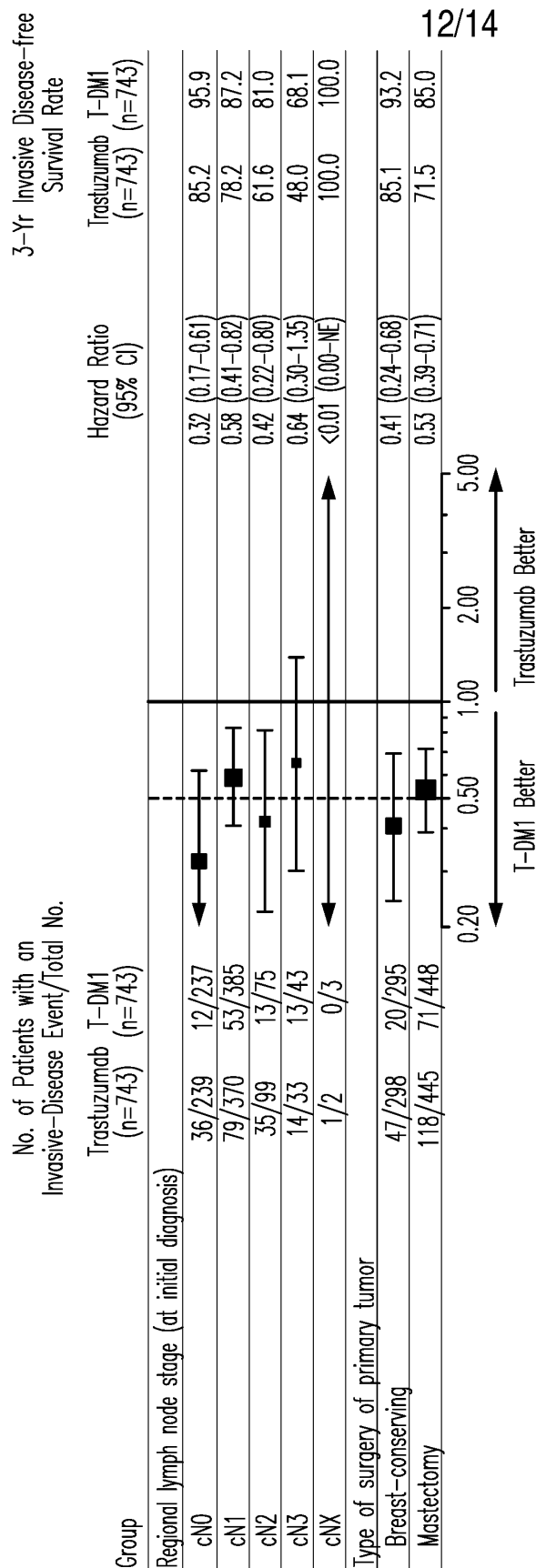


FIG. 6B continued

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Neoadjuvant therapy	Trastuzumab arm	T-DM1 arm
	IDFS events (events/no. patients)	
No prior P	23.7% (141/596)	13.0% (78/600)
	Unstratified HR=0.489 (95% CI, 0.371–0.645)	
	3-year IDFS	
	75.9%	87.7%
Prior P	IDFS events (events/no. patients)	
	17.3% (24/139)	9.0% (12/133)
	Unstratified HR=0.498 (95% CI, 0.249–0.995)	
	3-years IDFS	
	80.9%	91.4%

*CI denotes confidence interval, HER2 human epidermal growth factor receptor 2, HR hazard ratio, IDFS invasive disease-free survival, P pertuzumab, and T-DM1 trastuzumab emtansine.

FIG. 7

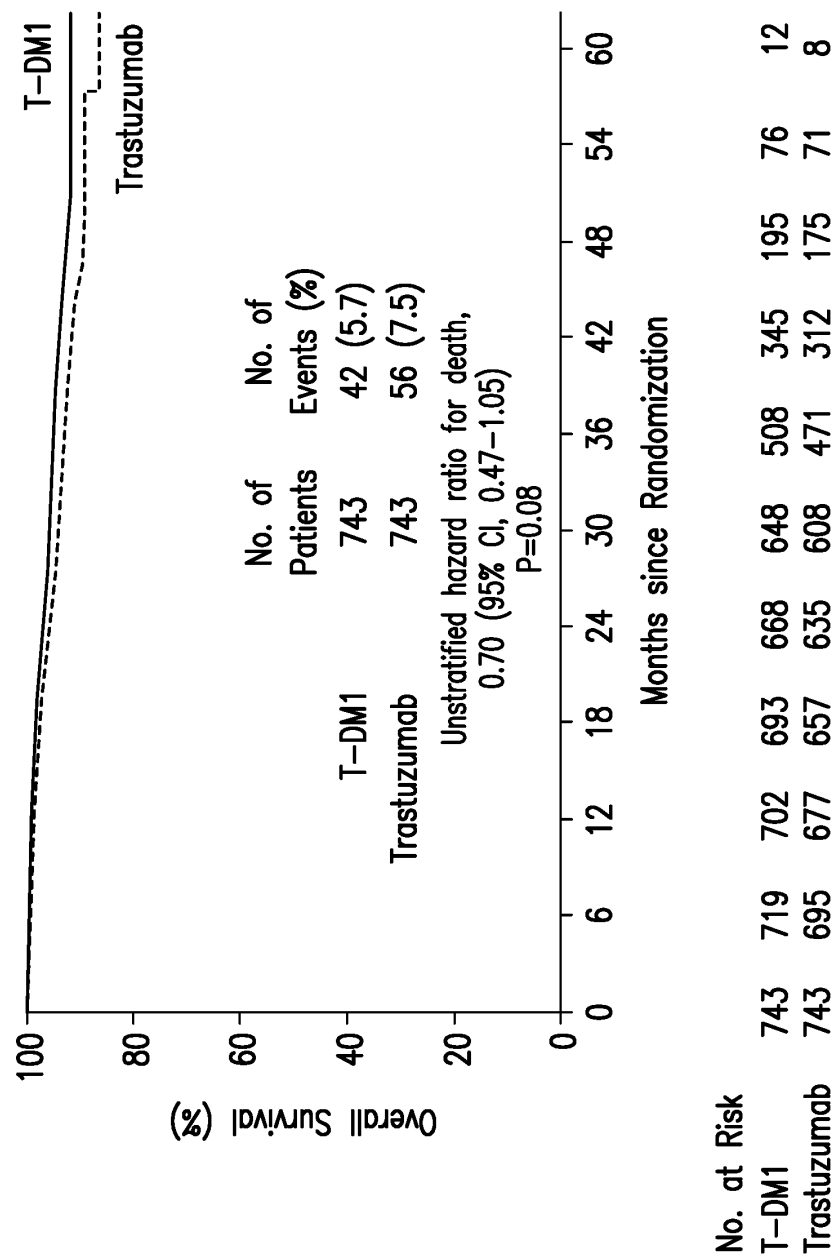


FIG. 8