

**Supplementary Table S1.** Comparison of baseline patient and disease characteristics assessed at eligibility in the ITT population versus in those with mRNA data derived from pre-NAT or post-NAT surgical samples (RNA-evaluable population). Note: the pre-NAT and post-NAT samples are not paired.

Characteristic	ITT Population			Patients with Pre-NAT RNA Data			Patients with Surgical Post-NAT RNA Data		
	Pooled ( <i>N</i> = 1486)	Trastuzumab ( <i>n</i> = 743)	T-DM1 ( <i>n</i> = 743)	Pooled ( <i>n</i> = 244)	Trastuzumab ( <i>n</i> = 122)	T-DM1 ( <i>n</i> = 122)	Pooled ( <i>n</i> = 815)	Trastuzumab ( <i>n</i> = 398)	T-DM1 ( <i>n</i> = 417)
Age, years									
Median (range)	49 (23–80)	49 (23–80)	49 (24–79)	47 (23–77)	47 (23–77)	48 (25–72)	49 (23–80)	49 (23–80)	50 (24–77)
Race, <i>n</i> (%)									
White	1082 (72.8)	531 (71.5)	551 (74.2)	174 (71.3)	92 (75.4)	82 (67.2)	587 (72.0)	275 (69.1)	312 (74.8)
Asian	129 (8.7)	64 (8.6)	65 (8.7)	11 (4.5)	4 (3.3)	7 (5.7)	74 (9.1)	38 (9.6)	36 (8.6)
Black or African American	40 (2.7)	19 (2.6)	21 (2.8)	8 (3.3)	2 (1.6)	6 (4.9)	23 (2.8)	11 (2.8)	12 (2.9)
American Indian <sup>a</sup> , Alaska Native, or Pacific Islander	87 (5.9)	51 (6.9)	36 (4.8)	24 (9.8)	13 (10.7)	11 (9.0)	43 (5.3)	29 (7.3)	14 (3.4)
Multiple/unknown	148 (10.0)	78 (10.5)	70 (9.4)	27 (11.1)	11 (9.0)	16 (13.1)	88 (10.8)	45 (11.3)	43 (10.3)
Clinical stage at presentation, <i>n</i> (%)									
Inoperable	375 (25.2)	190 (25.6)	185 (24.9)	63 (25.8)	30 (24.6)	33 (27.1)	185 (22.7)	94 (23.6)	91 (21.8)
Operable	1111 (74.8)	553 (74.4)	558 (75.1)	181 (74.2)	92 (75.4)	89 (73.0)	630 (77.3)	304 (76.4)	326 (78.2)
Hormone receptor status, <i>n</i> (%)									
ER negative and PgR negative/unknown	412 (27.7)	203 (27.3)	209 (28.1)	79 (32.4)	37 (30.3)	42 (34.4)	219 (26.9)	110 (27.6)	109 (26.1)

ER and/or PgR positive	1074 (72.3)	540 (72.7)	534 (71.9)	165 (67.6)	85 (69.7)	80 (65.6)	596 (73.1)	288 (72.4)	308 (73.9)
Neoadjuvant HER2-targeted therapy, <i>n</i> (%)									
Trastuzumab alone	1196 (80.5)	596 (80.2)	600 (80.8)	190 (77.9)	97 (79.5)	93 (76.2)	659 (80.9)	319 (80.2)	340 (81.5)
Trastuzumab plus pertuzumab	272 (18.3)	139 (18.7)	133 (17.9)	51 (20.9)	25 (20.5)	26 (21.3)	149 (18.3)	75 (18.8)	74 (17.8)
Trastuzumab plus other HER2-targeted therapy	18 (1.2)	8 (1.1)	10 (1.3)	3 (1.2)	0	3 (0.2)	7 (0.9)	4 (1.0)	3 (0.7)
Nodal status, <i>n</i> (%)									
Positive	689 (46.4)	346 (46.6)	343 (46.2)	111 (45.5)	52 (42.6)	59 (48.4)	385 (47.2)	194 (48.7)	191 (45.8)
Negative/not done	797 (53.6)	397 (53.4)	400 (53.8)	133 (54.5)	70 (57.4)	63 (51.6)	430 (52.8)	204 (51.3)	226 (54.2)
HER2 IHC status, <i>n</i> (%)									
IHC2+	326 (22.0)	168 (22.6)	158 (21.3)	44 (18.0)	18 (14.8)	26 (21.3)	198 (24.3)	97 (24.4)	101 (24.2)
IHC3+	1132 (76.2)	559 (75.2)	573 (77.1)	198 (81.2)	102 (83.6)	96 (78.7)	599 (73.5)	293 (73.6)	306 (73.4)
HER2 gene copy number, <i>n</i> (%)	<i>n</i> = 1415	<i>n</i> = 713	<i>n</i> = 702	<i>n</i> = 237	<i>n</i> = 120	<i>n</i> = 117	<i>n</i> = 794	<i>n</i> = 390	<i>n</i> = 404
4 to <6	180 (12.7)	91 (12.8)	89 (12.7)	22 (9.3)	9 (7.5)	13 (11.1)	116 (14.6)	58 (14.9)	58 (14.4)
≥6	1211 (85.6)	607 (85.1)	604 (86.0)	213 (89.9)	109 (90.8)	104 (88.9)	662 (83.4)	322 (82.6)	340 (84.2)
HER2 gene ratio, <i>n</i> (%)	<i>n</i> = 1415	<i>n</i> = 713	<i>n</i> = 702	<i>n</i> = 237	<i>n</i> = 120	<i>n</i> = 117	<i>n</i> = 794	<i>n</i> = 390	<i>n</i> = 404
2 to <4	405 (28.6)	203 (28.5)	202 (28.8)	64 (27.0)	26 (21.7)	38 (32.5)	247 (31.1)	123 (31.5)	124 (30.7)
≥4	988 (69.8)	498 (69.9)	490 (69.8)	171 (72.2)	92 (76.7)	79 (67.5)	534 (67.3)	260 (66.7)	274 (67.8)

Abbreviations: ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IDFS, invasive disease-free survival; IHC, immunohistochemistry; ITT, intent-to-treat; NAT, neoadjuvant therapy; PgR, progesterone receptor.

<sup>a</sup>Includes North, Central, and South American Indians.