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Supplemental Tables for:
Patterns of care and clinical outcomes of first-line trastuzumab-based therapy in HER2-positive metastatic breast cancer patients relapsing after (neo)adjuvant trastuzumab: an Italian multicenter retrospective cohort study
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Table S1. Baseline characteristics of patients with de novo stage IV disease.

Characteristic	Patients with de novo stage IV disease n=113 (%)
Age (range), years	53.57 (44.05 – 63.37)
Breast cancer diagnosis prior to 2007	55 (48.7)
Menopausal status	
Premenopausal	44 (38.9)
Postmenopausal	69 (61.1)
Histologic type	
Ductal carcinoma	96 (85.0)
Lobular carcinoma	2 (1.8)
Others	3 (2.7)
Unknown	12 (10.6)
Hormone receptor status	
Positive (ER and/or PR positive)	64 (56.6)
Negative (ER and PR negative)	44 (38.9)
Unknown	5 (4.4)
Grade (G)	
G1	0 (0.0)
G2	16 (14.2)
G3	27 (23.9)
Unknown	70 (61.9)

Table S2. First site of distant metastasis according to hormone receptor status irrespective of prior exposure to (neo)adjuvant trastuzumab.

	Hormone receptor positive n=186 (%)	Hormone receptor negative n=115 (%)	Hormone receptor unknown n=2 (%)	p value (HR+ vs HR-)
First site of distant metastasis				0.186
Brain	17 (9.1)	17 (14.8)	0 (0.0)	0.133
Liver	53 (28.5)	28 (24.3)	1 (50.0)	0.431
Lung	34 (18.3)	28 (24.3)	1 (50.0)	0.206
Bone	50 (26.9)	21 (18.3)	0 (0.0)	0.087
Others	32 (17.2)	21 (18.3)	0 (0.0)	0.815
First site of distant metastasis				
Visceral involvement	123 (66.1)	85 (73.9)	2 (100)	0.156
Non-visceral involvement	63 (33.9)	30 (26.1)	0 (0.0)	

Abbreviations: HR+, hormone receptor positive; HR-, hormone receptor negative.

Table S3. Characteristics of patients with de novo stage IV disease at the time of breast cancer diagnosis and features of the first-line treatment received.

Characteristic	Patients with de novo stage IV disease n=113 (%)
PFS follow-up (IQR range), years	1.02 (0.46 – 1.82)
OS follow-up (IQR range), years	2.59 (1.61 – 4.44)
First-site of distant relapse	
Brain	5 (4.4)
Liver	58 (51.3)
Lung	20 (17.7)
Bone	23 (20.4)
Others	7 (6.2)
Median number of metastatic sites (IQR range)	2 (1-3)
Strategy as first-line therapy	
CT (± ET) + trastuzumab	108 (95.6)
ET + trastuzumab	5 (4.4)
Trastuzumab alone	0 (0.0)
Type of first-line chemotherapy drugs	
Taxane-based	88 (81.5)
Vinorelbine	15 (13.9)
Capecitabine	1 (0.9)
Others	4 (3.7)
None	5 (4.4)
Type of first-line chemotherapy regimen	
Monotherapy	70 (64.8)
Combined therapy	38 (35.2)
Type of first-line endocrine therapy	
Tamoxifen ± LHRHa	7 (20.6)
AI ± LHRHa	26 (76.5)
Fulvestrant	1 (2.9)
None	79 (69.9)
Lines of therapy for metastatic disease, median (min – max)	
Chemotherapy	2 (0 – 8)
Anti-HER2 therapy	2 (1 – 8)
Endocrine therapy	0 (0 – 1)

Abbreviations: PFS, progression-free survival; IQR, interquartile range; OS, overall survival; CT, chemotherapy; ET, endocrine therapy; LHRHa, luteinizing hormone-releasing hormone analogues; AI, aromatase inhibitor.

Table S4. Objectives responses according to prior exposure to (neo)adjuvant trastuzumab.

	COHORT A No prior (neo)adjuvant trastuzumab n=202 (%)	**COHORT B Prior (neo)adjuvant trastuzumab n=101 (%)**	**p value**
Objective response rate (ORR)	114 (69.9)	49 (61.3)	0.176
Adjusted OR (95% CI)	0.62 (0.34 – 1.15)		0.131
Best objective response			
Complete response	41 (25.2)	20 (25.0)	0.979
Partial response	73 (44.8)	29 (36.3)	0.205
Stable disease	29 (17.8)	18 (22.5)	0.383
Progressive disease	20 (12.3)	13 (16.3)	0.395
Clinical benefit rate (CBR)	129 (79.1)	58 (72.5)	0.248
Adjusted OR (95% CI)	0.73 (0.37 – 1.46)		0.370
Non evaluable for response	39 (19.3)	21 (20.8)	0.606

Abbreviations: OR, odds ratio; CI, confidence intervals.

Table S5. Objectives responses according to prior exposure to (neo)adjuvant trastuzumab including patients with de novo stage IV disease.

	COHORT A No prior (neo)adjuvant trastuzumab n=315 (%)	**COHORT B Prior (neo)adjuvant trastuzumab n=101 (%)**	**p value**
Objective response rate	186 (71.0)	49 (61.3)	0.100
Adjusted OR (95% CI)	0.62 (0.34 – 1.10)		0.104
Best objective response			
Complete response	64 (24.4)	20 (25.0)	0.917
Partial response	122 (46.6)	29 (36.3)	0.104
Stable disease	40 (15.3)	18 (22.5)	0.131
Progressive disease	36 (13.7)	13 (16.3)	0.575
Clinical benefit rate	205 (78.0)	58 (72.5)	0.313
Adjusted OR (95% CI)	0.78 (0.41 – 1.49)		0.455
Non evaluable for response	52 (16.5)	21 (20.8)	0.192

Abbreviations: OR, odds ratio; CI, confidence intervals.