Treatment landscape of HER2-positive metastatic breast cancer (MBC) - Results from the Austrian AGMT_MBC-Registry

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Background

Real-world data are needed to characterize the current treatment landscape of HER2+ MBC and the potential sequencing of new anti-HER2 drugs recently approved. Here, we present data from the MBC-Registry of the Austrian Study Group of Medical Tumor Therapy (AGMT).

Patients and methods

The AGMT-MBC-Registry is a multicenter nationwide ongoing retrospective and prospective registry for MBC patients in Austria.

In this analysis, patients with known HER2 status, available survival data, at least one treatment line and diagnosis of metastatic disease after 01/04/2013 (pertuzumab available in Austria) were included.

Definitions

In case more than one tumor sample from one patient was available, the receptor status (and grade, Ki-67, and histologic subtype) of a metastasis was used, if the sample was taken ≤ 3 months after diagnosis of metastatic disease and if at least ER- and HER2-status were available. Otherwise, the receptor status of the latest primary tumor (or local recurrence) diagnosed before (or within 3 months of) the diagnosis of metastatic disease was used.

Figure 1. Consort diagram.

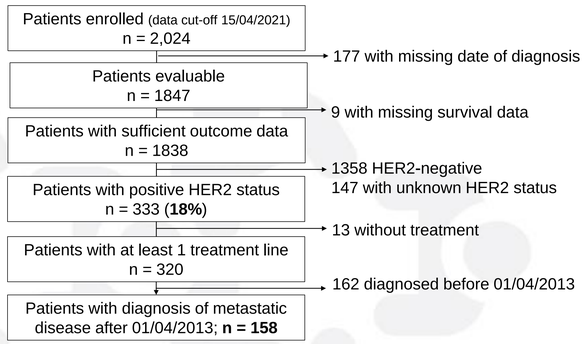


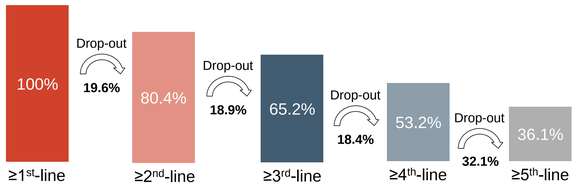
Table 1. Patient characteristics (n = 158)

Median age (range)*	64 years (26-94)
Stage at diagnosis	
stage I-III	84/158 (53.2%)
stage IV (*de novo* metastatic)	73/158 (46.2%)
unknown	1/158 (0.6%)
Menopausal status *	
postmenopausal	104/158 (65.8%)
premenopausal	24/158 (15.2%)
unknown	29/158 (18.4%)
male	1/158 (0.6%)
Metastatic sites *	
visceral disease	104/158 (65.8%)
non-visceral disease only	54/158 (34.2%)
brain or leptomeningal metastases	11/158 (7.0%)
Number of metastatic sites *	
median (range)	1 (1-9)
1	81/158 (51.3%)
2	41/158 (25.9%)
≥ 3	36/158 (22.8%)
Hormone-receptor (HR) status	
positive	101/158 (63.9%)
negative	57/158 (36.1%)
Histologic subtype	
no special type (NST)	109/158 (69.0%)
invasive lobular	6/158 (3.8%)
mixed NST and lobular	2/158 (1.3%)
other	24/158 (15.2%)
unknown	17/158 (10.8%)
Grading	
1	2/158 (1.3%)
2	59/158 (37.3%)
3	66/158 (41.8%)
unknown	31/158 (19.6%)
Treatment for early stage (stage I-III)	
(neo)adjuvant chemotherapy	64/84 (76.2%)
(neo)adjuvant trastuzumab ± pertuzumab	53/84 (63.1%)†
adjuvant endocrine therapy (for HR+ only)	40/52 (76.9%)
no (neo)adjuvant therapy	4/84 (3.6%)
Disease-free survival (DFS; stage I-III)	
< 24 months	23/84 (27.4%)
≥ 24 months	56/84 (66.7%)
NA	5/84 (6.0%)
Survival status	
alive	73/158 (46.2%)
lost to follow-up	8/158 (5.1%)
dead	77/158 (48.7%)

* at diagnosis of metastatic disease † 13 pt had a HER2-negative primary tumor

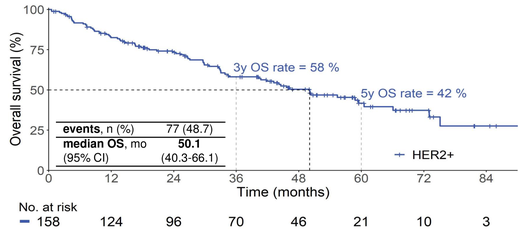
Drop-out rate

Figure 2. Estimated percentage of patients being treated in each therapy line and drop-out rates from 1st- to 5th-line.



Overall survival (OS)

Figure 3. OS after a median follow-up of 51.4 months (95%CI 46.8-58.3)



Efficacy of different treatment lines

Table 2. Progression-free survival (PFS), time to next treatment (TTNT), overall response rate (ORR) and clinical benefit rate (CBR) in different lines.

Line	Median PFS* (95%-CI)	Median TTNT* (95%-CI)	ORR*	CBR*
1st (n=158)	13.10 (10.60-16.60)	13.20 (10.50-15.75)	48%	70%
2nd (n=90)	7.70 (3.40-10.15)	7.90 (4.70-9.80)	32%	63%
3rd (n=49)	5.20 (3.00-7.00)	6.85 (3.65-9.25)	21%	44%
4th (n=28)	3.20 (0.15-3.60)	4.10 (0.70-4.90)	17%	30%
5th (n=15)	3.00 (0.70-3.40)	4.45 (3.30-5.40)	0%	17%
≥6th (n=14)	2.70 (2.00-3.90)	3.80 (1.25-4.95)	7%	21%

** calculated in patients with available data; ORR = partial response (PR) or complete response (CR); CBR = PR, CR or stable disease (SD) for at least 6 months*

Treatment landscape

Table 3. Treatments per therapy line.

	1st n=158	2nd n=90	3rd n=49	4th n=28	5th n=15
Trastuzumab + pertuzumab + chemo*	81 (51.3%)	9 (10.0%)	8 (16.3%)	2 (7.1%)	-
Trastuzumab + pertuzumab + ET	3 (1.9%)	4 (4.4%)	2 (4.1%)	-	-
Trastuzumab + chemo*	12 (7.6%)	6 (6.7%)	4 (8.2%)	6 (21.4%)	5 (33.3%)
Trastuzumab + ET	8 (5.1%)	12 (13.3%)	5 (10.2%)	-	-
T-DM1	15 (9.5%)	34 (37.8%)	4 (8.2%)	6 (21.4%)	3 (20.0%)
Lapatinib-based therapy	5 (3.2%)	7 (7.8%)	9 (18.3%)	3 (10.7%)	-
Neratinib-based therapy	-	-	3 (6.1%)	1 (3.6%)	3 (20.0%)
Tucatinib-based therapy	-	-	3 (6.1%)	-	-
Trastuzumab deruxtecan	-	-	1 (2.0%)	-	-
Chemo without anti-HER2 therapy*	11 (7.0%)	7 (7.8%)	6 (12.2%)	6 (21.4%)	2 (13.3%)
ET without anti-HER2 therapy	17 (10.8%)	4 (4.4%)	1 (2%)	2 (7.1%)	-
Other	6 (3.8%)	7 (7.8%)	3 (6.1%)	2 (7.1%)	2 (13.4%)

Chemo: chemotherapy; ET: endocrine therapy ** ± ET*

Conclusion

More than a half of patients with HER2+ MBC in Austria receive at least four treatment lines. Treatment benefit diminishes from line to line, underlining the medical need for more effective new compounds as well as studies looking at optimal sequencing of multiple treatment lines.

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Conflicts of Interest

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