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A retrospective population-based observational study in metastatic HER2-positive breast cancer patients in Denmark previously treated with T-DM1

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Background

Current guidelines in HER2-positive metastatic breast cancer (mBC) recommend the combination of trastuzumab with one of several chemotherapeutic agents for 3rd line or later treatments. This study aims to describe treatment of HER2-positive mBC patients in 3rd line or later previously treated with T-DM1 in a Danish real-world setting.

Methods

This observational population-based study included all women diagnosed with HER2-positive mBC in Denmark, previously treated with T-DM1. Patients were included on the date of progression leading to subsequent initiation of 3rd line treatment if the patient received T-DM1 in 1st or 2nd line. If the patient received T-DM1 in 3rd line or later the inclusion was based on the date of progression on T-DM1. Inclusion dates were between 1st of January 2014 and 31st of December 2019. The primary end points were overall survival (OS) and progression-free survival (PFS). For evaluation of the results on time on treatment (ToT) the competing risk setting should be taken into account. Estimates presented for ToT are for the event discontinuation only.

	All Patients (n=272)	CNS+ (n=77) (28%)	CNS- (n=195)(72%)
Age (years)			
Mean age (min-max)	59 (27-86)	54 (33-78)	62 (27-86)
Sites of Cancer			
Visceral	227	77 (100)	150 (77)
CNS as only visceral	NA	11 (14)	NA
Non-visceral	45	0	45 (33)
Number of sites			
1	26	2 (3)	24 (12)
2	52	8 (10)	44 (23)
3+	194	67 (87)	127 (65)
HER2 status			
Biopsy metastasis	224	67 (87)	157 (80)
Biopsy primary tumor	48	10 (13)	38 (20)
IHC			
FISH 2+	71	8 (10)	63 (32)
IHC 3+	201	69 (90)	132 (68)
ER status			
Positive	168	47 (61)	121 (62)
Negative	104	30 (39)	74 (38)
Prior treatment			
T-DM1	272		
Pertuzumab	167	44 (57)	123 (63)
Trastuzumab	269	76 (99)	193 (99)
Other anti-HER2	44	18 (23)	26 (13)
Taxanes	99	30 (39)	69 (35)
Hormone	98	28 (36)	70 (36)
Other systemic	268	76 (99)	192 (98)
Number of lines received for mBC			
Median (min-max)	3 (2-11)	3 (2-9)	2 (2-11)

Table 1: Baseline characteristics overall, and stratified by presence of CNS metastases

Results

In the treatment line subsequent to inclusion 43 (16%) patients received capecitabine combined with trastuzumab, 32 (12%) received a taxane combined with trastuzumab, 26(10%) received capecitabine combined with lapatinib, 23 (8%) received T-DM1, 21 (8%) received eribulin combined with trastuzumab, 21 (8%) received experimental treatment and 106 (38%) received other treatment modalities.

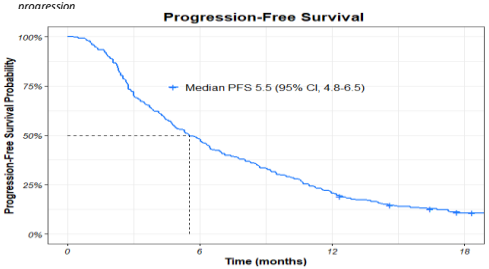
In the treatment line subsequent to inclusion median progression-free survival was 5.5 months (95% CI, 4.8-6.5).

Median overall survival was 18.5 months (95% CI, 16.2-21.3) across all lines following inclusion.

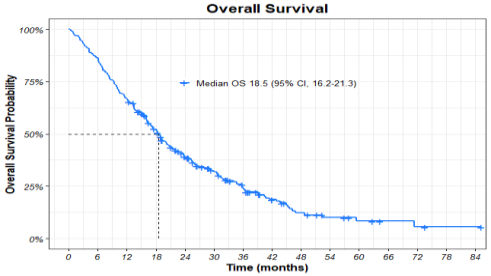
In the treatment line subsequent to inclusion median time of treatment was 29.3 months for patients without CNS presence at index (95% CI, 25.5-36.1) and 22.5 months (95% CI, 12.7-44.6) for patients with CNS presence at inclusion.

Treatment subsequent to inclusion until progression	No. Patients (%)
Total	272 (100)
Trastuzumab + Capecitabine	43 (16)
Trastuzumab + Taxane	32 (12)
Lapatinib + Capecitabine	26 (10)
T-DM1	23 (8)
Trastuzumab + Eribulin	21 (8)
Experimental	*21 (8)*
Other	*106 (38)*

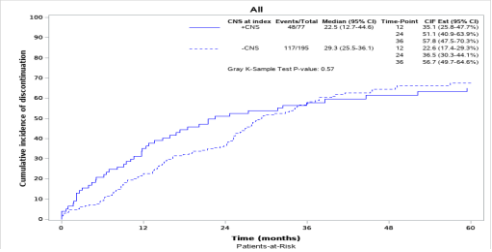
Table 2: most used treatment modalities subsequent to inclusion until disease progression



Median progression-free survival in patients in line subsequent to inclusion



Median overall survival across all treatment lines subsequent to inclusion



Cumulative incidence curve describing time on treatment of patients across all lines stratified by presence of CNS metastases at inclusion

Conclusion

In this real-world study, patients were treated with a wide variety of anti-cancer agents in 3rd line or later in HER2-postive mBC. These agents show efficacy in these pretreated patients, but there is still a need for effective therapies in the 3rd line or later treatment settings.

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