PRAEGNANT Real-World registry

Progression free survival (PFS) and overall survival (OS) of patients treated with trastuzumab emtansine (T-DM1) after previous treatment with pertuzumab in patients with advanced breast cancer (NCT02338167)

P6-17-22

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BACKGROUND

Both treatments, pertuzumab (PTZ) + trastuzumab (TZM) together with chemotherapy and trastuzumab emtansine (T-DM1) were developed in phase III studies[1,2] during overlapping time intervals. Therefore pertuzumab was not yet approved at the time when the EMILIA[2] study was conducted. Subsequently the knowledge, which is used to assess the benefit of T-DM1, comes only from a population without a pretreatment with pertuzumab. It is known that tumors acquire new resistance mechanisms with the increasing number of given therapy lines. In addition to or as a result of that, patients with more advanced therapy lines have usually a more unfavorable prognosis.

PTZ+TZM and chemotherapy has been established in many national and international guidelines as the standard first line therapy for HER2 positive metastatic breast cancer. T-DM1 is usually given after such a first line treatment with PTZ and trastuzumab (see SABCS 2018 poster P6-17-37).

Low evidence is known about the progression-free (PFS) and overall survival (OS) of patients treated with T-DM1 after PTZ. **Aim of this** study was to analyze a real world patient cohort of advanced breast cancer (ABC) patients who were treated with T-DM1 after a treatment containing pertuzumab in the metastatic setting with regard to patient characteristics, progression free survival (PFS), and overall survival (OS)

STUDY DESIGN AND METHODS

THE PRAEGNANT breast cancer registry is a prospective network including patients with advanced breast cancer, who have a life expectancy of at least three months. Patients can be included at any time point during the course of the disease (Figure 1). Patients are scheduled for regular study visits every three months. The data were collected by trained stuff and documented in an electronic case report form. Additionally quality of life is assessed and biomaterials are obtained at each change of therapy line.

All patients were identified who have started a therapy with T-DM1 after a completed treatment with pertuzumab in the metastatic setting.

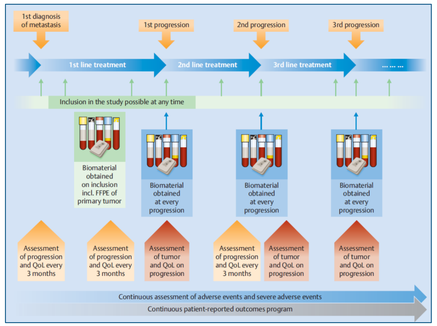

Figure 1: Recruitment design of the PRAEGNANT study

Study Objectives

Progression free survival and overall survival

Statistical considerations

Progression-free survival was defined from the date of therapy begin to the earliest date of disease progression (distant-metastasis, local recurrence, or death from any cause) or the last date known to be progression-free. Overall survival was defined from the date of therapy begin to death from any cause or the last date known to be alive. PFS and OS rates were estimated using the Kaplan-Meier product limit method.

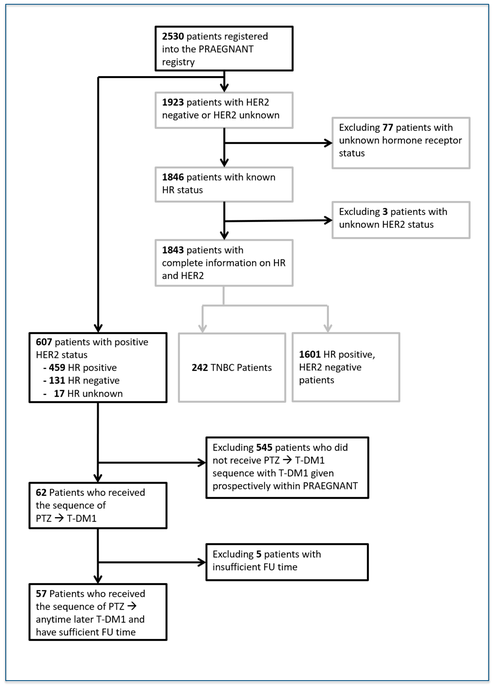

Figure 2: Patient selection

RESULTS

Patient selection: A total of 2530 patients were recruited into the PRAEGNANT registry up to June 2018. Of these patients 2450 could be classified according to molecular subtypes. 242 (9.9%) patients were classified as having a triple negative tumor, 1601 (65.3%) patients had a HER2 negative HR positive tumor and 607 (24.8%) were HER2 positive. Of those patients 62 could be identified who were treated with T-DM1 in any therapy line after a completed treatment with pertuzumab/trastuzumab and chemotherapy. These patients had to have started their treatment after study inclusion or not more than 90 days after study inclusion. Patient selection is shown in **Figure 2**. After applying all inclusion and exclusion criteria 57 patients could be included into this analysis.

Patient Characteristics: Patients were in average 55 years old. About half of the patients had a ECOG 0. Most of them had visceral metastases and about a quarter had brain metastases. Pertuzumab as the precedent therapy was mainly given in the 1st line (n=45; 78.9%). T-DM1 treatment was given in most of the cases in the 2nd line (n=33; 57.9%). Third line treatment was given in 14 patients (24.6%) and fourth or further line treatment occurred in 10 patients (17.5%) **(Table 1)**.

Survival Analyses: In the total cohort of 57 patients 47 PFS events occurred and the median progression free survival time was 4.8 months (95% CI: 3.1 – 8.0). The corresponding Kaplan-Meier curve is shown in **Figure 3a**. Looking at median PFS according to therapy lines, patients who received T-DM1 in the second line seemed to perform slightly better [median PFS: 7.7 months (95%CI: 2.8-12.2)] than patients in later therapy lines [3rd line: 4.2 months (95% CI: 4.2 – NA); 4th line and higher: 4.0 months (95% CI: 1.8-NA)] **(Figure 3b)**. Median overall survival was not achieved yet. Assessing the Kaplan Meier curves patients with higher therapy lines seemed to also have a worse prognosis than patients with T-DM1 treatment in earlier therapy lines **(Figure 4a and 4b)**.

Table 1: Patient and tumor characteristics

Characteristic		N (%) or Mean (±SD)
Age		55 (±11.4)
BMI		26.2 (±5.4)
M-stage at diagnosis	cM0	30 (52.6)
	cM1	27 (47.4)
Metastasis pattern	brain	15 (26.3)
	visceral	35 (61.4)
	bone	1 (1.8)
	others	6 (10.5)
ECOG status	0	28 (50.9)
	1	22 (40.0)
	2	4 (7.3)
	3	1 (1.8)
Therapy line at study inclusion	1st line met	33 (61.1)
	2nd line met	12 (22.2)
	3rd line met	5 (9.3)
	4+ line met	4 (7.4)
Lowest line of PTZ	1	45 (78.9)
	2	5 (8.8)
	3	4 (7.0)
	4+	3 (5.3)
Lowest line of TDM1	2	33 (57.9)
	3	14 (24.6)
	4+	10 (17.5)

CONCLUSIONS

- Median progression free survival is with 4.8 months (95 CI: 3.1-8.0) i.e. shorter than in the EMILIA2 study (9.6 months), the TH3RESA[3] study (7.5 months) and subgroup analyses of the KAMILLA[4] study.
- Despite small sample sizes the prognosis seems to depend – like in other studies and patients populations – on the therapy line.
- T-DM1 is a reasonable therapy after pertuzumab.
- Larger studies are needed to confirm our results.

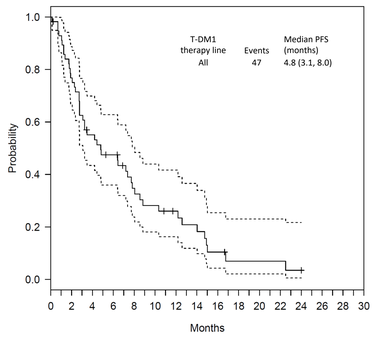

Figure 3a: Progression free survival in the overall cohort

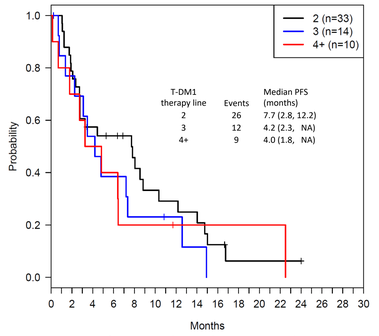

Figure 3b: Progression free survival according to T-DM1 therapy line

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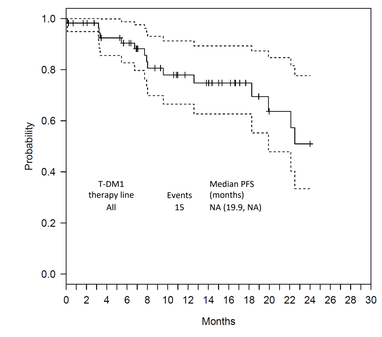

Figure 4a: Overall survival in the overall cohort

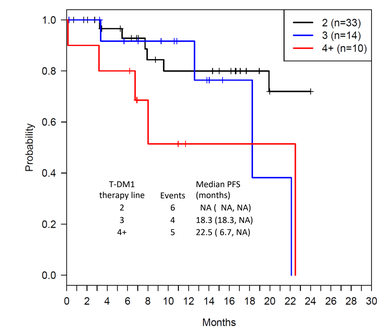

Figure 4b: Overall survival according to T-DM1 therapy line

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