

## Background

Up to 30% of metastatic breast cancer (BC) patients develop brain metastases (BM). Prognosis of patients with BM is poor and long-term survival is rare. Despite commonly known short median survival times of brain metastatic breast cancer patients differing between 7 and 8 months, long-term survivors with survival rates longer than 2 years make almost 25% of the whole cohort.<sup>1</sup> Identification of factors associated with long-term survival is important for improving treatment modalities.

**The aim of this retrospective analysis from the BMBC registry was to identify long-term survivors and characterize prognostic factors being associated with long-term survival.**

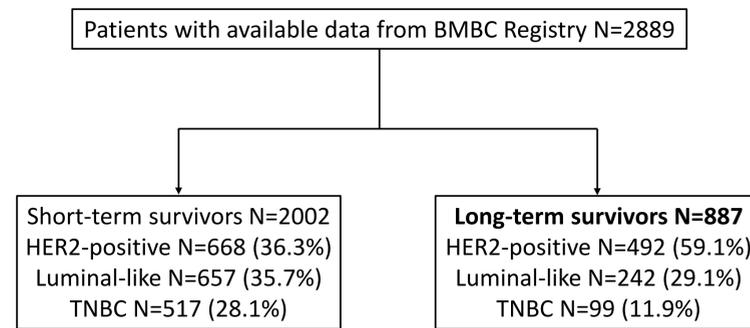
## Patients and Methods

Clinical data for this analysis derived from the **brain metastases in breast cancer (BMBC) registry**. A total of **2889** out of 3234 patients of the BMBC registry were available for this analysis. Long-term survival was defined as overall survival (OS) after diagnosis of BM in the upper third of the survival curve resulting in a cut-off of 15 months. **887 patients were categorized as long-term survivors**. Baseline characteristics were assessed by Wilcoxon test, Fisher's exact test resp. Pearson  $\chi^2$ -test between short-term vs long-term survivors. Associations with the assignment into the group of long-term survivors were analyzed by logistic regression models with 95% Wald confidence interval (CI). Differences in OS of long-term survivors between subtypes were analyzed by the log-rank-test and Kaplan-Maier curves. All reported p-values were two-sided, the significance level was set to 0.05.

### Objectives:

- To assess the OS after diagnosis of BM in long-term survivors
- To characterize exploratively the prognostic behavior of the following factors to be assigned in the group of long-term survivors: age, hormone receptor status, HER2 status, subtype, ECOG, number of BM, localization of BM, clinical symptoms, ECM at diagnosis of BM, localization of ECM, chemotherapy after diagnosis of BM
- Comparison of the OS after diagnosis of BM between the groups of BC subtypes (HER2-positive, Luminal-like, TNBC).

**Figure 1: Patient cohort including in the analysis**



**Table 1: Baseline characteristics**

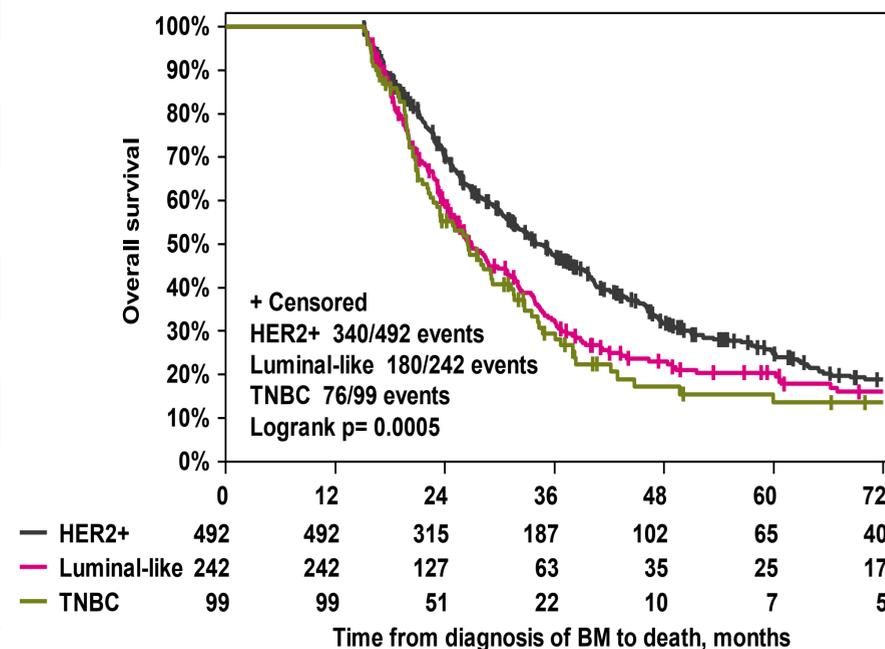
Parameter at diagnosis	Category	Short-term survivors N (valid %)	Long-term survivors N (valid %)	p-value
Age at first BC diagnosis, years	Median (range)	54.0 (10.0-98.0)	48.0 (20.0-92.0)	<0.001
Age at first BM diagnosis, years	Median (range)	59.0 (13.0-99.0)	53.0 (25.0-93.0)	<0.001
ECOG	0-1 2-4	457 (51.0) 440 (49.1)	306 (76.9) 92 (23.2)	<0.001
Hormone receptor	negative positive	826 (42.8) 1104 (57.2)	279 (33.1) 563 (66.9)	<0.001
HER2	negative positive	1180 (65.1) 633 (34.9)	342 (42.8) 458 (57.3)	<0.001
Number of BM	1 2-3 ≥4	453 (25.4) 476 (26.7) 853 (47.9)	337 (40.9) 218 (26.5) 269 (32.6)	<0.001
Leptomeningeal metastases	no yes	1652 (82.5) 350 (17.5)	795 (89.6) 92 (10.4)	<0.001
Clinical symptoms*	no yes	402 (20.1) 1600 (79.9)	235 (26.5) 652 (73.5)	<0.001
ECM*	yes no	351 (17.5) 1651 (82.5)	234 (26.4) 653 (73.6)	<0.001
ypT after NACT	ypT0 ypTis ypT1 ypT2 ypT3 ypT4a-d	83 (13.7) 33 ( 5.4) 174 (28.7) 180 (29.7) 71 (11.7) 65 (10.7)	60 (21.6) 22 ( 7.9) 95 (34.2) 58 (20.9) 22 ( 7.9) 21 (7.5)	<0.001

\*at diagnosis of BM; ECM, extracranial metastases; NACT, neoadjuvant chemotherapy

## Results

- Long-term survivors compared to short-term survivors were significantly **younger** at BC and BM diagnosis, showed **better ECOG** at time of BM diagnosis and **lower number of BM**. Furthermore, long-term survivors had significantly higher **pathological complete remission rate** (21.6% vs 13.7%, p<0.001), **less leptomeningeal metastases** (10.4% vs 17.5%, p<0.001) and **less extracranial metastases** (ECM, 73.6% vs 82.5%, p<0.001) (Table 1).
- The distribution of biological subtypes in long-term vs short-term survivors was 59.1% vs 36.3% for HER2-positive tumors, 29.1% vs 35.7% for luminal-like and 11.9% vs 28.1% for TNBC (p<0.001) (Fig. 1).
- Overall, median OS in long-term survivors was **30.9 months** (95% CI 28.8-32.6). Median OS according to different subtypes was 33.9 months (95% CI 31.5-37.9) in HER2 positive, 26.9 (95% CI 25.0-30.9) in luminal-like and 26.5 months (95% CI 22.7-31.2) in TNBC patients.
- Age, hormone receptor status, HER2 status, number of BM, ECM and chemotherapy were significantly associated with a categorization of long-term survivors in uni- and multivariate analyses (Table 2).**

**Figure 2. Kaplan-Meier OS in long-term survivors by different subtypes**



**Table 2: Prognostic factors in long-term survivors**

Parameter at diagnosis	Category	Univariate analysis		Multivariate analysis	
		Odds Ratio* (95% CI)	p-value	Odds Ratio* (95% CI)	p-value
Age**, years	≥60 vs <60	0.49 (0.42-0.58)	<0.001	0.59 (0.44-0.79)	<0.001
ECOG**	2-4 vs 0-1	0.31 (0.24-0.41)	<0.001	0.45 (0.33-0.61)	<0.001
Hormone receptor	positive vs negative	1.51 (1.27-1.79)	<0.001	1.87 (1.39-2.50)	<0.001
HER2 status	positive vs negative	2.50 (2.11-2.96)	<0.001	2.74 (2.06-3.64)	<0.001
Number of BM	2-3 vs 1	0.62 (0.50-0.76)	<0.001	0.79 (0.55-1.13)	0.191
	≥4 vs 1	0.42 (0.35-0.52)	<0.001	0.46 (0.33-0.65)	<0.001
Leptomeningeal metastases	yes vs no	0.55 (0.43-0.70)	<0.001	0.99 (0.64-1.53)	0.949
Clinical symptoms**	yes vs no	0.70 (0.58-0.84)	<0.001	0.94 (0.66-1.34)	0.726
ECM**	yes vs no	0.59 (0.49, 0.72)	<0.001	0.65 (0.46-0.93)	0.017
Chemotherapy***	yes vs no	2.80 (2.38-3.30)	<0.001	2.19 (1.64-2.92)	<0.001

\*An odds ratio ≥1 means to have a higher probability to be assigned to the group of long-term survivors; \*\* at diagnosis of BM; \*\*\*after diagnosis of BM; ECM, extracranial metastases

## Conclusions

**Our analysis identified factors associated with long-term survival of breast cancer patients with brain metastases and characterized clinical features of this patient cohort. Patients with better ECOG status, younger age, lower number of BM, less extended visceral metastases were more likely to show a long-term survival. Those patients might be more eligible for extended local and systemic treatment.**

**Further research is needed to understand the factors leading to long-term survival of patients with brain metastases.**

## References

- Witzel I, Laakmann E, Weide R, Neunhöffer T, Park-Simon TJ, Schmidt M, Fasching PA, Hesse T, Polasik A, Mohrmann S, Würschmidt F, Schem C, Bechtner C, Würstlein R, Fehm T, Möbus V, Burchardi N, Loibl S, Müller V. Treatment and outcomes of patients in the Brain Metastases in Breast Cancer Network Registry. Eur J Cancer. 2018 Oct;102:1-9. doi: 10.1016/j.ejca.2018.07.004. Epub 2018 Aug 9. PMID: 30099223.