Outcome of patients with HER2-positive brain metastatic breast cancer: a 10-year retrospective study

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BACKGROUND

Brain metastases (BM) are a major clinical issue in patients with Human Epidermal Growth Factor Receptor-2 (HER2) positive breast cancer (BC), remaining often the cause of death despite extra-cerebral disease control with HER2-targeted therapies.

Considering long-term neurocognitive effects following whole brain radiotherapy, better knowledge of the patient's outcomes will help to provide an adapted therapeutic strategy.

The aim of this real-life study was to highlight factors related to survival outcome in a HER2-positive BMBC population and to identify prognostic risk categories.

METHODS

Patients treated between January 2009 and December 2020 for a HER2-positive BMBC at three French centers (ICANS, Centre Paul Strauss and University Hospital of Strasbourg) were included.

Primary endpoint was overall survival (OS). Secondary endpoints were visceral progression free survival (PFS) and cerebral PFS. Cox logistic regression was carried out to identify prognosis survival factors. A prognostic score was defined providing the identification of patient's categories with similar risks.

RESULTS

Ninety-four patients with HER-2 positive BMBC were included with a 3.7 years-median follow-up. Median age at BM diagnosis was 54 years (95% IC 51 - 57), with a *performans status* ≤ 1 in 61 patients (65%). Positive tumoral hormone receptor was present in 62% of cases. Median time between diagnosis of breast cancer and diagnosis of BM was 3.6 years (95% IC 2.7 - 4.6). Twenty-nine patients (31%) had exclusively brain metastasis. Forty patients (43%) had ≥ 5 lesions while 24 (26%) had only one. Median largest BM size was 18.5 mm (95% IC 16 - 21). Concomitant extra-CNS progression was observed in 42 patients (45%). At the last follow-up, 62 patients (66%) had died.

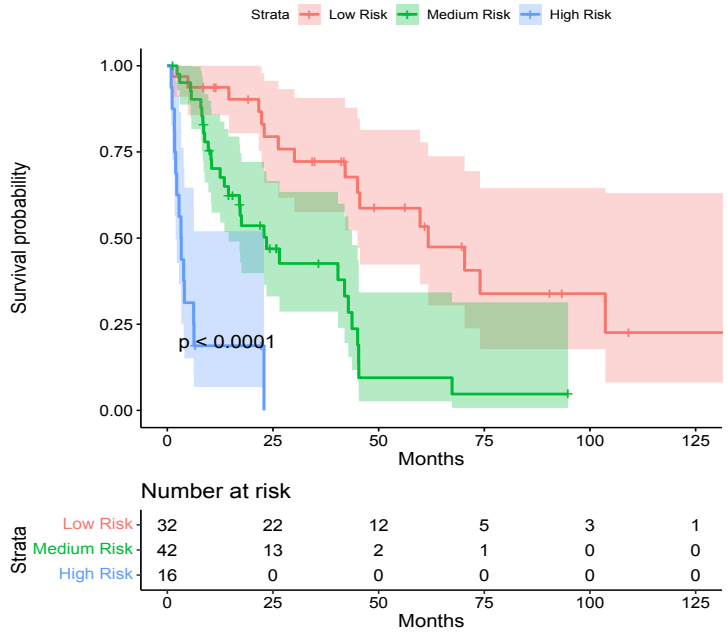
Median OS was 18.4 months (95% CI 12.8 - 24.0). Cerebral PFS was 8.3 months (95% IC 4.4 - 12.1).

Multivariable analysis of overall survival factors

	HR (95% CI)
Age < *vs* ≥ 50 years	**0.42 (0.19 - 0.89)**
Performans status < *vs* ≥ 2	**0.35 (0.17 - 0.70)**
Number of brain metastasis ≥ 5 *vs* < 5	**2.22 (1.20 - 4.12)**
Concomitant extra-CNS* progression yes *vs* no	**2.31 (1.09 - 4.93)**
Number of lines before CNS metastatic diagnosis ≥ 2 *vs* < 2	**2.09 (1.00 - 4.35)**

**CNS central nervous system*

	Low risk (95% IC)	Medium risk (95% IC)	High risk (95% IC)
OS	41.9 m (30.5-53.3)	17.1 m (11.5-22.7)	3.2 m (0.4-6.1)
Visceral PFS	22.0 m (11.5-32.5)	8.6 m (4.0-13.2)	2.2 m 0-4.5)
Cerebral PFS	13.5 m (4.1-22.9)	8.6 m (6.4-10.7)	2.9 m (0.8-5.0)



Three different risk categories (low, medium and high risk) were identified, with a respectively 41.9 (95% CI 30.5 – 53.3), 17.1 (95% CI 11.5 – 22.7) and 3.2 (95% CI 0.4 - 6.1) month-median OS (p<0.001).

DISCUSSION

Based on retrospective data, a prognostic risk score was identified which could help to choose the best therapeutic strategy. The intermediate and high risks categories strongly support the need for a more efficient treatment. On the other hand, in the low category, the optimal therapeutic management needs to be debated considering the risk of neurological deterioration.

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The first author declares that there is no conflict of interest regarding the publication of this article.