

## Brain metastases in breast cancer: analysis of the role of HER2 status and treatment in the outcome of 94 patients

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### ABSTRACT

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**Aims and background.** We investigated the impact of human epidermal growth factor receptor 2 (HER2) and prognostic factors in the outcome of patients with breast cancer that developed brain metastases.

**Methods.** The data from 94 patients who received multidisciplinary therapy from 2001 to 2007 were retrospectively reviewed. Patients were assigned according to their HER2 status, and overall survival and time to brain metastases recurrence/progression were evaluated. The prognostic value of age, presence of extracerebral metastases, recursive partitioning analysis class, hormone therapy, systemic therapy and trastuzumab was assessed.

**Results.** The median overall survival and time to brain disease progression were 7.1 and 6.5 months, respectively. HER2 positivity ( $P = 0.006$ ), treatment with trastuzumab ( $P = 0.025$ ), chemotherapy ( $P = 0.011$ ) and recursive partitioning analysis class I-II ( $P < 0.001$ ) were associated with prolonged survival on univariate analysis. On multivariate analysis, only recursive partitioning analysis class I-II ( $P < 0.001$ ) and triple-negative disease ( $P = 0.04$ ) remained significant for overall survival, whereas time to brain metastases progression was only associated with recursive partitioning analysis class I-II ( $P = 0.001$ ). The time from the diagnosis of primary disease to brain metastasis was slightly shorter in the HER2+ patients than in HER2- patients (36 vs 39 months). Intensified local treatment of brain metastasis incorporating whole-brain radiotherapy and/or radiosurgery and neurosurgery did not affect survival. Patients with triple-negative disease presented a significantly lower survival than the rest of the cohort (4 vs 8 months;  $P = 0.012$ ).

**Conclusions.** Recursive partitioning analysis class I-II was found to be the strongest independent predictive factor. Treatment with trastuzumab in HER2+ patients appeared to improve overall survival, probably due to the better control of systemic metastatic disease, but did not maintain significance in multivariate analysis. The dismal prognosis of patients with triple-negative breast cancer highlights the need to develop novel therapies to improve the poor survival.

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**Key words:** brain metastases, breast cancer, HER2, recursive partitioning analysis, trastuzumab, triple-negative disease.

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