186P HER2-positive breast cancer and CNS metastases: Prognostic factors and clinical outcome

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Background: Since the introduction of trastuzumab-containing therapies, patients (pts) with HER2-positive breast cancers (BC) are experiencing longer progression-free (PFS) and overall survival (OS). However, the extending life expectancy of these pts is associated with an increased incidence of distance recurrences and, particularly, central nervous system (CNS) metastases. Aim of this study is the evaluation of factors which could affect prognosis from diagnosis of CNS metastatic disease to death.

Methods: Records of pts with HER2-positive BC treated at Humanitas Cancer Center between 2000 and 2017 were retrospectively reviewed. OS was estimated by Kaplan Meier method and differences between groups by log-rank test. Cox proportional Hazard model was used to estimate Hazard ratio (HR) with 95% confidence intervals (CI). Significance was set at a p value of 0.05.

Results: Globally, 1171 pts with HER2-positive BC were retrospectively analyzed. 283 pts (24%) developed metastatic disease; 16 (6%) developed only CNS metastases, 174 (61%) other-than CNS metastases, 93 (33%) both. Among pts with CNS metastases, median age of diagnosis was significantly younger than median age of pts with other-than CNS metastases (51 years old, range 31-81 vs 57 years old, range 30-89, $p = 0.012$). The development of CNS metastases was associated with a worse prognosis, with an almost 5-fold increased risk of death compared with other-than CNS metastases (HR 4.7, CI 3.5; 6.4). Median time from diagnosis of CNS metastases to death was 13 months. The number of CNS metastatic lesions (single vs multiple lesions) was associated with a different 3-year survival (39% vs 18% $p = 0.003$). The administration of a brain radiation treatment had a favorable association with 3-year survival ($p < 0.001$). Pts who received the newest HER2-targetting therapies (pertuzumab and/or T-DM1 and/or lapatinib) had a 3-year OS of 30.6%, compared with 22.5% for those who did not receive the above mentioned treatments ($p = 0.025$).

Conclusions: Pts affected by HER2-positive BC who develop CNS metastases have a poor prognosis. A multimodality therapeutic approach shows an impact on survival, although limited. Still, greater efforts in understanding vulnerability of CNS metastases should be made.

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