Aim: HER2-positive (HER2+) breast cancer (BC) is a heterogeneous disease, with a minority of patients presenting an excellent prognosis. Recent findings suggest that the efficacy of HER2-directed therapy may differ according to hormone receptor (HR) status, and this raised the question if HR status defines different subtypes of HER2+ BC. We conducted a multicenter analysis of HER2+ early BC patients to determine relapse free survival (RFS) and overall survival (OS), and to investigate the role of HR in outcome.

Methods: We retrospectively enrolled HER2+ (IHC 3+ or 2+ amplified) early BC patients treated with adjuvant chemotherapy with or without trastuzumab (T) in 7 Italian oncologic centres until December 2011. A review of clinical and treatment data was carried out for analysis.

Results: 769 chemotherapy-treated HER2+ early BC patients have been analysed and divided into two groups, T-untreated (N = 304, cohort A), and T-treated (N = 465, cohort B). Overall, the median follow-up was 68 months (range, 1-171). Three-year RFS for cohort A was 81.3%, whereas it was 92% for cohort B (p <0.0001). Five-year OS was 88.4% and 95.8% for the cohort A and B, respectively (p = 0.0001). At multivariate analysis, in the whole population, factors related to absence of relapse were older age, earlier stage, T therapy and hormonal treatment. HR-negative disease had a trend, although not significant (p = 0.6), towards a worse 3-year RFS with respect to HR-positive disease. Overall, 356 patients have triple (ER, PgR, HER2) positive (TP) tumors, 132 in the cohort A and 224 in the cohort B, and all underwent also endocrine adjuvant treatment. Three-year RFS for TP patients was 84.6% in the cohort A and 93.7% in the cohort B (p = 0.002). Considering only TP patients with ER staining in 50% or more cancer cells (TP50), 3-year RFS was 90.6% in the cohort A and 93.3% in the cohort B (p = 0.03). Thus, in TP50-patients, addition of T to therapy provides only slight RFS benefit, suggesting a very favourable prognosis.

Conclusions: Although the benefit given by addition of T to adjuvant chemotherapy is clear in all subgroups analyzed, our data suggest the existence of a subset of TP BC, characterized by high levels of ER expression, that is driven both by HER2 and ER signalling, with a biological behaviour similar to ER-positive, HER2-negative BC.

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