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ESTROGEN RECEPTOR AS A RESISTANCE MECHANISM TO TRASTUZUMAB

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HER2-positive hormone-sensitive (HER2+/HR+) breast cancers have recently been singled out as a separate entity. It has been suggested that elevated estrogen receptor (ER) expression and/or activity may represent an avoidance mechanism or an alternative pathway leading to resistance to anti-HER2 therapy.

The aim of the study was to examine the disease outcome as the clinical benefit rate (CBR), progression-free survival (PFS), and overall survival (OS), both in the group of patients with HER2-positive metastatic breast cancer treated with first-line systemic therapy of trastuzumab along with chemotherapy and in patients with different status of hormone receptors HR+/HER2+ (ER+ and/or PR+/HER2+) compared to HR-/HER2+ (ER-/PR-/HER2+).

The study included 121 patients with pathohistologically confirmed HER2+ metastatic breast cancer treated with trastuzumab along with chemotherapy during 2017 and monitored until June 2020.

The mean age of the patients was 55.45 ± 9.83 years. 53.7% of the patients were HR-positive and 46.3% HR-negative. Progression-free survival was statistically significantly different regarding the HR status. Patients with HR- have longer PFS compared to patients with HR + (15 and 8 months, respectively). Patients with HR- tumors have a 62% lower risk of disease progression compared to HR+ tumors (HR 0.382; 95% CI 0.261-0.558, $p < 0.001$). The overall survival was statistically significantly different regarding the HR status ($p = 0.034$). Patients with HR- have longer survival compared to patients with HR+ (43 and 35 months, respectively). Hormone receptor negative tumors have a 43% lower risk of fatal outcome compared to hormone-sensitive tumors (HR 0.576; 95% CI 0.342-0.972, $p = 0.039$).

Given that HR+/HER2- tumors have a poorer outcome with trastuzumab treatment, future clinical trials should focus on the combination of hormonotherapy and anti-HER2 therapy in this subtype of breast cancers.

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