

## PRESENTATION: ORAL PRESENTATION (GENERAL SESSION)

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## 1074 – Human epidermal growth factor receptor 2-low is not a distinct subgroup in breast cancer patients undergoing neoadjuvant chemotherapy

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**Introduction:** Breast cancer is a heterogeneous disease, and patients with low expression of human epidermal growth factor receptor 2 (HER2) benefit from antibody-drug conjugate therapies.

**Objective:** To investigate the association between HER2-low status and survival and pathologic complete response (pCR) in breast cancer patients undergoing neoadjuvant chemotherapy.

**Methods:** Prospectively collected data were analyzed from 2010 to 2021 for a total of 544 patients with locally advanced breast cancer subjected to neoadjuvant chemotherapy. HER2 expression was determined by immunohistochemistry and *in situ* hybridization, and HER2-low was defined as an immunohistochemistry score of 1+ or 2+ and non-amplified *in situ* hybridization. Kaplan–Meier methods and Cox regression models were used for survival analyses, and logistic regression for pCR.

**Results:** The study identified 78 HER2-low/hormone receptor (HR)–, 90 HER2-low/HR+, 76 HER2+/HR+, 74 HER2+/HR–, 92 luminal, and 134 triple-negative breast cancers (TNBC). Overall survival was strongly associated with hormone receptor (HR) status (hazard ratio [HR] 0.5; 95% confidence interval [CI] 0.3–0.8) and clinical stage (HR 2.4; 95%CI 1.6–3.6), independent of HER2-low status. Consequently, patients were stratified into subgroups according to HR: ER+ group (HER2-low/HR+, HER2+/HR+ and luminal) and ER- group (HER2-low/HR–, HER2+/HR– and TNBC). HER2+ patients achieved the highest pCR rate (52.7% in ER- group [p<0.001] and 33% in ER+ group [p<0.001]). HER2-low/HR+ and HER2-low/HR- patients achieved similar pCR rates (6.7% and 30.8%, respectively) compared to luminal tumors (8.7%; p= 0.80) and TNBC (25.4%; p=0.50), respectively. The prognosis of HER2-low tumors was similar to that of luminal or HER2+/HR+ tumors (HR 1.2; 95%CI 0.6–2.3 and HR 2.3; 95%CI 0.8–6.3), and TNBC or HER2+/HR- (HR 0.9; 95%CI 0.6–1.5 and HR 0.8; 95%CI 0.2–3.4), respectively.

**Conclusion:** HER2-low does not define an independent predictive and prognostic subgroup.

**Ethics:** Research Ethics Committee Approval (CAAE 38438620.3.0000.5440).

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**Keywords:** breast cancer; molecular subtype; neoadjuvant therapy.