

<https://doi.org/10.29289/259453942025V35S1045>

Immunoexpression of markers related to the human epidermal growth factor receptor-type 2 (HER2) pathway in cases of pure positive HER2 breast carcinoma treated with trastuzumab

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Objective: To evaluate the immunoexpression of possible markers involved in the human epidermal growth factor receptor-type 2 (HER2) pathway in breast carcinoma with pure HER2 overexpressing treated with trastuzumab. **Methods:** This study analyzed 90 patients diagnosed with pure HER2-positive breast carcinoma treated with trastuzumab at the Brazilian Institute for Cancer Control (IBCC) and the São Paulo Hospital from the Federal University of São Paulo (HSP/Unifesp) between 2009 and 2018. Immunohistochemistry assessed HER2 pathway markers (MUC4, IGF-1, IGF-1R, EGFR, p21, p27, p53, p16, cyclin D1, PTEN, CDK4, Bcl-2, VEGF, AR, MDM2, and TNF α) in paraffin-embedded tumor and compromised lymph node samples, correlating them with clinicopathological variables. Statistical analyses were performed using the IBM Statistics Package for Social Sciences (SPSS), version 25, with p-values ≤ 0.05 considered significant. Associations were verified through Pearson's χ^2 and Fisher's exact tests, while survival analysis used the Kaplan-Meier. **Results:** Resistance to trastuzumab occurred in 40% of cases; overall survival was 4.13 years (95% confidence interval [CI] 5.1–12.5), and disease-free survival was 3.6 years (95%CI 5.1–13.1). In tumor samples, cyclin D1 correlated with nuclear grade (p=0.049) and recurrence (p=0.038); IGF-1 with tumor size (p=0.015) and death (p=0.046); and p16 (p=0.016) and PTEN (p=0.050) correlated with treatment response. Poor prognosis markers included p53 with histological grade (p=0.003) and nuclear grade (p=0.048), and IGF-1R with lymph node involvement (p=0.016). In lymph nodes, TNF α (p=0.043) and CDK4 (p=0.011) correlated with good prognosis, while p53 (p=0.045) remained a poor prognosis marker. **Conclusion:** Cyclin D1, IGF-1, p16, and PTEN showed potential as good prognosis markers, while p53 and IGF-1R were associated with worse outcomes. In lymph nodes, TNF α and CDK4 were favorable markers, whereas p53 retained its poor prognosis role.

Keywords: breast cancer; receptor, ErbB-2; trastuzumab; immunohistochemistry.