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1085 – Prognostic impact of her2-low status in patients with breast cancer: a systematic review of the literature

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Introduction: Breast cancer (BC) is a biologically heterogeneous disease and HER2 expression presents important prognostic implications. Recently, the HER2-low BC has been recognized, defined as HER2 immunohistochemistry (IHC) 1+ or 2+ without gene amplification, whereas HER2-zero tumors show no detectable expression. However, the prognostic significance of HER2-low status in BC remains unclear. This review evaluated the prognostic significance of HER2-low compared with HER2-zero in invasive BC.

Methods: The systematic review followed PRISMA guidelines and was registered in PROSPERO (CRD420261335199). Searches were conducted through the PubMed and LILACS databases using the terms “HER2-low” AND “breast cancer prognosis”, restricted to the last five years and free full text. The PICO criteria included: Participants, adult patients (≥18 years) diagnosed with invasive BC with HER2 status assessed by immunohistochemistry; intervention, HER2-low tumors, defined as HER2 1+ or HER2 2+ with negative gene amplification results; comparison, HER2-zero tumors (HER2-0); outcome, clinical prognosis, including overall survival (OS), disease-free survival (DFS), recurrence, and breast BC-specific mortality. Of the 400 articles identified and screened, 41 were included.

Results: Retrospective cohorts and secondary analyses of clinical trials evaluated HER2-negative BC across early, locally advanced, and metastatic settings. Most did not demonstrate clinically meaningful prognostic differences between HER2-low and HER2-zero tumors regarding OS or DFS, with survival curves frequently overlapping after adjustment for clinicopathological variables. However, other studies reported a modest subgroup difference. In hormone receptor-positive disease, HER2-low tumors were associated with improved DFS or lower recurrence risk. In triple-negative-BC, findings were heterogeneous, with some studies showing comparable outcomes and others reporting survival differences. Across therapeutic settings, including neoadjuvant chemotherapy and CDK4/6 inhibitor-based therapy, HER2-low status did not consistently predict survival outcomes.

Conclusion: Current evidence suggests that HER2-low BC do not present consistent prognostic difference compared with HER2-zero tumors. Further prospective studies are necessary to clarify the clinical significance of HER2-low expression.

Ethics: Public data – Literature review.

Registry: PROSPERO CRD420261335199.

Keywords: Invasive breast cancer; HER2 expression; immunohistochemistry.