

<https://doi.org/10.29289/259453942025V36S11175>

1175 – HER2MtGx score predicts high risk of recurrence and death in luminal breast cancer

Laura de Martin Coletti, Anastácia de Souza Freias, Joao Paulo Cheles de Lima, Isabela Panzeri Carlotti Buzatto, Daniel Guimarães Tiezzi

¹Universidade de São Paulo, Faculdade de Medicina – Ribeirão Preto (SP), Brazil.

²Hospital das Clínicas de Ribeirão Preto, Setor de Mastologia – Ribeirão Preto (SP), Brazil.

Introduction: Molecular profiling has been demonstrated to be a powerful tool for identifying breast cancer patients at high risk of recurrence and death. A metagene score (HER2MtGx), derived from a 31-gene signature across human epidermal growth factor receptor 2 (HER2), Luminal, and Basal subspaces, was recently proposed and shown to identify patients who do not benefit from HER2-targeted therapy.

Objective: To investigate how this model can identify high-risk patients with estrogen receptor-positive (ER+)/HER2- tumors.

Methods: Exploratory analyses were performed to assess HER2MtGx as a prognostic tool for ER+/HER2- breast cancer in the METABRIC (n=85) and TCGA (n=558) datasets. Prognostic factors (age, clinical stage, and histological grade) and the HER2, Basal and Luminal metagene scores estimated by the HER2MtGx model were used as independent variables. Survival data were right-censored at 7.5 years, and disease-specific survival was analyzed using Kaplan–Meier and Cox regression model. Time-dependent receiver operating characteristic (ROC) curve estimation was applied to survival data to estimate the best metagene score cutoff to discriminate between low- and high-risk patients.

Results: Multivariate analysis showed age (hazard ratio [HR] 1.01; 95% confidence interval [CI] 1.0–1.02), stage (stage 2: HR 2.0; 95%CI 1.4–2.9; stage 3: HR 4.5; 95%CI 2.8–7.3), grade 3 (HR 1.5; 95%CI 1.1–2.0), and the Luminal score (HR 0.7; 95%CI 0.5–0.8) as significant prognostic factors. The Luminal score classified 217 (14%) patients as high risk. The metagene risk score was not associated with stage (p=0.50). A strong association was observed with histological grade (p<0.001). Disease-specific survival was 82.0% (95%CI 80.2–85.3) in low-risk patients compared with 70.1% (95%CI 63.3–77.7) in high-risk patients (p=0.002).

Conclusion: The HER2MtGx model can identify patients at high-risk with ER+/HER2- invasive breast cancer.

Ethics: Public data.

Funding: National Council for Scientific and Technological Development (CNPq), Grant No. 307801/2025-0.

Keywords: molecular subtype; breast cancer; gene expression; computational biology.