Invasion factors uPA/PAI-1 and HER2 status provide independent and complementary information on patient outcome in node-negative breast cancer.

Abstract:

PURPOSE: The independent clinical relevance of invasion factors urokinase-type plasminogen activator (uPA)/PAI-1 and HER2 status was evaluated in lymph node-negative breast cancer patients (N = 118) without adjuvant systemic therapy after long-term follow-up of more than 10 years (median, 126 months). PATIENTS AND METHODS: Levels of uPA and its inhibitor PAI-1 were prospectively measured by enzyme-linked immunosorbent assay in primary tumor tissue extracts. HER2 gene amplification (HER2_AMP) was evaluated by fluorescence in situ hybridization (FISH; Ventana Medical Systems HER-2/neu probe; Tucson, AZ), and HER2 protein overexpression (HER2_EXP) was evaluated by immunohistochemistry (IHC; Oncogene Science antibody Ab-3; Cambridge, MA) on parallel-cut formalin-fixed paraffin-embedded tissue sections. RESULTS: uPA/PAI-1 was high (either one or both factors were high) in 44% of the tumors. HER2_AMP was detected by FISH in 33% of the patients, and HER2_EXP was found by IHC in 44% of the patients. In a multivariate analysis of established and tumor-biologic prognostic factors, uPA/PAI-1 was the only independent prognostic factor for disease-free survival ([DFS]; P<.001; relative risk [RR], 8.3; 95% confidence interval [CI], 3.4 to 20.4). Although
HER2_AMP and HER2_EXP did not reach significance for DFS, they were significant for overall survival (OS), even in multivariate analysis (HER2_AMP: \( P = .004 \); RR, 3.7; 95% CI, 1.5 to 9.2; HER2_EXP: \( P = .009 \); RR, 3.4; 95% CI, 1.4 to 8.7). CONCLUSION: After long-term follow-up, uPA/PAI-1 levels in primary tumor tissue reliably and strongly indicate an aggressive course of disease in lymph node-negative breast cancer independent of HER2 status. The particular prognostic effect of HER2 status on OS may reflect its ability to predict resistance to systemic therapy.