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PAI-1 and HER2 interaction in advanced breast cancer disease: evidence for added benefit from trastuzumab in HER2-negative patients.

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Abstract

PURPOSE:

The urokinase plasminogen activator (uPA) and the plasminogen activator inhibitor 1 (PAI-1) are associated with an aggressive course in breast cancer and are used to determine whether chemotherapy is needed in node-negative patients. The objective of the study was to evaluate the prognostic value of uPA and PAI-1 protein expression in advanced breast cancer patients treated with trastuzumab.

METHODS:

Formalin-fixed paraffin-embedded tumor tissue samples were retrospectively collected from 230 patients with advanced breast cancer treated with trastuzumab and 130 patients treated with 1st line taxanes. uPA, PAI-1, ER, PgR, HER2 and Ki67 protein expression was evaluated by immunohistochemistry.

RESULTS:

Central review of HER2 status revealed that only 144 (63 %) of the trastuzumab-treated patients were truly HER2-positive. Median survival was 50.7 months for the HER2-positive and 30.1 months for the HER2-negative patients ($p = 0.006$) treated with trastuzumab. In multivariate Cox regression analysis of the trastuzumab cohort, a significant interaction was found, in terms of survival, between HER2 status and PAI-1 protein expression in the stroma (Wald's $p = 0.002$). Positive PAI-1 protein expression in the stroma of HER2-negative patients was associated with lower risk of death (HR 0.35, 95 % CI 0.19-0.65, Wald's $p = 0.0008$). Such an association was not observed in HER2-positive patients treated with trastuzumab or in the non-trastuzumab (validation) cohorts.

CONCLUSIONS:

Our results suggest that positive stromal PAI-1 protein expression may identify a subgroup of HER2-negative advanced breast cancer patients who might benefit from treatment with trastuzumab. Further studies are warranted to validate these findings in larger cohorts.