

Triple-negative phenotype is of adverse prognostic value in patients treated with dose-dense sequential adjuvant chemotherapy: a translational research analysis in the context of a Hellenic Cooperative Oncology Group (HeCOG) randomized phase III trial.

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Source

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Abstract

PURPOSE:

It is well recognized that breast cancer is a heterogeneous disease. The purpose of the current study was to classify patients according to the immunohistochemical phenotype of their tumors in an effort to evaluate the outcome of the respective groups of patients and specifically of those with triple-negative breast cancer (TNBC) following dose-dense sequential adjuvant chemotherapy.

METHODS:

A total of 595 patients with high-risk breast cancer were treated with adjuvant anthracycline-based dose-dense sequential chemotherapy with or without paclitaxel in the context of a randomized study. ER, PgR, HER2, Ki67, EGFR, and CK5 protein expression were evaluated in 298 formalin-fixed paraffin-embedded tumor samples by immunohistochemistry (IHC). HER2 was also evaluated by chromogen in situ hybridization (CISH). HER2 status and Ki67 protein expression differentiated luminal IHC subtypes (luminal B tumors being HER2 and/or Ki67-positive).

RESULTS:

Among the 298 tumors, the immunohistochemical panel classified 37 (12%) as luminal A, 198 (66%) as luminal B, 27 (9%) as HER2 enriched, and 36 (12%) as TNBC. The median follow-up time was 97 months. Patients with luminal A tumors had the best prognosis, with improved disease-free survival (log-rank, $P = 0.033$) and overall survival ($P = 0.006$) compared with the other three tumor subtypes. The three subtypes had an increased risk for relapse and death compared with luminal A in multivariate analysis, as well. No benefit from paclitaxel treatment was detected in any of the four subtypes or the total cohort. Hierarchical clustering based on mRNA expression of ER, PgR, and HER2 by quantitative RT-PCR identified patient groups that were comparable to the subtypes identified by IHC.

CONCLUSIONS:

The results of this study confirm that triple negative, luminal B and HER2-enriched phenotypes identified by IHC are of adverse prognostic value in high-risk breast cancer patients treated with dose-dense sequential adjuvant chemotherapy.