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Prognostic significance of RACGAP1 mRNA expression in high-risk early breast cancer: a study in primary tumors of breast cancer patients participating in a randomized Hellenic Cooperative Oncology Group trial.

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Source

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Abstract

PURPOSE:

RACGAP1 is a Rac GTPase-activating protein involved in cell growth regulation, cell transformation and metastasis. The aim of the present study was to explore the prognostic and/or predictive significance of RACGAP1 mRNA expression on disease-free survival (DFS) and overall survival (OS) in high-risk early breast cancer patients and compare it to that of Ki67 protein expression and to the Nottingham prognostic index (NPI).

METHODS:

A total of 595 high-risk breast cancer patients were treated in a two-arm trial evaluating postoperative dose-dense sequential chemotherapy with epirubicin followed by CMF with or without paclitaxel. RNA was extracted from 314 formalin-fixed paraffin-embedded primary tumor tissue samples followed by one-step quantitative RT-PCR for assessing RACGAP1 mRNA expression.

RESULTS:

High RACGAP1 mRNA expression (above the median) was associated with poor DFS (log-rank, $p = 0.002$) and OS ($p < 0.001$). High histological grade, as well as high Ki67 protein expression, was more frequent in the high-expression group of RACGAP1. Results of the Cox multivariate regression analysis revealed that high RACGAP1 mRNA expression independently predicted poor overall survival (Wald's $p = 0.008$). High Ki67 protein expression was also an adverse prognostic factor for death ($p = 0.016$), while high NPI score values were not.

CONCLUSIONS:

High RACGAP1 mRNA expression, as assessed by qRT-PCR, was found to be of adverse prognostic significance in high-risk early breast cancer patients treated with dose-dense sequential chemotherapy. The utility of RACGAP1 mRNA expression in patient selection for treatment with aggressive chemotherapy regimens should be further explored and validated in larger cohorts.