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Molecular subtypes of breast cancer in relation to paclitaxel response and outcomes in women with metastatic disease: results from CALGB 9342

Lyndsay N Harris[1], Gloria Broadwater[2], Nancy U Lin[1], Alexander Miron[1], Stuart J Schnitt[3], David Cowan[4], Jonathan Lara[5], Ira Bleiweiss[6], Donald Berry[7], Matthew Ellis[8], Daniel F Hayes[9], Eric P Winer[1] and Lynn Dressler[4]

[1]Dana-Farber Cancer Institute, 44 Binney Street, Boston, Massachusetts 02115, USA
[2]Duke University Medical Center, 2301 Erwin Road, Durham, North Carolina 27710, USA
[3]Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Boston, Massachusetts 02215, USA
[4]University of North Carolina, 250 East Franklin Street, Chapel Hill, North Carolina 27514, USA
[5]St. Barnabas Medical Center, 94 Old Short Hills Road, Livingston, New Jersey 07039, USA
[6]Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, New York 10029, USA
[7]MD Anderson Cancer Center, 1515 Holcolmb Boulevard, Houston, Texas 77030, USA
[8]Washington University Medical Center, 660 S. Euclid Avenue, St. Louis, Missouri 63110, USA
[9]University of Michigan Comprehensive Cancer Center, 1500 E. Medical Center Drive, Ann Arbor, Michigan 48109, USA

Corresponding author: Lyndsay N Harris, lyndsay.harris@yale.edu

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Abstract

Introduction The response to paclitaxel varies widely in metastatic breast cancer. We analyzed data from CALGB 9342, which tested three doses of paclitaxel in women with advanced disease, to determine whether response and outcomes differed according to HER2, hormone receptor, and p53 status.

Methods Among 474 women randomly assigned to paclitaxel at a dose of 175, 210, or 250 mg/m^2, adequate primary tumor tissue was available from 175. Immunohistochemistry with two antibodies and fluorescence *in situ* hybridization were performed to evaluate HER2 status; p53 status was determined by immunohistochemistry and sequencing. Hormone receptor status was obtained from pathology reports.

Results Objective response rate was not associated with HER2 or p53 status. There was a trend toward a shorter median time to treatment failure among women with HER2-positive tumors (2.3 versus 4.2 months; $P = 0.067$). HER2 status was not related to overall survival (OS). Hormone receptor expression was not associated with differences in response but was associated with longer OS ($P = 0.003$). In contrast, women with p53 over-expression had significantly shorter OS than those without p53 over-expression (11.5 versus 14.4 months; $P = 0.002$). In addition, triple negative tumors were more frequent in African-American than in Caucasian patients, and were associated with a significant reduction in OS (8.7 versus 12.9 months; $P = 0.008$).

Conclusion None of the biomarkers was predictive of treatment response in women with metastatic breast cancer; however, survival differed according to hormone receptor and p53 status. Triple negative tumors were more frequent in African-American patients and were associated with a shorter survival.

Introduction

The taxanes (paclitaxel and docetaxel) are among the most active drugs for treatment of breast cancer and are an important component of treatment in the neoadjuvant, adjuvant, and metastatic settings. These drugs act, at least in part, by stabilizing microtubules and inducing G_2/M arrest, with subsequent apoptosis in malignant cells. Paclitaxel, the first taxane that was developed, has substantial antitumor activity. As a result,

CALGB – Cancer and Leukemia Group B; CI = confidence interval; ER = estrogen receptor; FISH = fluorescent *in situ* hybridization; HER = human epidermal growth factor receptor; IHC = immunohistochemistry; NSABP = National Surgical Adjuvant Breast and Bowel Project; OS = overall survival; PR = progesterone receptor; TTF = time to treatment failure.