

ASCO 2010 Abstract #511

Potential biologic causes of the racial survival disparity in adjuvant trials of ER-positive breast cancer.

Author(s): K. S. Albain, W. E. Barlow, S. Shak, G. N. Hortobagyi, D. F. Hayes, for The Breast Cancer Intergroup of North America; Loyola University Medical Center, Maywood, IL; Cancer Research and Biostatistics, Seattle, WA; Genomic Health, Redwood City, CA; University of Texas M. D. Anderson Cancer Center, Houston, TX; University of Michigan Medical Center, Ann Arbor, MI

Background: An analysis of SWOG adjuvant breast cancer clinical trials (n = 6,676) found African American (AA) patients (pts, n = 662) had significantly worse survival than others (adjusting for treatment, tumor factors, BMI and SES) overall and in ER-positive (ER+) and ER-negative cohorts separately (JNCI 2009; 101:984). As triple negativity could not fully explain the disparity, we analyzed the ER+ S8814 phase III study to assess if level of ER-positivity or expression of single genes within the 21-gene Recurrence Score (RS) assay might inform this critical issue.

Methods: S8814 (ER+, node+, postmenopausal: tamoxifen vs. CAF plus tam; Lancet 2009; 374:2055) was analyzed for disease-free survival (DFS) and overall survival (OS) for AA vs. others, adjusting for other factors. Within the subset available for RS analysis of prognosis/prediction of CAF benefit (Lancet Oncol 2010; 11:55), outcome of AA vs. others was assessed overall; and by ER level, the composite RS, and each of the genes analyzed by RT-PCR.

Results: Of 1,477 pts, 139 (9%) were AA, who derived similar benefit from CAF as did others. However, outcomes were worse for AA after adjusting for treatment and other prognostic factors: DFS AA vs. others HR = 1.44 and for OS = 1.70. 27 of 367 pts in the RS sample were AA, for whom DFS was also worse (logrank p = 0.073; adjusted HR 1.65; 5-year DFS 67% AA, 79% others). There was no significant difference in RS by race, although fewer AA had low RS (33% vs. 40%) and more had high RS (41% vs. 32%). There was no significant difference by race in ER level by Allred IHC score or by RT-PCR for each of the 4 ER genes. However, all 5 genes in the proliferation group by RT-PCR had higher quantitative gene expression in AA vs others (p < 0.05 for CCNB1, MKI17, MYBL2, BIRC5; p = 0.051 for AURKA). While Cox regression models that adjusted for nodes, CAF and RS made a marginal impact on the DFS HR by race (1.60), the HR decreased substantially to 1.23 upon adjustment for proliferation.

Conclusions: AA on ER+ early breast cancer trials have worse survival than others, due in large part to tumors with higher proliferation and not to differences in degree of endocrine responsiveness. If confirmed in other studies, this finding might impact choice of adjuvant therapy.