RE: A two-gene expression ratio predicts clinical outcome in breast cancer patients treated with tamoxifen

We recently reported a novel biomarker of two-gene expression ratio that outperformed the current positive and negative predictors of outcome in patients with estrogen receptor (ER)-positive early-stage breast cancer treated with adjuvant tamoxifen (Ma et al., 2004). While the cases in our original 60-patient discovery cohort were closely matched for tumor size, grade, and lymph node status (28 cases node-negative, 25 node-positive and 7 cases not evaluated), almost all cases (19/20) in the initial validation cohort were lymph node-negative. The bias toward lymph node-negative patients in our initial validation cohort was not by design, but was consistent with the fact that lymph node-positive patients usually receive chemotherapy in addition to adjuvant tamoxifen (EBCTCG, 1998) and would have been excluded from our study. Subsequent to this publication, we have further assessed the predictive power of this two-gene ratio biomarker in an independent cohort of breast cancer patients from a randomized prospective clinical trial of adjuvant tamoxifen (D. Sgroi et al., 2004, ASCO Annual Meeting Proceedings, abstract). Results from this study confirm our initial observations and suggest that the two-gene signature is a more robust predictor in lymph node negative patients, as compared with lymph node positive patients. We are currently carrying out additional studies using archived tissue samples from large randomized prospective trials of adjuvant tamoxifen to further evaluate the clinical utility of our gene expression ratio biomarker.

Dennis C. Sgroi,[1,2,*] Daniel A. Haber,[1] Paula D. Ryan,[1] Xiao-Jun Ma,[3] and Mark G. Erlander[3]

[1]Department of Pathology, Harvard Medical School
Molecular Pathology Research Unit
Massachusetts General Hospital
Boston, Massachusetts 02129
[2]Massachusetts General Hospital Cancer Center
Harvard Medical School
Boston, Massachusetts 02129
[3]Arcturus Bioscience, Inc., 400 Logue Avenue
Mountain View, California 94043
*Correspondence: dsgroi@partners.org

References

Ma, X.J., Wang, Z., Ryan, P.D., Isakoff, S.J., Barmettler, A., Fuller, A., Muir, B., Mohapatra, G., Salunga, R., Tuggle, J.T., et al. (2004). A two-gene expression ratio predicts clinical outcome in breast cancer patients treated with tamoxifen. Cancer Cell 5, 607–616.

Early Breast Cancer Trialists' Collaborative Group (EBCTCG). (1998). Tamoxifen for early breast cancer: An overview of the randomized trials. Lancet 351, 1451–1467.