

Can we identify a group of breast cancer patients with a good prognosis despite four or more positive (4+) axillary nodes using a tissue microarray (TMA)?

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Background: Although breast cancer with 4+ axillary lymph nodes generally carries a poor prognosis, we hypothesized that a good prognostic subgroup of such patients would be identifiable by immunohistochemical (IHC) biomarkers.

Methods: Patients with primary breast cancer with 4+ axillary nodes and no metastatic disease at diagnosis were identified from a large clinically annotated TMA of formalin-fixed paraffin-embedded archival breast cancers and analyzed for eight IHC based biomarkers: estrogen receptor, HER2, carbonic anhydrase IX, EGFR, CK 5/6, progesterone receptor, p53, Ki67. Expression of each biomarker was scored 0 or 1 to indicate good or bad prognosis based on univariate analysis of relapse free survival (RFS). Patients were banded as having a total score of 0 (i.e. each biomarker predicted a good outcome), 1-4 or 5-8. Kaplan Meier and Cox regression analysis of RFS outcomes was performed. 10 year RFS for each band was compared to the mean of predicted outcomes based on the prognostic tool Adjuvant! (www.adjuvantonline.com).

Results: 313 eligible patients were identified and complete data were available for 228. The subset of 228 was similar to the larger group of 313 with respect to RFS and conventional prognostic factors. 10 year RFS for the 228 patients was 39.5% (standard error, SE 3.4%). The subgroup of 37 (16%) scoring zero for all 8 biomarkers had a mean 10 year RFS of 77.6% (SE 7.0). Mean 10 year RFS for the bands scoring 1-4 (154 patients, 68%) and 5-8 (37 patients, 16%) were 34.9% (SE 4.1) and 19.0% (SE 6.9) respectively. Mean 10 year RFS predictions by Adjuvant! were 35.9% (SE 2.6), 34.5% (SE 1.2) and 34.3% (SE 2.3) respectively. In multivariate analysis with conventional prognostic factors, the banded biomarker score retained statistical significance for predicting RFS ($p=0.0007$) along with estrogen receptor status ($p=0.03$) and tumour size ($p=0.01$).

Conclusions: This TMA biomarker panel identified a breast cancer subgroup with good prognosis despite extensive axillary node involvement. Long term outcome was markedly better than that predicted by conventional prognostic factors. If validated, treatment decisions and clinical trial stratification might be modified using this new score.