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CORRESPONDENCE

Re: Clinical Validity/Utility, Change in Practice Patterns, and Economic Implications of Risk Stratifiers to Predict Outcomes for Early-Stage Breast Cancer: A Systematic Review

In a recent issue of the Journal, Hornberger et al. (1) systematically reviewed the clinical validity/utility of early breast cancer (EBC) risk stratifiers using Simon's standardized level-of-evidence (LOE) grading (2). The authors focused mainly on multigene predictors, selecting four gene expression signatures, one immunohistochemistry-based risk classifier, and the Adjuvant! Online decision tool.

To have a complete picture on the topic of EBC risk stratifiers, we think it is also important to consider the risk classifiers serine protease urokinase-type plasminogen activator (uPA) and its inhibitor plasminogen activator inhibitor type 1 (PAI-1). Indeed, in the "American Society of Clinical Oncology 2007 Update of Recommendations for the Use of Tumor Markers in Breast Cancer" (3), Harris et al. identified uPA and PAI-1 as LOE 1 markers in node-negative EBC. The results of the prospective, randomized ChemoN0 trial on the clinical utility of this risk stratifier have been published (4), and results of the randomized NNBC3 trial are awaited in 2013 (5).

Therefore, according to the grading system described by Simon et al. (2), uPA and PAI-1 are currently the only LOE 1, category A (ie, based on the results of prospective, randomized trials) markers for risk stratification in EBC. Conversely, the 21-gene recurrence score should be presently graded, at best, as LOE 1, category B evidence (ie, based on data obtained using archived specimens) because, as stated by Hornberger et al. (1), no category A study on any of the EBC risk stratifiers they selected has been completed. Indeed, although archived specimens can be used to provide reliable evaluations of the clinical validity of biomarkers, nothing can replace a prospective, randomized trial to validate a biomarker.

We thus consider it important to highlight the existence of the LOE 1, category A uPA and PAI-1 risk stratifiers and to specify that the 21-gene recurrence score is at best LOE 1, category B evidence (while waiting for the results of category A studies) in the framework of a global and systematic overview of risk stratifiers in EBC.

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