Commentary: Improving Breast Cancer Testing for Patients—The Secret Sauce Is Collaboration

By M. Elizabeth H. Hammond, MD

Breast cancer treatment is becoming increasingly personalized, as more and more studies appear that define the molecular basis of treatment response. As many as two thirds of breast cancers are estrogen receptor (ER) and/or progesterone receptor (PgR) positive, with their growth influenced by activation of the ER pathway. The purpose of ER/PgR testing is to identify patients with breast cancer whose tumors express ER and/or PgR (hormone receptor positive) and who should therefore be considered candidates for treatment with endocrine therapies, which may include options like tamoxifen, an aromatase inhibitor, and/or suppression of ovarian function, as appropriate. These treatments can substantially improve survival in patients with hormone receptor–positive invasive breast cancer.

Immunohistochemistry (IHC) is an established assay to determine the ER/PgR status of a tumor by measuring protein amounts of ER and PgR in breast cancer cells. However, up to 10% to 20% of IHC test results throughout the world may be inaccurate (false positive or false negative). This significant level of testing inaccuracy led ASCO and the College of American Pathologists (CAP) to convene an expert panel to address the causes of the inaccuracies and develop a guideline to improve testing performance. The guideline¹ was published in June 2010 jointly by *Journal of Clinical Oncology* and *Archives of Pathology and Laboratory Medicine*, and a summary² appears in this issue of *Journal of Oncology Practice*.

The guideline builds on a previous successful collaboration between ASCO and CAP resulting in a guideline for HER2 testing in breast cancer. In both documents, the principal strategies for improving testing accuracy are specified: specimen handling, testing parameters, reporting requirements, and quality assurance (QA) programs. The guideline defines the threshold for a positive ER or PgR test; defines specimen handling requirements; and emphasizes appropriate use of QA practices, including laboratory proficiency testing and accreditation by agencies such as CAP that require adherence to guideline elements.

For ER/PgR testing, the emphasis on specimen handling has been strengthened. Data have recently been published that illustrate the serious consequences of treatment delay as a result of fixation on testing accuracy. A recently published study³ from Intermountain Healthcare found that samples taken on weekends were much more likely to be ER negative than those taken during the week. Studies conducted in Asian countries by Nichols et al⁴

showed that breast cancer specimens in those countries were usually ER negative unless specimen handling issues were addressed. Laboratories are now required to record the time the tumor was removed, the time the tissue was placed in fixative, and the fixative duration. Remotely obtained specimens should be bisected and placed in fixative to be sure that the tumor is quickly exposed to fixative.

Increased attention to simple measures such as the handling of tissue specimens, the uniform fixation of specimens, the standardization and validation of lab assays, rigorous reporting procedures, and greater access to treatment interventions has the potential to significantly improve breast cancer outcomes around the world. Collaboration among medical specialists is necessary to achieve the best patient outcomes.

The ASCO/CAP Panel chose to specifically focus on IHC assays for ER/PgR testing based on its widespread use, its worldwide impact, and the large body of evidence available. In the future, the ASCO/CAP Panel may review new methods and predictive assays to identify patients most likely to benefit from endocrine therapies as new high-level data on validated assays and outcomes become available.

In conjunction with the publishing of the guideline, ASCO and CAP have developed clinical tools and resources for oncologists and pathologists that summarize the findings and recommendations. These resources include a slide presentation on the ASCO Web site and the guideline summary in *JOP*. In addition, CAP has developed a Breast Predictive Factors Testing Certificate Program and associated Continuing Medical Education, which will also allow pathologists to gain special expertise in the development and implementation of these tests. Patients seeking additional information should visit MyBiopsy.org.

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Author's Disclosures of Potential Conflicts of Interest

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