Ancillary Prognostic and Predictive Testing in Breast Cancer

Focus on Discordant, Unusual, and Borderline Results

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KEYWORDS

• ER testing • HER2 testing • Fluorescence in situ hybridization (FISH) • Molecular testing • Breast cancer • OncotypeDX • Predictive testing

ABSTRACT

Ancillary testing in breast cancer has become standard of care to determine what therapies may be most effective for individual patients with breast cancer. Single-marker tests are required on all newly diagnosed and newly metastatic breast cancers. Markers of proliferation are also used, and include both single-marker tests like Ki67 as well as panel-based gene expression tests, which have made more recent contributions to prognostic and predictive testing in breast cancers. This review focuses on pathologist interpretation of these ancillary test results, with a focus on expected versus unexpected results and troubleshooting borderline, unusual, or discordant results.

ROLE OF ANCILLARY TESTS IN BREAST CANCER TREATMENT

OVERVIEW

To serve as a valued member of a breast cancer treatment team, today's practicing surgical pathologist needs to learn to think like a "diagnostic oncologist" with an in-depth understanding of the treatment implications of the details of the their cancer diagnoses.[1–6] This is especially critical when performing or interpreting additional prognostic and predictive markers because these have become the primary branch-point in clinical decision-making algorithms for breast cancer treatment. The pathologist's role in the breast cancer treatment team has changed from just rendering a diagnosis of breast cancer, to providing translation and integration of all the available biologic information on an individual patient's cancer, such that the treatment team and patient can make individualized treatment decisions for each unique case (**Fig. 1**).

Key Points

ROLE OF ANCILLARY TESTING IN BREAST CANCER

- Breast cancer treatment guidelines organize patients into different treatment groups on the basis of hormone receptor and HER2 test results
- The 8th edition of the American Joint Committee on Cancer staging manual adds a clinical Prognostic Staging system that includes traditional TNM plus results of ancillary tests

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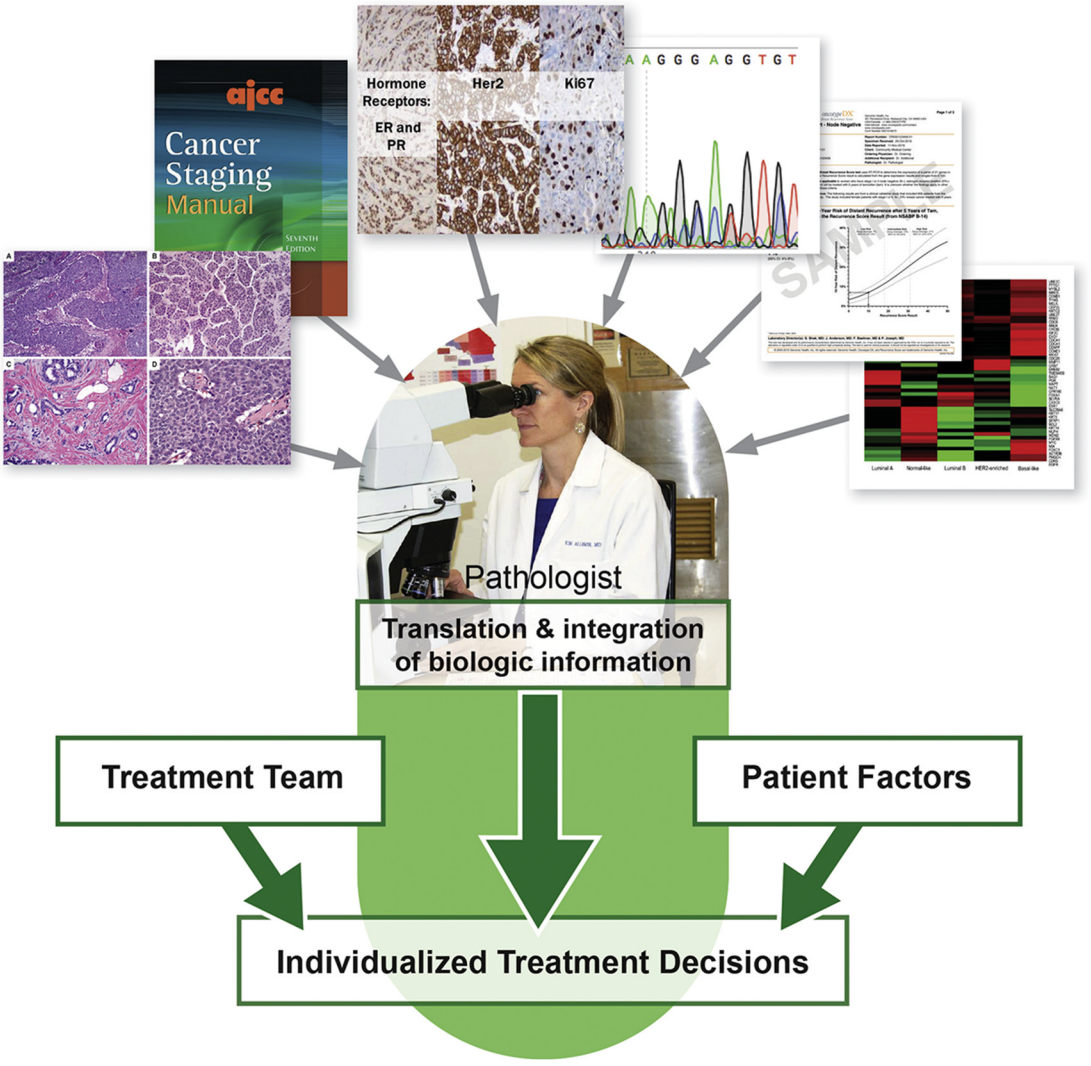

Fig. 1. Predictive and prognostic ancillary testing in breast cancer have increasingly placed the pathologist in a new role as a "diagnostic oncologist" who performs, interprets, and integrates pathology data on each patient's tissue such that individualized treatment decisions can be made.

Most breast cancer treatment guidelines, such as the National Comprehensive Cancer Network (NCCN) guidelines and St Gallen recommendations, are organized by hormone receptor and human epidermal growth factor receptor 2 (HER2) status.[7–9] It is critical that these test results are correct because treatment algorithms are different for breast cancers grouped into the following categories: (1) estrogen receptor (ER)-positive, HER2-negative, (2) ER-positive, HER2-positive, (3) ER-negative, HER2-positive, and (4) negative for ER and HER2.[10] Molecular data on gene expression also support segregation of breast cancers into similar groups with hormone receptor expression associated with the luminal molecular subtypes, HER2 overexpression associated with the HER2-enriched subtype and the "triple-negative" breast cancers associated with the basal-like molecular subtype.[11–18] However, the overlap of these groups as defined by gene expression versus traditional immunohistochemistry (IHC)/in situ hybridization (ISH) is imperfect.[19] In addition, gene expression profiling results are subject to variability by testing platform and are currently not as accessible as traditional testing methods.[20–22] As such, most treatment guidelines use the well-validated, traditional hormone receptor and HER2 biomarkers (as assessed by IHC or ISH) as the basis for treatment recommendations. A rough overview of how these ancillary markers are associated with clinical and pathologic characteristics, as well as the gene expression/molecular subtypes, is shown in **Fig. 2**.