Individualizing Care for Women With Early-Stage Breast Cancer: The Role of Molecular Assays

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Traditionally, a variety of factors were used to make adjuvant treatment decisions in breast cancer, but none of those factors, except grade, has a consistent association with sensitivity to chemotherapy or endocrine therapy. However, oncologists now are able to use molecular assays as a component of decision making for adjuvant therapy. This article focuses on the use of two of those molecular assays and their implications for nurses.

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Breast cancer is the most common cancer affecting women in the United States. In 2013, an estimated 232,340 new cases will be diagnosed in the United States (American Cancer Society [ACS], 2013). Several well-established factors are associated with an increased risk of breast cancer, including family history, nulliparity, early menarche, advanced age, and a personal history of breast cancer (ACS, 2013).

Of all women with breast cancer, 5%–10% may have a germline mutation of the *BRCA1* and *BRCA2* genes (ACS, 2013). Cancer genetics primarily focuses on the likelihood of developing cancer, but genomics is the study of how genes interact and are expressed as a whole. Certain genomics and gene expression profiling tools focus on the cancer itself and can determine the aggressiveness of the cancer (prognosis) and the likely benefit from treatment (prediction).

Breast cancer has several biologic subtypes that have distinct behavior and responses to treatment, including estrogen receptor– (ER) or progesterone receptor (PR)–positive, HER2-positive, and triple-negative (ER/PR/HER2-negative) (see Figure 1). ER is expressed in 75% of breast cancers overall and is slightly more common in postmenopausal women and less in younger women (Osborne & Schiff, 2011). ER expression is related to patient age and correlates with lower tumor grade, lower tumor proliferation, less aneuploidy, less frequent amplification of HER2 and concomitant loss of the p53 tumor suppressor gene, positive expression of PR, metastases, and lower rates of disease recurrence (Osborne & Schiff, 2011).

In the past, oncologists struggled to determine prognosis and chemotherapy treatment for patients with early-stage, ER-positive breast cancer. Traditionally, factors used to make treatment decisions included patient age, size of tumor, lymph node status, histologic grade, ER or HER2 status, and comorbid illness (Paik et al., 2004) (see Figure 2). Unfortunately, none of those factors, with the exception of grade, has a consistent association with sensitivity to chemotherapy or endocrine therapy. Weighing those factors, oncologists would provide subjective recommendations for treatment, leading to variable recommendations among oncologists. Based on those recommendations, many patients received adjuvant systemic chemotherapy with limited benefit but substantial toxicity.

Breast oncologists now are able to use molecular assays as a component of decision making for adjuvant therapy and to distinguish the patients that might benefit most from a combination of endocrine therapy and chemotherapy versus endocrine monotherapy. Molecular markers promise the ability to estimate prognoses and predict responses to particular treatments with greater precision than is possible with clinical findings alone. The markers ultimately would allow the care of patients with cancer to be more individualized (Bast & Hortobagyi, 2004). Available data suggest that information generated from genomic tests has resulted in a change in treatment decision making in 25%–30% of breast cancer cases (Lo et al., 2010).

Two of the molecular assays for breast cancer treatment are Oncotype DX® and MammaPrint®. They provide better data to predict clinical outcome than the traditional anatomic and pathologic data and standards.

21-Gene Assay

Oncotype DX is a 21-gene reverse transcription polymerase chain reaction assay that measures the expression of 21 genes. Those genes include 16 cancer-related genes and five reference genes. The genes are identified in the RNA extracted from formalin-fixed, paraffin-embedded samples of tissue from primary breast cancer.

To establish the levels of expression of the 21 genes, the genes are manipulated by an empirically derived, prospectively defined mathematical algorithm to calculate a recurrence score (RS). That score is used to assign a patient to one of three groups by estimated risk of distant