# Accurate Identification of HER2-Positive Patients Is Essential for Superior Outcomes With Trastuzumab Therapy

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**Purpose/Objectives:** To review the clinical significance, methods of testing, and outcomes of trastuzumab (Herceptin®) treatment for *HER2* gene amplification and HER2 protein overexpression in breast cancer.

**Data Sources:** Published articles and abstracts, online resources, a clinical handbook, and product information.

**Data Synthesis:** *HER2* gene amplification or HER2 protein overexpression can be found in 20%–25% of breast cancers and is important pathogenic and prognostic information. HER2 also predicts patient response to trastuzumab. Patients with HER2-positive metastatic breast cancer benefit from trastuzumab whether selected by immunohistochemistry, which measures the HER2 protein, or fluorescence in situ hybridization (FISH), which measures the *HER2* oncogene. However, patients who are identified accurately as *HER2* gene-amplified by FISH derive the greatest benefit.

**Conclusions:** Accurate testing is crucial for appropriate identification of patients for trastuzumab therapy. FISH is the most reproducible and accurate method.

**Implications for Nursing:** Education regarding HER2 testing and trastuzumab helps patients to make informed decisions and facilitates active participation in their care as well as enhances dialogue with physicians.

## Key Points . . .

- HER2 testing is recommended for all newly diagnosed patients with breast cancer because *HER2* gene amplification or HER2 protein overexpression correlates with poor clinical outcomes.
- HER2 testing is critical because HER2-positive patients may benefit from trastuzumab therapy, which has been shown to significantly improve response rates, time to disease progression, and overall survival.
- Immunohistochemistry and fluorescence in situ hybridization (FISH) have been approved for the determination of HER2 status; however, FISH has demonstrated superior sensitivity and specificity. Patients with *HER2* gene amplification by FISH have been shown to benefit from trastuzumab therapy.

Breast cancer is the most commonly diagnosed cancer among women and the second leading cause of cancer death (Jemal et al., 2005). The American Cancer Society estimated that more than 211,000 new cases of breast cancer would be diagnosed in the United States in 2005 and more than 40,000 women would die as a result of the disease (Jemal et al.). Breast cancer survival is determined by a variety of prognostic and predictive indicators. Breast cancer's prognostic factors (e.g., tumor size and type, number of positive lymph nodes, nuclear grade, absence or presence of estrogen and/or progesterone receptors) (National Comprehensive Cancer Network [NCCN], 2005; Rosenzweig, Rust, & Hoss, 2000) influence the clinical outcome of the disease regardless of treatment, whereas predictive factors, such as HER2 overexpression or amplification, correlate with prognosis because they are linked to patients' responses to particular therapies.

Several newly recognized prognostic and predictive factors have begun to be used in the management of breast cancer (NCCN, 2005). One factor is the human epidermal growth factor receptor-2, or HER2. Overexpression of HER2 is associated strongly with a poor prognosis in breast cancer, indicating a more aggressive disease and shortened overall survival (Slamon et al., 1987, 1989). The five-year overall survival rate for HER2-positive patients is significantly shorter than for those who are HER2 negative (58% versus 77%, respectively; p = 0.004) (Sjogren, Inganas, Lindgren, Holmberg, & Bergh, 1998). Using multivariate survival analysis, Slamon et al. (2001) found *HER2* gene amplification to be more predictive for clinical outcome than any other prognostic factor, with the exception of the number of positive lymph nodes (Slamon et al., 1987, 1989). NCCN and American Society of Clinical Oncology (ASCO) guidelines recommended HER2 testing for all patients with newly diagnosed breast cancer (Bast et al., 2001; NCCN). HER2 testing is critical because of the demonstrated survival benefit of trastuzumab (Herceptin®, Genentech, Inc., South San Francisco, CA) therapy in combination with chemotherapy for

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