

HER-2/neu, Serum

FOR MONITORING SOLUBLE HER-2/NEU PROTEIN IN PATIENTS WITH METASTATIC BREAST CANCER.

Test Highlights

- In HER-2/neu-positive metastatic breast cancer patients, concentrations of serum HER-2/neu reflect disease progression and response to therapy, regardless of the treatment regimen.
- Serum HER-2/neu testing can help detect HER-2/neu-positive tumors in patients whose primary tissue tests were initially HER-2/neu negative.
- Changes in the concentration of serum HER-2/neu reflect clinical response to trastuzumab-based therapy.

Disease Overview

- Breast cancer is the most common malignancy in women. Approximately 15–20 percent of breast cancers show amplification in the human epidermal growth factor receptor-2 gene (HER-2). Also referred to as HER-2/neu, amplification of this gene is the primary mechanism of HER-2/neu overexpression. This overexpression leads to increased dimerization and subsequent activation of the HER-2/neu tyrosine kinase which, in turn, results in increased cellular replication. HER-2/neu positivity is associated with a poor prognosis (higher rate of recurrence and mortality) and is usually associated with resistance to endocrine therapies.
- Targeted therapies directed against the extracellular portion of HER-2/neu are able to inhibit HER-2/neu-overexpressing breast cancers. Trastuzumab (Herceptin®) has been shown to prolong the overall survival of patients with metastatic breast cancer whose tumors overexpress HER-2/neu. Trastuzumab reduces the risk of recurrence by one-half and mortality by one-third. Due to high drug costs and cardiac toxicity, the clinical use of trastuzumab requires the identification of susceptible patient populations whose tumors overexpress HER-2/neu.
- Assessment of tissue HER-2/neu status is determined by immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH) and is the standard for the evaluation of newly diagnosed carcinomas of the breast. Although these tissue tests are approximately 80–85 percent accurate in determining HER-2/neu status, studies show that HER-2/neu status of the primary breast cancer does not always accurately reflect the HER-2/neu status of metastatic breast cancer.¹

Pathophysiology

The extracellular domain of HER-2/neu can be released from normal or malignant cells and can be reproducibly and accurately measured in serum.

Indications for Ordering

- Monitor response to metastatic breast cancer therapy.
- Identify patients with an elevated serum HER-2/neu but a negative HER-2/neu tissue test.
- Predict therapeutic response and clinical course of metastatic breast cancer.

Clinical Utility

- In a multicenter study of 307 patients with metastatic breast cancer receiving trastuzumab-based therapies, patients who did not achieve a more than 20 percent decline in serum HER-2/neu had a lower response rate, a shorter duration of response, a shorter time to disease progression, and an overall decreased survival compared to those who did achieve a decrease of more than 20 percent.²
- A significant decrease in serum HER-2/neu from baseline concentrations was observed in a study of 55 metastatic breast cancer patients who experienced an objective response to trastuzumab-based therapy as early as day eight of treatment onward. In contrast, serum HER-2/neu concentrations in patients with progressive disease demonstrated no significant change.³
- In a study of 58 metastatic breast cancer patients, 12 percent were HER-2/neu negative in the primary tumor but HER-2/neu positive in the metastases.¹ Similarly, numerous reports have demonstrated that approximately 30 percent of women with HER-2/neu negative primary breast cancer can develop elevated serum HER-2/neu concentrations when diagnosed with metastatic disease.⁴ Together, these results suggest that serum HER-2/neu may be useful as a surrogate marker for the presence of HER-2/neu positive tumor and might identify patients who could potentially benefit from trastuzumab-based therapies.

Limitations

- Serum HER-2/neu is a test to complement, not replace, testing for HER-2/neu in tissue.
- Serum HER-2/neu should be performed at the time that metastatic breast cancer is diagnosed to establish a baseline concentration.
- The clinical utility of serum HER-2/neu as a prognostic indicator for early recurrence has not been fully established.

Methodology

HER-2/neu is measured using a commercially available two-site enzyme-linked immunosorbent assay (HER-2/neu, Siemens Medical Solutions Diagnostics). Trastuzumab therapy does not interfere with test performance.

References

1. Zidan J, et al. Comparison of HER2 overexpression in primary breast cancer and metastatic sites and its effect on biological targeting therapy of metastatic disease. *Br J Cancer* 2005; 93:552–6.
2. Ali SM, et al. Serum HER-2/neu and relative resistance to trastuzumab-based therapy in patients with metastatic breast cancer. *Cancer* 2008; 113:1294–301.
3. Köstler WJ, et al. Monitoring of serum Her-2/neu predicts response and progression-free survival to trastuzumab-based treatments in patients with metastatic breast cancer. *Clin Cancer Res* 2004; 10:1618–24.
4. Carney WP, et al. HER-2/neu diagnostics in breast cancer. *Breast Cancer Res* 2007; 9:207–17.

Test Information

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For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.