Lot 1:

The Serum HER-2 Blood Test Can Provide Valuable Clinical Information in both HER-2 Positive and HER-2 Negative Metastatic Breast Cancer Patients.

The HER-2 oncogene encodes a transmembrane tyrosine kinase growth factor receptor that is expressed on cells of epithelial origin. The full length glycoprotein has a molecular weight of 185,000 Daltons (p185) with a 97-115kDa extracellular domain (ECD) that is released into circulation and can be measured in the serum component of blood in both normal individuals and cancer patients. The Oncogene Science serum HER-2 (sHER-2) ELISA test measures the level of the ECD by using 2 monoclonal antibodies to the ECD that capture and quantitate HER-2 levels in serum (1&2). Numerous clinical studies demonstrate that monitoring changes (increases or decreases) in sHER-2 levels in metastatic breast cancer (MBC) patients can be an early indicator of cancer progression or response to therapy and correlates with clinical status (2-17). In fact, increasing sHER-2 levels can precede progression by up to 2 years prior to clinical symptoms (18). Clinical studies have shown that a normal sHER-2 level is < 15 ng/mL while an elevated (above normal) level is 15 ng/mL or greater (2). The prevalence of elevated sHER-2 levels greater than 15 ng/mL is 10–15% (5–22.9%) in primary breast cancer (3) and as high as 90% of MBC patients (4,5). An increase or decrease of 20% or more from one patient blood draw to another is a significant change in the HER-2 level. An increase of 20% or more reflects disease progression while decreases of greater than 20% reflect therapy response or stable disease (2, 10-12).   In a recent report by Petersen et al, 48 HER-2 tissue positive patients treated with Trastuzumab for up to six years or until death were monitored with the sHER-2 test. A significant decrease in sHER-2 of ≥20% correlated with no disease progression in 20 out of 21 clinical courses while a significant increase in serum HER-2 of ≥20% correlated with disease progression in the disease in 40 out of 44 clinical courses. Patients with no recurrence after Trastuzumab treatment (n=18) had a median sHER-2 concentration of 10.5 ng/ml, whereas patients alive with recurrence (n=13) had a median sHER-2 of 20.1 ng/ml (p=0.002). Patients who died due to recurrence (n=17) had a median sHER-2 of 232.4 ng/ml at the latest measurement before death, (p=<0.0000001) compared to patients without recurrence (16). A decrease in sHER-2 levels greater than 20% at a median of 30 days from pre-treatment samples in anti-HER-2 therapy treated patients was strongly associated with progression free survival (11&12). In contrast, increases in sHER-2 levels greater than 20% from visit to visit, persistently high levels (13–15), or failure to achieve at least a 20% drop in early weeks of anti-HER-2 therapy (17) is strongly associated with shorter progression free survival. Patients with sHER-2 levels that are consistently less than normal have significantly longer survival while patients with sHER-2 levels continuously greater than normal have shorter survival (13-15). In a meta-analysis of 4030 breast cancer patients, patients with serum HER-2 levels > 15ng/ml had a 3.39-4.57 odds of recurrence within 2 years than patients with serum HER-2 levels < 15ng/ml. The meta-analysis agreed with numerous previous studies that elevated serum HER-2 levels > 15ng/ml is a strong prognostic indicator of poor clinical outcome (19).

MBC patients with elevated sHER-2 levels should be monitored periodically to detect early cancer progression. Since the Oncogene Science HER-2/neu ELISA test measures the ECD in the circulation, levels are independent of therapy type and the test is not restricted to those receiving HER-2 targeted therapies.

Many reports have also documented that there is a significant number of breast cancer patients with a primary breast tumor that was classified as HER-2 negative but who develop a recurrent HER-2 tissue positive metastatic tumors. Since selection for HER-2 targeted therapies is based on the IHC/FISH results of the primary tumor there is a significant population of women who may be missing an opportunity to be treated with approved HER-2 targeted therapies or missing the opportunity to participate in clinical trials with new HER-2 targeted therapies. Since many studies show that the HER-2 status of a MBC tumor may be positive in patients with a HER-2 negative primary tumor, elevated sHER-2 levels may be an additional way of identifying those MBC patients incorrectly classified as HER-2 negative (18,20-23). Therefore routine testing for elevated sHER-2 levels can complement HER-2/neu tissue testing. In conclusion, periodic monitoring of all MBC patients for elevated sHER-2 levels can provide valuable information for patient management in both the HER-2 tissue positive and HER-2 tissue negative patients. The serum HER-2 test can also be used in clinical research studies to investigate the clinical value of measuring serum HER-2 levels in other epithelial cancers. For instance, studies show that sHER-2 levels can be elevated in patients with gastric cancer (24), prostate cancer (25), non-small cell lung cancer (26,27) and ovarian cancer (28).

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