

Retrospective Studies Support the Use of the Siemens Serum HER-2/neu Test in HER-2/neu-Positive Breast Cancer

Changes in serum HER-2/neu levels provide prognostic information

Cancer patients are routinely monitored to evaluate disease status and prognosis. Bramwell et al. evaluated the prognostic utility of serum HER-2/neu levels in 158 women with metastatic breast cancer (median age: 61; range: 20 to 84; 87 percent postmenopausal). Samples were collected 8 weeks after definitive diagnosis and before initiation of systemic therapy and then every 6 to 12 weeks thereafter until death.¹

The study showed that patients with elevated baseline serum HER-2/neu levels had poorer survival rates. In univariate analysis, elevated serum HER-2/neu levels had a relative risk (RR) of 1.029 for poor survival; in multivariate analysis, serum HER-2/neu levels greater than 12 ng/mL were the most prognostic for poor survival, with a relative risk of 6.097.¹

This study provided additional data that supports the usefulness of serum HER-2/neu measurements in monitoring metastatic breast cancer patients.¹

Changes in serum HER-2/neu levels are associated with relative resistance to trastuzumab-based therapies

Trastuzumab-based therapies have a response rate of 45 percent (95 percent CI: 39–51 percent) in HER-2/neu-positive breast cancer patients.² Patients who are unresponsive to trastuzumab-based therapies may be responsive to other HER-2/neu-targeted therapies and thus would benefit from timely identification.

A multicenter study by Ali et al. evaluated the utility of the changes in serum HER-2/neu levels to predict resistance to trastuzumab and to establish a clinically relevant cutoff. The study included 307 patients with metastatic breast cancer. Of these patients, 191 (62 percent) had a significant decline (>20 percent) in serum HER-2/neu levels and 116 (38 percent) did not.³ The objective response rate for trastuzumab-based therapies was 57 percent among patients who achieved a significant decline in serum HER-2/neu (>20 percent), compared with 28 percent for patients who did not. Patients who achieved a significant decline also had a significantly longer time to disease progression (320 days vs. 180 days; $P < 0.0001$), longer duration of response (369 days vs. 230 days; $P < 0.008$), and longer overall survival (898 days vs. 593 days; $P < 0.018$).³

Among patients in this study with 3+ IHC and FISH amplification of HER-2/neu, overall response rate, duration of response, time to progression, and overall survival were also better (Figure 1).³

This study suggests that serum HER-2/neu measurements can aid in assessing relative resistance to trastuzumab-based therapies.

Serum HER-2/neu changes from baseline and clinical outcomes

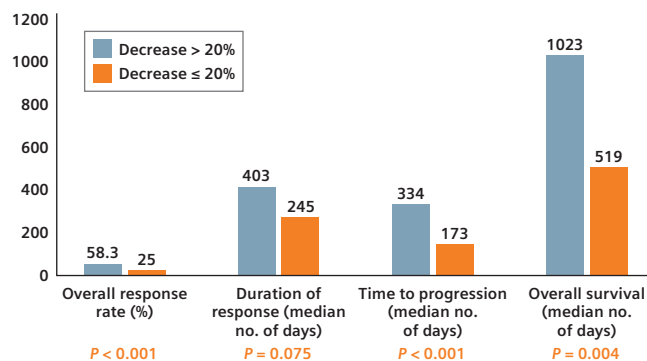


Figure 1. Among patients with 3+ IHC and FISH amplification of HER-2/neu, those with decreases in serum HER-2/neu levels > 20 percent had a better overall response rate, duration of response, time to progression and overall survival.

HER-2/neu expression can differ in primary and metastatic breast cancer

Current trastuzumab treatment recommendations are based on analysis of the primary tumor only. In some patients, the HER-2/neu status of the primary tumor and metastatic lesions are discordant. Patients who are negative for HER-2/neu in the primary tumor but positive in the metastatic lesion may be eligible for HER-2/neu-targeted therapies.

In a study by Lower et al. comparing HER-2/neu expression in primary and metastatic tumors in 382 breast cancer patients, 128 cases (34 percent) were discordant (positive at one site and negative at the other site). Median survival from the time of original diagnosis was significantly different between groups: for group 1 (negative primary/negative metastasis), 2105 days; for group 2 (positive primary/negative metastasis), 1787 days; for group 3 (negative primary/positive metastasis), 3368 days; and for group 4 (positive primary/positive metastasis), 2290 days. Patients from group 3 (negative primary/positive metastasis) experienced the longest survival. When IHC 2+ staining patterns were excluded from the analysis, over 20 percent of specimens were still discordant, but the differences in survival were no longer significant.⁴

The authors concluded that “the significant discordance between HER-2/neu expression in primary and metastatic tumors suggests that determination of HER-2/neu status in metastatic disease should be attempted.”⁴

References

1. Bramwell V, et al. *Breast Can Res Treat.* 2009;114(3):503-11.
2. Trastuzumab package insert. Available from http://www.accessdata.fda.gov/drugsatfda_docs/label/2000/trasgen020900LB.htm#desc
3. Ali SM, et al. *Cancer.* 2008;113(6):1294-301.
4. Lower EE, et al. *Breast Can Res Treat.* 2009;113(2):301-6.

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