

Total HER2 and HER2 homodimer levels predict response to trastuzumab.

Author Block: K. Leitzel, A. Lipton, W. Koestler, E. Fuchs, S. M. Ali, J. Weidler, Y. Wu, J. Sperinde, W. Huang, M. Bates; Penn State / Hershey Medical Center, Hershey, PA; Medical University of Vienna, Vienna, Austria; Penn State / Hershey Medical Center; Lebanon VAMC, Hershey, PA; Monogram Biosciences, South San Francisco, CA; Monogram Biosciences, South San Francisco, CA

Abstract:

Background: Current methods used to select HER2 positive patients with metastatic breast cancer for treatment with trastuzumab are semi-quantitative and yield response rates of less than fifty percent. Using a novel assay to quantitate total HER2 and HER2 homodimer levels, we examined the relationship between these measurements and clinical outcomes in a cohort of trastuzumab-treated metastatic breast cancer patients, previously assessed as IHC 3+ or FISH+ for HER2 overexpression or amplification.

Methods: The VeraTag assay was used to measure total HER2 expression (H2T) and HER2 homodimers (H2D) in 106 formalin-fixed, paraffin-embedded primary tumor specimens. Using test for trend, multivariate Cox proportional hazards, and Kaplan-Meier analyses, the results were correlated with objective response, time-to-progression (TTP), and overall survival following trastuzumab-containing treatment.

Results: Higher levels of H2T ($p=0.008$) or H2D ($p=0.001$) correlated with higher probability of objective response to trastuzumab therapy in a quartile analysis. Using the median value of the H2T distribution as a cutoff, higher H2T correlated with longer TTP (median TTP 11.6 mo vs. 5.4 mo, $p=0.055$), as did higher H2D (median TTP 11.6 mo. vs. 5.8 mo., $p=0.055$). Using incremental scanning to identify an optimal cutoff, higher H2T correlated with longer TTP (median TTP 11.3 mo. vs. 4.2 mo., $p=0.003$), as did higher H2D (median TTP 11.1 mo. vs. 4.2 mo., $p=0.016$). Using the optimal cutoff, higher H2T showed a non-significant trend toward longer overall survival (median survival 37.4 mo. vs. 28.7 mo., $p=0.2$). Cox multivariate models identified H2T above vs. below the optimal cutoff as a statistically significant correlate of both TTP (HR=0.41, $p=0.0002$) and overall survival (HR=0.45, $p=0.009$). Also in multivariate analyses, H2D above vs. below the optimal cutoff was a statistically significant correlate of both TTP (HR=0.64, $p=0.03$) and overall survival (HR=0.6, $p=0.02$).

Conclusions: In metastatic breast cancer patients previously selected by IHC or FISH, higher total HER2 and HER2 homodimer levels as measured by the VeraTag assay predict those patients more likely to respond to trastuzumab-containing therapy.

Grant support: Supported by a grant from Komen for the Cure Foundation.

: