Prognostic value of HER2 on breast cancer survival

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Background
HER2 overexpression and overamplification have originally been described as a prognostic factor indicating a poor prognosis. However the highly effective anti-HER2 treatment was approved in 2006 after several large randomized trials showing that the prognosis in HER2 positive women could be improved. Few data has been generated comparing HER2 positive patients treated with trastuzumab with comparable HER2 negative patients. Aim of this analysis was to investigate the prognostic relevance of HER2 status in a post trastuzumab approval study.

Methods
The SUCCESS trial is an open-label, multicenter, randomized controlled, phase III study comparing FEC-docetaxel (Doc) vs. FEC-Doc-gemcitabine (Doc-G) regime and 2 vs. 5 year treatment with zoledronate in 3754 patients with primary breast cancer (N+ or high risk). All patients were treated per protocol with trastuzumab, if HER2 status was shown to be positive by local pathology. Furthermore HER2 status was a stratification factor. The prognostic value of HER2 status with respect to overall survival (OS) and progression-free survival (PFS), disregarding the above stated treatment arms, was studied with Cox proportional hazards regression models in univariate as well as multivariate analyses adjusted for age, BMI, tumor size, nodal status, grading, estrogen receptor status and progesterone receptor status.

Results
2628 patients were included into this analysis. Median follow-up time was 4.8 years, 221 deaths and 412 recurrences were recorded until data base closure. HER2 was not a prognostic factor in the univariate analysis (OS: HR = 0.86, 95% CI: 0.63 to 1.19; PFS: HR = 0.95, 95% CI: 0.76 to 1.19). In the multivariate analysis of all of the above stated prognostic factors of were of prognostic relevance. HER2 was of prognostic relevance with a HR of 0.67 (OS, 95% CI: 0.48 to 0.92) and 0.79 (PFS, 95% CI: 0.62 to 0.99) indicating that patients with a positive HER2 status had a better prognosis.

Conclusion
Patients treated with trastuzumab showed a more favourable prognosis compared to HER2 negative patients in this prospectively randomized trial, possibly due to the therapeutic effect of HER2-targeted treatment.

Acknowledgment