the prognostic value of HER-2/neu status in premenopausal patients with hormoneresponsive breast cancer.
Jakesz R, Hausmaninger H, Kubista E, Gnant M, Seifert M, Kwasny W, Steger G, Samonigg H, Tausch C, Stierer M, the ABCSG. Vienna University, Vienna, Austria

Background: HER-2/neu status in breast cancer tissue has shown to be a marker for aggressive tumor biology. In the palliative setting, HER-2/neu status is predictive for response to Herceptin® (trastuzumab). Furthermore, several retrospective trials indicate anthracycline sensitivity and tamoxifen resistance. Little is known about HER-2/neu status in premenopausal patients with hormone-responsive tumors.

Patients and Methods: Austrian Breast & Colorectal Cancer Study Group (ABCSG) Trial 5 has shown that combination endocrine treatment with adjuvant tamoxifen (20mg, 5a) and goserelin (3.6mg q 4w, 5a) is superior to i.v. cyclophosphamide, methotrexate and fluorouracil (CMF) in 1040 premenopausal patients with hormone-responsive breast cancer (J Clin Oncol, in press). We investigated whether HER-2/neu status is prognostic and/or predictive for these patients (n=572), or either one of the treatment groups.

Results: Strongly positive HER-2/neu (++) status was detected in 12.2% of all patients at 5 years, representing a significant predictor of worse overall survival (OS) (92% vs. 82%; p<0.01) and relapse-free survival (77% vs. 72%; p=0.07). No significant interaction was established in analyses of results according to treatment groups. Analyzing results further, interaction showed to be significant between the prognostic value of HER-2/neu status and tumor grading. HER-2/neu status failed to affect OS in the presence of G3 tumors, but was highly significant (p<0.0001) in patients with better-differentiated tumors (95% vs. 82% OS at 5 years).

Conclusions: HER-2/neu status represents an indicator for poorer outcome in this homogeneous patient group. No treatment interaction was demonstrated either for endocrine or cytotoxic treatment. HER-2/neu status shows additional, inferior prognostic significance in patients with G1 and G2 tumors, but not so in G3 tumors.