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Titel des Beitrags: Triple-negative high-risk breast cancer derives particular benefit from dose intensification of adjuvant chemotherapy: results of WSG AM-01 trial.

Abstract: BACKGROUND: This paper evaluates the prognostic and predictive impact of protein expression of various molecular markers in high-risk breast cancer (HRBC) patients with >9 involved lymph nodes, who received different chemotherapy dose-intensification strategies within a prospective randomized WSG AM-01 trial. MATERIALS AND METHODS: Paraffin-embedded tumors from 236 patients, who were randomly assigned to dose-dense conventional chemotherapy with four cycles of E(90)C(600) followed by three cycles of C(600)M(40)F(600) every 2 weeks (DD) or a rapidly cycled tandem high-dose regimen with two cycles of E(90)C(600) every 2 weeks followed by two cycles of E(90)C(3000)Thiotepa(400) every 3 weeks (HD), were available for retrospective central pathological review (116 HD/120 DD). Expression of estrogen receptor (ER), progesterone receptor (PR), MIB-1, epidermal growth factor receptor, and Her-2/neu was evaluated immunohistochemically using tissue microarrays. Results were correlated with follow-up data and treatment effects by proportional hazard Cox regression models (including interaction analysis). RESULTS: After
a median follow-up of 61.7 months, 5-year event-free survival (EFS) as well as overall survival (OS) rates for the 236 patients were significantly better in the HD arm: EFS: 62% versus 41% [hazard ratio (HR) = 0.60, 95% CI 0.43-0.85, P = 0.004]; OS: 76% versus 61% (HR = 0.58, 95% CI 0.39-0.87, P = 0.007). In multivariate analysis, HD, tumor size<3 cm, positive PR, negative MIB-1 staining, and grade 1/2 were associated with favorable outcome. Interaction analysis showed that regarding predictive effects, triple negative (ER/PR/Her-2/neu) and G3 tumors derived most benefit from HD.

CONCLUSION: Tandem HD improves both EFS and OS in HRBC. This therapy effect may be partly attributable to superior efficacy in the subgroup of triple-negative tumors and/or G3 with their poor prognostic marker profile.