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# Evaluation of the prognostic value of HER-2 and VEGF in breast cancer patients participating in a randomized study with dose-dense sequential adjuvant chemotherapy.

Kostopoulos I, Arapantoni-Dadioti P, Gogas H, Papadopoulos S, Malamou-Mitsi V, Scopa CD, Markaki S, Karagianni E, Kyriakou V, Margariti A, Kyrkou E, Pavlakis K, Zaramboukas T, Skordalaki A, Bourli A, Markopoulos C, Pectasides D, Dimopoulos MA, Skarlos D, Fountzilas G.

**Source**

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**Abstract**

**PURPOSE:**

To assess the prognostic and predictive significance of HER-2 overexpression and high expression of VEGF in high-risk patients with breast cancer treated with dose-dense sequential chemotherapy.

**PATIENTS AND METHODS:**

From June 1997 until November 2000, 595 patients were randomized to three cycles of epirubicin (E) 110 mg/m2 followed by three cycles of paclitaxel (T) 250 mg/m2 followed by three cycles of "intensified" CMF (cyclophosphamide 840 mg/m2, methotrexate 47 mg/m2 and fluorouracil 840 mg/m2) or to four cycles of E, followed by four cycles of CMF. HER-2 was assessed by immunohistochemistry (IHC) in 394 patients, and by fluorescence in situ hybridization (FISH) in cases scored as 2+ by IHC. VEGF was evaluated in 323 patients by IHC.

**RESULTS:**

HER-2 overexpression was detected in 123 patients (31%) and high expression of VEGF in 233 (72%). The rate of HER-2 overexpression was significantly higher in patients with positive VEGF staining (35% vs. 21%, p=0.02). Overexpression of HER-2 was significantly associated with negative hormonal status, high histologic grade and larger tumors. HER-2 overexpression was a significant negative predictor of DFS (p=0.002), but not of OS. Adjusting for HER-2 overexpression, DFS and OS did not significantly differ between treatment groups. Positive VEGF staining was not associated with receptor status, number of positive nodes, grade, tumor size, incidence of relapse or death.

**CONCLUSIONS:**

For both treatments, HER-2 overexpression was a significant negative prognostic factor for DFS but not for OS, while high expression of VEGF was not significantly associated to either DFS or OS. No predictive ability of HER-2 status or VEGF overexpression for T treatment was evident.