Expression of endothelin-A-receptor predicts unfavourable response to neoadjuvant chemotherapy in locally advanced breast cancer.

Abstract:

Endothelin-1 (ET-1) and its receptors (ETAR and ETBR), referred to as the endothelin (ET) axis, are overexpressed in breast carcinomas and appear to influence tumour growth and progression. The objective of this study was to determine the effect of expression of the ET axis in breast carcinomas on response to cytotoxic chemotherapy. The study included 44 patients with locally advanced breast cancer participating in a prospective phase III study evaluating high-dose neoadjuvant chemotherapy of epirubicin and cyclophosphamide. Expression of ET-1, ETAR and ETBR was determined by semiquantitative immunohistochemical analysis of breast cancer tissue from prechemotherapy tru-cut biopsies. Immunohistochemical staining was positive for ET-1 in 61.5%, for ETAR in 35% and for ETBR in 35.9% of breast carcinomas. Pathological response to chemotherapy was significantly decreased in ETAR-positive patients (P=0.002). In total, 50% of ETAR-positive patients as compared to 7.7% of ETAR-negative patients attained pathologically "no change". Logistic regression confirmed ETAR as an independent predictive marker for pathological response (P=0.009). These data indicate that increased expression of ETAR in breast carcinomas is associated with resistance to chemotherapy.
Determination of ETAR status may serve as a predictive marker for identifying patients less likely to be responsive to conventional chemotherapy.