Expression of angiogenic markers in the peripheral blood of docetaxel-treated advanced breast cancer patients: a Hellenic Cooperative Oncology Group (HeCOG) study.

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Source

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Abstract

It is well known that low-dose metronomic chemotherapy has antiangiogenic activity. The aim of the present trial was to investigate the antiangiogenic properties of weekly docetaxel in patients with metastatic breast cancer. In total, 157 metastatic breast cancer patients received 35 mg/m2 docetaxel weekly as a recommended treatment. Blood samples were collected before the start of chemotherapy (baseline) and during treatment. Nitric oxide (NO) and vascular endothelial growth factor A (VEGF-A) plasma levels were measured at baseline and during treatment, while VEGF-A, endothelial nitric oxide synthase (eNOS) and thrombospondin-1 (THBS-1) peripheral blood mRNA levels were measured at baseline, in 127 patients and 39 female healthy controls. In general, the treatment was well-tolerated. Sixty-one patients (38%) achieved an objective response (4% complete and 34% partial response), while 52 (33%) had stable disease and 27 (17%) progressed. At a median follow-up of 33.5 months (range 2.8-45.0), 118 patients (74%) demonstrated disease progression and 94 (59%) had died. Median progression-free survival (PFS) was 8.8 months and median overall survival (OS) was 27.7 months. Median baseline level of plasma NO was significantly lower in patients than in healthy controls ($p=0.010$), while none of the plasma markers significantly changed upon docetaxel treatment. In addition, the median relative quantification value for THBS-1 mRNA was significantly higher ($p<0.001$) in patients as compared to healthy controls. NO plasma levels were positively associated with the number of organs involved ($p=0.008$). In multivariate analysis, low eNOS mRNA levels showed adverse prognostic significance for OS and high THBS-1 mRNA levels were found to be associated with shorter OS and PFS, independently from established clinical prognostic factors. Although an antiangiogenic activity of weekly docetaxel was not demonstrated in the present study, some interesting observations regarding the prognostic role of a number of blood angiogenic markers could be made.