Expression of angiogenic markers in the peripheral blood of patients with advanced breast cancer treated with weekly docetaxel.

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Source

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Abstract

BACKGROUND:

Metronomic chemotherapy targets the inhibition of tumor growth primarily through antiangiogenic mechanisms. The aim of the present study was to investigate the antiangiogenic properties of weekly metronomic docetaxel administration in patients with metastatic breast cancer.

PATIENTS AND METHODS:

In total, 157 patients with metastatic breast cancer received docetaxel at 35 mg/m(2) on a weekly basis as first-line treatment. Blood samples were collected before and during treatment. Plasma protein levels and peripheral blood mRNA expression of human epidermal growth factor-2 (HER2), interleukin-8 (IL8) and transforming growth factor beta-1 (TGF-β1) were measured by enzyme-linked immunosorbent assays (ELISA) and quantitative reverse transcription-polymerase chain reaction (qRT-PCR), respectively in 127 patients and 39 healthy controls.

RESULTS:

Sixty-one patients (38%) achieved an objective response (4% complete and 33% partial responses), 52 (33%) had stable disease, and in 27 patients (17%) the disease progressed. At a median follow-up of 33.5 months, 118 patients (74%) demonstrated disease progression and 94 (59%) had died. The median overall survival (OS) was 27.7 months, while the median progression-free survival (PFS) was 8.8 months. Median baseline plasma HER2 protein levels were significantly higher in patients than in controls (Mann-Whitney test, $p=0.033$). In addition, the median relative quantification (RQ) values for blood IL8 mRNA were significantly lower in patients ($p<0.001$) compared to healthy controls, while the median RQ values for TGF-β1 mRNA were significantly higher ($p<0.001$). Furthermore, plasma HER2 protein levels (Wilcoxon signed ranked test, $p<0.001$), as well as blood IL8 mRNA ($p=0.026$) and TGF-β1 mRNA levels ($p=0.016$) decreased significantly upon treatment. Univariate Cox regression analysis showed that high baseline plasma protein levels of IL8 were of adverse prognostic significance for OS (Wald's $p=0.031$), while high blood HER2 mRNA levels were marginally associated with longer OS ($p=0.060$). In multivariate analysis, plasma IL8 protein lost its prognostic significance, while high blood HER2 mRNA levels were associated with significantly improved OS (Wald's $p=0.022$).

CONCLUSION:

Our study demonstrated a potential in vivo antiangiogenic activity of weekly docetaxel. Some interesting observations were made regarding the prognostic role of baseline plasma IL8 protein levels and blood HER2 mRNA levels, however, further research is required in order to validate

these findings in larger cohorts, and to fully understand the angiogenic processes and optimize treatment strategies.