Pharmacogenomics J. 2014 Jun;14(3):248-55. doi: 10.1038/tpj.2013.36. Epub 2013 Sep 24.

Vascular endothelial growth factor polymorphisms and clinical outcome in patients with metastatic breast cancer treated with weekly docetaxel.

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Abstract

The aim of the study was to evaluate the association of vascular endothelial growth factor (VEGF) genotypes with treatment efficacy in a phase II trial. This study evaluated weekly docetaxel, as first-line treatment for metastatic breast cancer. Existing data from in vitro and animal model experiments suggest that docetaxel at low doses has anti-angiogenic activity. DNA was extracted from blood samples of 86 patients participating in the trial. Genotyping was performed for selected single-nucleotide polymorphisms (SNPs; VEGF-2578, -1498, -1154, and +936). Moreover, due to the highly polymorphic nature of the studied areas, we were able to analyze additional registered SNPs. All candidate genotypes were evaluated for associations with overall survival (OS), progression-free survival (PFS) and response rate. The VEGF-1154 GG genotype was more frequent in patients not responding to treatment compared with responders (42.9% vs 0.0%, P=0.048). Moreover, the VEGF-2578 AA genotype was associated with longer PFS compared with CC (hazard ratio (HR)=0.40; 95% confidence interval (CI) 0.17-0.98; pairwise P=0.0457). Patients with the VEGF-1190 GG genotype demonstrated shorter PFS compared with those with the alternative genotypes (GA and AA) combined (HR=3.85; 95% CI: 1.20-12.50; P=0.0224). In addition, the VEGF-2551/-2534 homozygous del18bp and VEGF-2430/-2425 homozygous ins1bp genotypes were associated with worse PFS compared with no deletion and no insertion, respectively (HR=2.49; 95% CI: 1.02-6.07; pairwise P=0.0442 and HR=2.57; 95% CI: 1.05-6.27; pairwise P=0.0385, respectively). Furthermore, patients with the VEGF-1498 CC genotype exhibited longer median OS compared with those with the alternatives genotypes (CT and TT) combined (HR=0.27; 95% CI: 0.08-0.89; P=0.0311). In multivariate analysis, the VEGF-2578 AA genotype retained its significance (P=0.0220) for PFS. Our results support the association of specific VEGF genotypes with clinical outcome in patients with metastatic breast cancer treated with a potentially anti-angiogenic regimen, such as weekly docetaxel. However, current results should be validated prospectively in larger cohorts.

PMID: 24061601 [PubMed - in process]