Circulating VEGF and eNOS variations as predictors of outcome in metastatic colorectal cancer patients receiving bevacizumab

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Background: Novel predictive biomarkers are needed to improve patient selection and optimize the use of bevacizumab in metastatic colorectal cancer (mCRC).We analysed the potential of five circulating biomarkers to predict bevacizumab efficacy and monitor response.

Materials and Methods: Peripheral blood samples collected at baseline, at first clinical evaluation and at progression were available for 129 patients enrolled in the prospective multicentric *ITACa* trial and randomized to receive FOLFOX4/FOLFIRI (CT) with (64 patients) or without bevacizumab (65 patients). VEGF-A, eNOS, EPHB4, COX2 and HIF-1α mRNA levels were measured by qRT-PCR. Baseline marker expression levels and their modulation during therapy were analysed in relation to objective response, progression-free survival and overall survival (OS).

Results: VEGF and eNOS expression was significantly correlated in both groups (Spearman's correlation coefficient = 0.80; P < 0.0001 and 0.75; < 0.0001, respectively). Bevacizumab-treated patients with > 30% reduction in eNOS and VEGF levels from baseline to first clinical evaluation showed better OS than the others (median OS 31.6 months, 95% CI 21.3-49.5 months and median OS 14.4 months, 95% CI 9.0-22.7 months, respectively, HR 0.38, 95% CI 0.19-0.78, P = 0.008).

Conclusions: A reduction in eNOS and VEGF expression from baseline to first clinical evaluation may indicate a response to bevacizumab.