

The trough levels of bevacizumab significantly affects the outcome of the treatment in patients with metastatic colorectal cancer: A Turkish Oncology Group Study

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Background

There are controversial reports regarding the blood levels of the monoclonal antibodies and clinical efficacy (1). However, the role of trough levels of bevacizumab has not been studied as a predictor parameter in patients with colorectal cancer. In this trial we aimed to investigate the role of angiogenic factors and bevacizumab (Beva) trough levels on the efficacy of Beva plus chemotherapy combination in metastatic colorectal cancer patients (mCRC).

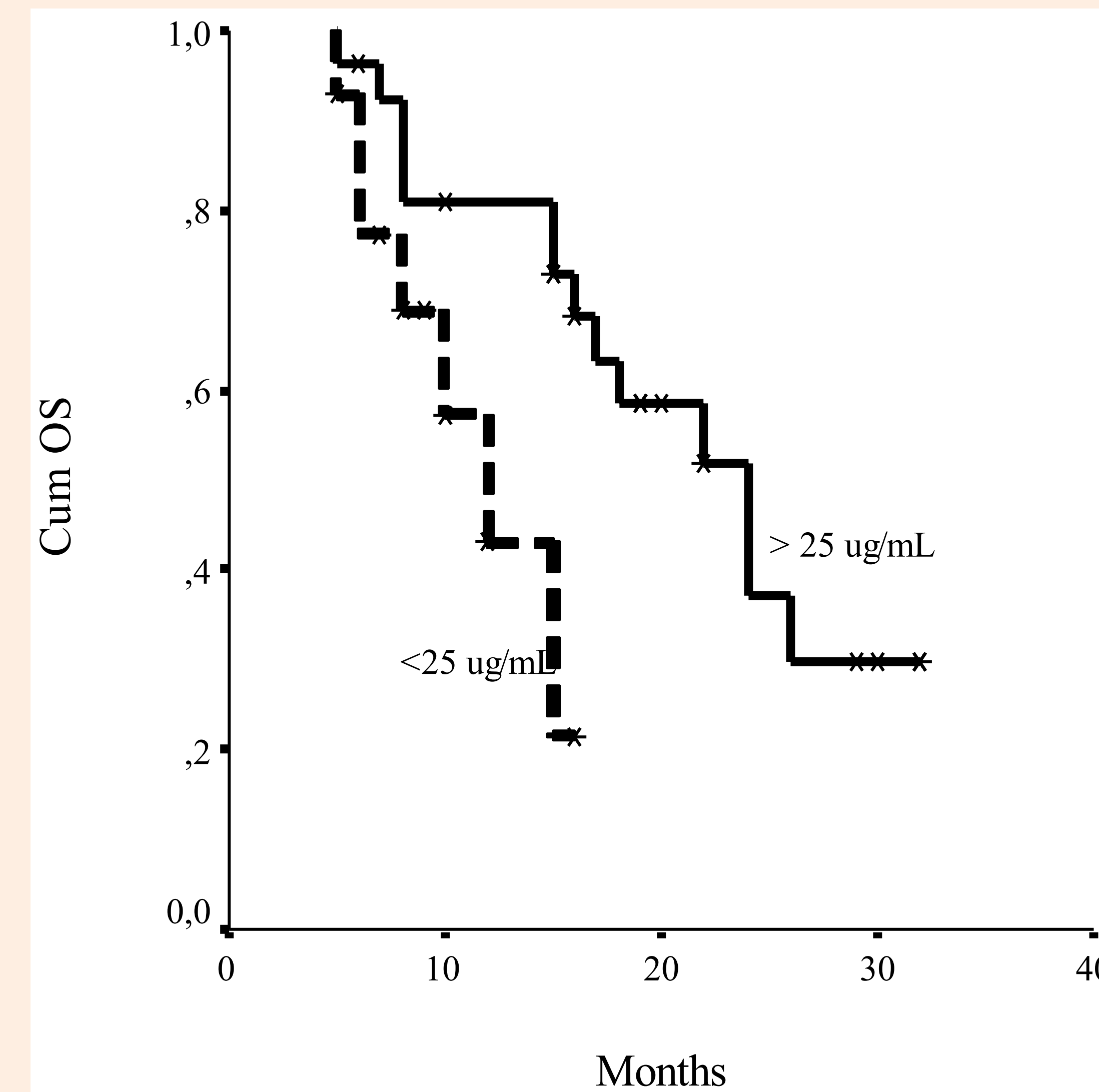
Methods

Eighty-eight patients with mCRC whom treated with Beva plus either irinotecan or oxaliplatin based chemotherapy regimens were prospectively included. The serum levels of angiogenic factors including hepatocyte growth factor (HGF), PlGF, VEGF, PDGF, bFGF, Annexin-1, Angiopoietin-2, Endothelin-1 and MMP9 were measured before the onset of the Beva. The trough levels of Beva on the 14th day of the first cycle and following the eighth cycle and anti-Beva Ab levels in the 3rd month of the treatment were assayed by ELISA (Shikari Matriks Biotek, TR).

Results

The median age was 60 years old (range: 28-70). Beva (5mg/kg, q2w) has been implemented to the chemo backbone either at the first line setting (in 35% of the patients) or second line (65%). The chemo backbone was irinotecan based in 51% of the patients. The median number of treatment cycles was 6. The objective response and disease stabilization rates were 35% and 77%, respectively. The median overall survival (OS) time was 15 months. There was no significant OS difference between the chemo backbones. Though not significant, only the patients with lower HGF levels (<1750 pg/ml) had favorable OS time when compared to the higher group (22 mo vs 15 mo). The pretreatment levels of the other factors including VEGF had no impact on OS. The median trough levels of bevacizumab after the first cycle and eighth cycle were 27,6 and 76,5 ug/ml, respectively. No correlation was found between the serum VEGF levels and trough levels of Beva.

The patients with lower trough levels (≤ 25 ug/ml) at the first cycle had significantly lower OS times when compared to the patients with higher levels (> 25 ug/ml) (12 mo vs 24 mo, $p=0.0198$). The presence of anti-Beva Abs (15% of the patients) had no impact on treatment outcomes.



Overall survival curves according to the bevacizumab trough levels on the 14th day of the first cycle

Conclusion

In conclusion our results show that the pretreatment angiogenic factor levels are not predictors of outcomes for Beva plus chemotherapy in mCRC patients. The development of anti-Beva Abs seems to have no effect on the efficacy of the Beva treatment. The trough levels of Beva at the first cycle could be a good predictor of survival for Beva treatment in patients with mCRC.

References

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