months, HR 0.43, 95% CI 0.23-0.8, p = 0.007). Regarding serum proteins modulation during therapy, patients with a > 20% reduction from baseline to first clinical evaluation in IL-8 levels showed a better PFS and OS compared to those with a < 20% reduction or an increase (HR 0.41, 95% CI 0.22-0.77, p = 0.005 and HR 0.43, 95% CI 0.23-0.79, p = 0.007, respectively).

Conclusion: Our data suggest that baseline IL-8 and TSP-1 levels could represent potential prognostic markers in patients with mCRC receiving B-based chemotherapy and that IL-8 modulation from baseline to the first clinical evaluation may indicate better clinical outcomes.

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Introduction: Bevacizumab (B) plus chemotherapy (CT) is a common choice for first-line treatment of metastatic colorectal cancer (mCRC). Molecular predictors of B efficacy have not been identified yet. Previous studies have assessed circulating levels of pro- and anti-angiogenic factors at baseline and during therapy in relation to B response with conflicting results. We analyzed the potential role of 22 angiogenesis associated proteins (FGF-basic, HGF, sTIE-2, sVEGFR-1, sVEGFR-2, Ang-2, EGF, IL-6, IL-8, PLGF, VEGF-A, VEGF-C, VEGF-D, PDGF-bb, Ang-1, SDF-1alpha, MDC, Galectin, TSP-1, Endocan, eNOS, HIF-1alpha) in relation to patient outcomes.

Methods: Serum samples collected at different times (baseline, first clinical evaluation and disease progression) were available for 58 patients treated by CT (FOLFOX4/FOLFIRI) with B out of the 176 patients enrolled in the randomized multicenter ITACa trial (NCT01878422). Levels of all serum proteins were determined using a Bio-Plex 200 array reader, based on Luminex X-Map Technology. Baseline marker expression levels and their modulation during therapy were correlated with objective response (OR), progression-free survival (PFS) and overall survival (OS).

Results: Higher baseline vascular endothelial growth factor C (VEGF-C) levels and macrophage-derived chemokine (MDC) levels were associated with higher OR rate (Odd Ratio=7.69, 95% CI 2.13-27.78, p = 0.002 and Odd Ratio=3.58, 95% CI 1.12-11.37, p = 0.031, respectively). Baseline IL-8 levels were associated with PFS and OS, in particular patients with IL-8 <145 pg/mL showed a better median PFS and OS compared to those with higher levels (12.6 vs 6.5 months; Hazard Ratio [HR] 5.09, 95% CI 2.00-12.97, p < 0.001 and 28.8 vs 8.7 months, HR 6.06, 95% CI 2.12-17.37, p < 0.001, respectively). Moreover, patients with thrombospondin-1 (TSP-1) levels ≥12000 ng/mL showed a better median OS compared to those with lower levels (34.5 vs 13.1