P – 140 Correlation between values of specific biomarkers and outcome in metastatic colorectal cancer patients treated with regorafenib

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Introduction: Regorafenib is an oral small-molecule multiple kinase inhibitor indicated as a third-line treatment for patients with metastatic colorectal cancer (mCRC). Regorafenib has shown significant benefits in overall survival (OS) and progression-free survival (PFS) in mCRC patients in two phase III trials (CORRECT and CONCUR). Moreover, a retrospective exploratory analysis investigated the clinical activity of regorafenib in biomarker subgroups in the CORRECT study. The present study aimed to evaluate the role of specific biomarkers potentially involved in the clinical activity of regorafenib.

Methods: We determined the concentration of 4 proteins of interest in plasma samples collected from 17 mCRC pts before starting regorafenib (baseline). The proteins selected on the basis of their roles in angiogenesis and colorectal cancer pathogenesis were TNF-α, TGF-β, chemokine ligand 5 (CCL5), and chemokine ligand 4 (CCL4). They were analysed with ELISA test and concentrations were expressed in pg/ml. The values obtained were compared with the values of 7 healthy controls, in order to evaluate the differences in the concentration of the cytokines examined. All analyses were carried out using GraphPad (Version 5) and $P < .05$ was considered the statistical significance level. Additional ongoing analysis include other cytokines that will give us further informations.

Results: We found that TNF-α basal level is significantly higher in CRC patients compared to healthy volunteers. Moreover, progressed patients (PD) (n = 12), have higher basal levels of TNF-α, CCL5, and TGF-β compared with responders (R) (complete response n=1, partial response n = 1 or stable disease [SD] n = 3). The median values of cytokine distribution in R patients are similar to that of healthy volunteers. Furthermore, high TGF-β negatively correlates with PFS, indicating that this cytokine is associated with tumour progression. We also observed that plasma basal levels of CCL4 are significantly lower in PD compared to R patients. We assigned a score (qREGOSCORE) to each patient depending on the combination of pro- or anti-tumoural roles of each cytokine. Notably, this score was significantly higher in PD pts than in R pts and also correlated with PFS. These results might discriminate mCRC patients that will respond better to treatment

Conclusion: Our data showed that in R pts, the baseline cytokine profile approached the values observed in healthy volunteers. On the contrary, pts that did not benefit from treatment could be identified by different cytokine profiles. However, it must be stressed that our population is small and the data should be verified on a larger number of pts. It might also be of interest to extend analyses to other cytokines and cell populations not yet determined in our study.