

Manuscript Review

Number ID	Review Info	Specific Comments To Authors	Answering Reviewers
03551817	Conclusion: Rejection Scientific Quality: Grade C (Good) Language Quality: Grade A (Priority publishing)	<p>This is a valuable retrospective study. But the authors collected 17 blood samples of patients treated with regorafenib or 6 healthy volunteers, the samples are not enough. I suggest the authors collect more samples of patients and healthy volunteers. Meanwhile, the authors evaluate more cytokines such as ILs.</p>	<p>We are aware that our population is small and data should be verified on larger and independent series of patients. It might also be of interest to extend analysis to other cytokines and cells population not determined in our study.</p>
03004570	Conclusion: Minor revision Scientific Quality: Grade B (Very good) Language Quality: Grade B (Minor language polishing)	<p>This manuscript is a retrospective cohort study about the relationship between some circulating cytokines and the clinical outcome in mCRC patients treated with regorafenib. As the authors mentioned, this is a “proof of concept” study. The number of patients is very low but this is expected in forth and fifth line treatment in mCRC. They demonstrated that a cytokine signature may be predictive for the response to regorafenib, if validated in future trials. Avoiding ineffective treatments is a clinically important issue. I recommend some minor changes: How was the primary site of 9 colon cancer patients (right or left)? In the Discussion section, citation of references should be corrected as [17-19] and [20-22] in place of [17-18-19] and [20-21-22] respectively. Figures are informative and nice.</p>	<p>The requested changes have been made. In particular the primary tumour location was specified by numbering patients with left and right colon cancer. References have been changed as required</p>