Thank you very much the editors and all the reviewers for their positive and constructive comments on our manuscript.

Reviewer ID: 02445585

This manuscript by Ozkan Kanat, et al. extensively updates the clinical use of anti-angiogenesis drugs in advanced colorectal cancer. It is informative and readable for scientists in this field. A minor concern is about the general structure of this review article. The Introduction section is actually a comprehensive review of the agent Bevacizumab, but it will be better to have a general description about colorectal cancer, therapeutic options and a bridge paragraph of anti-angiogenesis treatment. Bevacizumab and other anti-angiogenesis agents would be the main body of the article, which will then end with a conclusive remark.

Answer to Reviewer:

The introduction section was revised and changes made were highlighted with yellow.

Reviewer ID 02904061

The authors conducted a mini review about therapeutic strategies for patients with mCRC progressing following first-line bevacizumab-based therapy. It suggested that Treatment options include the continuation or reintroduction of bevacizumab, or switching to a different antiangiogenic monoclonal antibody such as aflibercept or ramucirumab. The clinical trials were mentioned in the manuscript. However, there are several minor concerns should be elucidated. 1. The title of the review is “Existing therapeutic strategies for patients with metastatic colorectal cancer progressing following first-line bevacizumab-based therapy”,while this manuscript only mentioned antiangiogenic therapy,but didn’t include such as immunotherapy,I recommend the authors to change the title. 2. A minor problem in this manuscript is the inconsistency of the form in which the results of trials were presented. Some of the results were provided with 95% CI, some others were not. I recommend the authors to make them in the same manner as possible. 3. In page 5,” The phase III VELOUR trial. approximately 30% of patients had received first-line bevacizumab-based therapy”, Whether the percentage of patients who had received first-line bevacizumab-based therapy in the experimental arm and the control arm was matched? 4. In page 9,” two small phase II studies, the SPIRITT and PRODIGE 18”,all enrolled patients were with KRAS wild-type,not with RAS wild-type. 5. In page 9, the authors wrote “However, the SPIRITT study demonstrated that a switch from bevacizumab to panitumumab may be associated with an increased tumor response (32% vs. 19%)”,maybe a little mistake,shoud be (19% vs.32%)”.

Answer to reviewer:

The title was revised and the changes in the title was highlighted with yellow. The information about the 95% CI was added to appropriate sections and was highlighted with yellow. The RAS status of patients enrolled to SPIRIIT and PRODIGE 18 studies was revised and the changes were highlighted with yellow.

The percentage of patients who had received first-line bevacizumab-based therapy in the experimental arm and the control arm was emphasized again according to the reviewer's recommendation.

In page 9, the response rates were reorganized according to the reviewer's suggestion.

Reviewer ID 03439017

The paper describes a better approach to the treatment of colorectal cancer that is interesting and may be accepted for publication.

Answer to reviewer: Thank you very much for your positive and provocative comments.

Reviewer ID 02683307

This is well written ms.

Answer to reviewer:

Thank you very much for your positive and provocative comments