Reviewer's report

Title: Low Mmp 9 and VEGF levels predict good oncologic outcome in mid and low rectal cancer patients with neoadjuvant chemoradiation

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Reviewer: david tougeron

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Kurt et al reported the link between VEGF apoptotic and angiogenic markers and response to CRT for rectal cancer. This study included 29 patients. The authors demonstrated that Bax, VEGF and MMP-9 levels are associated with complete response to CRT. It is an important topic to predict response to CRT in rectal cancer. The manuscript is well written and well discussed. Nevertheless, this study has some limitations.

Major Compulsory Revisions

- In the abstract and in the discussion sections, association of PCR and outcome (DFS and OS) should be deleted because it wasn’t the main end point of the study. It is already well-known in large randomised trials and this same result on 29 patients is unnecessary.
- In page 10 the authors say “In this study, the group with Dworak [22] scores of 0 to 3 (partial responders) were compared with the group with Dworak scores of 4 (complete responders).” Nevertheless, score of 0 is absence of regression and then not partial response, this point should be corrected.
- Results sections should be divided in different small paragraphs like “patient characteristics”, association of apoptotic and angiogenic markers and response to CRT” and “association of apoptotic and angiogenic markers and DFS/OS”...
- Figures 1 and 2 can be deleted because the link between complete response and survival is well-known and this study of 29 patients does not add anything more about it. Nevertheless, results could be presented in the text.
- Some tables can be also deleted : table 1 “exclusion criteria” (this point is explain in the text and numbers of patients could be added in the text) and table 7 (because there isn’t significant results).
- Tables 3, 4 and 6 should be presented in only one Table.
- Tables 2 should describe all patients but not divided patients with or without complete response because it isn’t the main goal of the study. Absence of difference between patient with and without PCR could be only explained in the text.
- For the multivariate analysis of OS and DFS, you must first performed a univariate analysis and introduce only significant variables in the multivariate model. Is there significant results in univariate analysis (PCR, MM9, Bax, T, N stage...).
- What are p values for association between PCR and OS and DFS?
- Conclusion is not in accordance with the results: there is no association with OS/DFS and VEGF and MMP-9 but only with PCR. This point must be explained in the conclusion and in the abstract.
- The results should be stratified: * correlation between clinical variables/ apoptotic and angiogenic markers and PCR.
  * correlation between clinical variables/ apoptotic and angiogenic markers and DFS/OS

Minor Essential Revisions

- In the abstract “MMP-9 and VEGF levels were higher in the PPR group than the PCR group (p=0.051).” Each p values for MMP-9 and VEGF should be detailed.
- There are some errors in syntax and grammar like absence of “]” in page 5 or “peritonitis carcinomatosa” in page 6.
- Methods section is too long, paragraph on “CRT”, “surgery”, “postoperative chemotherapy” and “follow-up” could be reduced.
- In page 12 the authors say “A low level of MMP-9 was significantly correlated with T downstaging seen between clinical and pathological stagings (p<0.04).” I think that it is p=0.04. I think there are some mistakes in the results sections using < instead of = for the p value.
- In the results section, all data concerning apoptotic and angiogenic markers and association with T or N staging should be grouped.
- In my opinion, manuscript is too long. Some paragraph could be reduced. Discussion about PCR and OS/DFS could be deleted.

Discretionary Revisions
None

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests