Author’s response to reviews

Title: Capecitabine plus bevacizumab versus capecitabine in maintenance treatment for untreated characterised KRAS exon 2 wild-type metastatic colorectal cancer: a retrospective analysis in Chinese postmenopausal women

Authors:

Jinsong Su (sujinsong5512@163.com)
Jiajie Lai (342756019@qq.com)
Ruikun Yang (gzhpyrk@163.com)
Bo Xu (80947061@qq.com)
Ying Zhu (zhuying10246@hotmail.com)
Mingdong Zhao (zhaomd886@aliyun.com)
Chen Yang (yangchen8866@aliyun.com)
Guanzhao Liang (gzhliang1989@aliyun.com)

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Dear Editors and Reviewers:

Thank you for your letter and for the comments of the editors and reviewers. Thank you for consideration of our manuscript for publication in your journal. We have reviewed the manuscript according to the reviewers’ comments. Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. Based on the comment and request, we have studied comments carefully and have made modification. Below you will find our point-by-point responses to your comments:

Editor Comments:

Response: We have already revised the relevant content in revised manuscript(Page 7, Lines 31-53). "Symptom assessment were performed every 3 months for the entire study period. Metastatic recurrence was confirmed mainly on the basis of imaging data. The rating rules for adverse events was based on Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.0. Medical therapy was performed in line with institutional guidelines. Assessment of response or progression was on the basis of either MRI or endorectal ultrasound. Temporary diverting ostomy was mainly based on the general situation of patients," instead of "Patients had symptom assessment and physical examination every 3 months in one year and at least every 6 months thereafter. Metastatic recurrence was identified based on physical examination or imaging. Adverse events were graded according to Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.0. Medical therapy to maintain blood pressure within normal limits and antiemetic support were prescribed according to institutional guidelines. All patients were assessed with interval imaging either with MRI or endorectal ultrasound for response or progression. Creation of a temporary diverting ostomy was at the discretion of the primary surgeon. Proctoscopy, CT, and MRI were repeated within 2-3 weeks for all patients."


Response: We have already revised the relevant content in revised manuscript (Page 8, Lines 6-19). "A retrospective, multi-centre study was performed, in which eligible patients received 6-cycle CAPOX-B induction therapy, as described by Nakayama et al.[19]. CAP-B maintenance therapy (intravenous B 7.5 mg/kg once a day and intravenous CAP 1000 mg/m2 twice daily) or CAP maintenance therapy (intravenous CAP 1000 mg/m2 twice daily) was performed for patients with stable or better following 6-cycle CAPOX-B induction therapy. The primary endpoints were mPFS and mOS. The secondary endpoint was safety." instead of "A retrospective, multi-centre study was performed, in which eligible patients received 6-cycle CAPOX-B induction therapy (intravenous oxaliplatin 130 mg/m2 on day 1, intravenous bevacizumab 7.5 mg/kg on day 1, oral capecitabine 1000 mg/m2 twice daily given as intermittent treatment for 2 weeks followed by a 1-week treatment-free interval every 3 weeks). CAP-B maintenance therapy (intravenous bevacizumab 7.5 mg/kg on day 1 and intravenous capecitabine 1000 mg/m2 twice daily) or capecitabine maintenance therapy (intravenous capecitabine 1000 mg/m2 twice daily) was carried out for patients with stable or better after 6-cycle CAPOX-B induction therapy. "
Response: We have already revised the relevant content in revised manuscript (Page 8, Lines 6-19). "The X-square test or Mann–Whitney U-test was used to compare categorical data. Continuous data were expressed as mean ± SD. A two-sample Student’s t test was applied to analyse differences in continuous data. The primary endpoints were compared using the log-rank test and were assessed by the Kaplan-Meier methods to estimate the mean and median with 95% CI. Cox hazard model were executed to assess the effect of CAP-B and CAP on PFS and OS. Statistical programming and analyses were produced using SPSS software, version 24.0 (IBM, Armonk, New York, USA). All statistical tests were two-sided. Differences were considered statistically significant at P < 0.05." instead of "Categorical variables are expressed as counts and percentages and analysed using the χ²-test or Mann–Whitney U-test. Continuous numerical variables are expressed as the means and SD and analysed using Student’s t-test. mPFS and mOS estimated using the Kaplan-Meier method were compared between groups by the log-rank test. Cox regression analyses were executed to adjust for age, site of primary tumour, number of metastatic sites, and performance status. SPSS version 24.0 (IBM, Inc., Chicago, IL, USA) was used. A P < 0.05 was considered a statistically significant difference for all statistical tests."

2. The Availability of data and materials section refers to the raw data used in your study and presenting tables and figures is not sufficient to state that all data is contained within the manuscript and additional files. Please only use this statement if you have indeed provided all raw data on which your study is based. We strongly encourage all authors to share their raw data, either by providing it in a supplementary file or depositing it in a public repository and providing the details on how to access it in this section. If you do not wish to share your data, please clearly state this in this section along with a justification. Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets):

- The datasets generated and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS]

- The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

- All data generated or analysed during this study are included in this published article [and its supplementary information files].

- The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.

- Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.
• The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [third party name].

• Not applicable. If your manuscript does not contain any data, please state 'Not applicable' in this section.

Please note that if you do wish to share your raw data and do not have consent from all patients to publish this data it will need to be de-identified.

Response: We have already revised the relevant content in The Availability of data and materials section:

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

3. Please also note that if you include your raw data as a supplementary file you will need to provide, after the References, a section titled “Additional files” where you list the following information about each of your supplementary files: * File name (e.g. Additional file 1), * Title of data, * Description of data. All additional files will also need to have been cited in the main manuscript.

For more information and a list of suitable availability statements, please see our Submission guidelines: https://bmcinfectdis.biomedcentral.com/submission-guidelines

Response: Done

4. Please move the statement “All authors have no actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations” found under your “Declarations” heading to replace your existing “Competing interests” statement.

Response: Done

5. Please change the section heading “Materials and Methods” to “Methods”.

Response: "Methods" instead of "Materials and Methods"

6. At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours.
All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.

Response: Done

Reviewer reports:

If improvements to the English language within your manuscript have been requested, you should have your manuscript reviewed by someone who is fluent in English. If you would like professional help in revising this manuscript, you can use any reputable English language editing service. We can recommend our affiliates Peerwith for help with English usage (https://bmc.peerwith.com/bmge/language-editing). Please note that use of an editing service is neither a requirement nor a guarantee of publication. Free assistance is available from our English language tutorial (https://www.springer.com/gb/authors-editors/authorandreviewertutorials/writinginenglish) and our Writing resources (http://www.biomedcentral.com/getpublished/writing-resources). These cover common mistakes that occur when writing in English.

Response: We used an English language editing service: American Journal Experts.

--------------------Declarations--------------------

> Ethics approval and consent to participate

Done

> Consent to publication

Done

> Availability of data and materials

For all journals, BioMed Central strongly encourages all datasets on which the conclusions of the manuscript rely to be either deposited in publicly available repositories (where available and appropriate) or presented in the main paper or additional supporting files, in machine-readable format (such as spreadsheets rather than PDFs) whenever possible. Please see the list of recommended repositories in our editorial policies.

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> Competing interests
All financial and non-financial competing interests must be declared in this section. See our editorial policies for a full explanation of competing interests. If you are unsure whether you or any of your co-authors have a competing interest please contact the editorial office.

The authors declare that they have no competing interests.

> Funding

All sources of funding for the research reported should be declared. The role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript should be declared.

Done

> Authors' contributions

The individual contributions of authors to the manuscript should be specified in this section. Guidance and criteria for authorship can be found in our editorial policies.

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> Acknowledgements

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> Authors' Information

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