Author’s response to reviews

Title: Disease characteristics and treatment patterns of Chinese patients with colorectal cancer: a retrospective study using medical records from China

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Author’s response to reviews:
Thank you very much for your comments. Below are our point-by-point responses. The reviewers’ comments are in bold text and the responses are in plain text. The corrections are underlined (the corrections here are same with that in the main manuscript).

Reviewer 1:

Comments to the Authors

This paper is generally well written, and it describes the real-world demographics and disease prognosis of CRC patients and treatment sequences among metastatic CRC in China with a large population. But I have a serious concern regarding the content. First, this paper has the huge potential to achieve the higher level analysis because of the detailed treatment strategies. However, we can't see the more detailed subgroup analysis about the survival of different combinations of chemotherapy regimens.

Reply:

Thank you very much for your comments. We agreed that the investigation of different combinations of treatment regimens on survival would provide a more comprehensive view of effectiveness of treatments for advanced CRC. As the current study used data extracted from multi-center electronic medical records (EMRs), death information was poorly documented and disease progression information was not directly captured. This limitation is common in using EMR databases in China, and it is not possible to link an EMR database to the National Death Registry. In addition, information on confounders, for examples, diet, smoking, alcohol, was not available in the database. Out concern is that the interpretation of survival analyses can be challenging when the outcome information is not accurate, and results were not nicely adjusted by confounders. Thus, the aim of the current study was designed as exploring the disease characteristics and treatment patterns of patients with colorectal cancer in China. To clarify this issue, in the Discussion, we added “Finally, some key information might not be available or well documented in EMR databases in China. For examples, death information was poorly documented and disease progression information was not directly captured. It is not possible to link an EMR database to the National Death Registry to obtain Deaths. Information on confounders, for examples, diet, smoking, alcohol, was not available in the database. Thus, in the current study, we were not able to provide a more comprehensive view of effectiveness of regimens on survival. It is evident that further real-world evidence, especially from Registries or prospective studies, is required.”

Second, this study has a large population, and it's better to provide the more difference between Chinese and Westerners.

Reply:

Thank you very much for your comments. We agreed with the reviewer. Thus, in addition to the existing discussion on treatment regimens, we expand our discussion to include treatment
patterns in Western countries as a reference. Please see corresponding sentences (original and the newly added) in Discussion section, line 326-330, page 17 and down below.

“Our study found that FOLFOX and other oxaliplatin-based regimens dominated first-line while FOLFIRI and other irinotecan-based regimens dominated second-line. This is consistent with findings from other studies. For example, a study with 1,655 adult mCRC patients in the US reported that about 40% of patients received FOLFOX in first-line therapy, and about 26% of patients received FOLFIRI in second-line therapy [15]. Another US based study reported similar findings [16]. As to third-line therapy, no dominated treatments were identified in China. Importantly, targeted biologics were not frequently used in China until third-line treatment, treatment cycles in third-line was short and some patients moved back to their previously used therapy. In contrast, in the US, the most common third line treatment regimens are EGFR-containing therapies, such as combination of cetuximab and irinotecan, panitumumab or cetuximab monotherapy [15]. In other countries, such as Canada, although oxaliplatin and irinotecan were also the most common chemotherapy backbones for first- and second-line, chemotherapy was usually not used alone [18,19].”

Reviewer 2:

Comments to the Authors

1. Title could be precised as « Disease characteristics and treatment patterns of Chinese patients with metastatic colorectal cancer: a retrospective study using medical records from China »

Reply:

Thank you very much for your suggestion. We have revised the article title as suggested. Please see revisions in Title section, line 1-2, page 1 and down below.

“Disease characteristics and treatment patterns of Chinese patients with metastatic colorectal cancer: a retrospective study using medical records from China”.

2. In abstract, conclusion is too long and should be shortened.

Reply:

Thank you very much for your comment. We have revised it accordingly. Please see revisions in Abstract section, line 63-70, page 3-4 and down below.

“Our findings reflected a lack of consensus on the choice of third-line therapy and limited available options in China. It is evident to continue promoting early CRC diagnosis and to increase the accessibility of treatment options for mCRC patients. As the only nationwide large-scale study among CRC and mCRC patients before more biologics became available in China, our results can also be used as the baseline to assess treatment pattern changes before and after
more third-line treatment were approved and covered into the National Health Insurance Plan in China between 2017 - 2018.”

There are now 272 words in total in the Abstract.

3. Results could be also shortened in a way that only main results are reported in the manuscript, other result already appear in figures and tables.

Reply:

Thank you very much for your comment. We have shortened the result in Abstract section. Please see the revised version in Abstract section, line 54-62, page 3 and down below.

“Among mCRC patients (3,878/8,136, 48%), the fluorouracil, leucovorin, and oxaliplatin (FOLFOX) and other oxaliplatin-based regimens were the most widely-used first-line treatment (42%). Fluorouracil, leucovorin, irinotecan (FOLFIRI) and other irinotecan-based regimens dominated the second-line (40%). There was no a dominated regimen for the third-line. The proportion of patients receiving chemotherapy with targeted biologics increased from less than 20% for the first- and second- lines to 34% for the third-line (p&lt;0.001). The most common sequence from first- to second-line was from FOLFOX and other oxaliplatin-based regimens to FOLFIRI and other irinotecan-based regimens (286/1,200, 24%).”

There are now 272 words in total in the Abstract.


Reply:

Thank you very much for your comments. We have read your recommended paper and other relevant papers as well. We agreed with the reviewer that the bevacizumab is not a standard of care in third line in current clinical practice. In the manuscript, we did not consider bevacizumab as the standard care of mCRC in third line. Nevertheless, to strengthen our findings, we have broadened our discussion with following sentences, also in Discussion section, line 347-350, page 18.

“There have been some major changes in mCRC treatment, especially in the third line since 2017. For example, Bevacizumab (Avastin®) has been included into the national reimbursement list and Regorafenib (Stivarga®) has been approved by CFDA. On September 5th, 2018, Fruquintinib (Elunate®) was approved in China’s market. These new treatment options on market have increased regimen choice and likely expenditures. Despite of that, the optimal use of these agents along with chemotherapy needs further investigation as a phase II multicenter trial
reported little objective responses to the combination of bevacizumab and chemotherapies among advanced CRC patients [41].”