Reviewer’s report

Title: Capecitabine and oxaliplatin combined with bevacizumab are feasible for treating Japanese patients at least 75 years of age with metastatic colorectal cancer

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Reviewer: Efrat Dotan

Reviewer’s report:

The authors responded well to most of the concerns raised by the reviewers. In review of the revised manuscript the following issues were identified:

Major:

1. Introduction: the introduction is very lengthy. It emphasizes the data on tx of mCRC in general, the PK information of capecitabine, and data on XELOX. However the main point of the paper is the use of this regimen in older patient. There is no review of the literature in this regard. As noted in the earlier comments there should be some reference to the recent data from large clinical trials among older mCRC patients.

2. Methods: page 10 lines 9-12 – the authors added description of how neuropathy was graded. It is not clear from this that there was any dose reduction allowed for oxaliplatin. If no dose reduction was allowed that would be odd and should be clarified.

3. Methods: Page 9 line 5 – The sentence: “no prior chemotherapy or treatment of recurrent lesions with only 5-FU without adjuvant chemotherapy”. This is listed as inclusion criteria – this is confusing and not clear what this means… patients could get 5FU only for metastatic disease? and then enroll on the study? patient’s were not allowed to have adjuvant therapy? Please clarify.

4. Results: Page 14, line 7-8: With regards to evaluation of other factors related to older patients. The authors responded that the following factors were evaluated: CCR, ASA score, ASA-PS score, age, BMI, and gender. Although the association with CCr was reported the text does not address the other factors. If no association was seen, that should clearly be state.

5. Results: Page 13 line 7-9: The following sentence is not clear: “Fourteen, 12, and two pt. received the protocol treatment after discontinuation of oxaliplatin, capecitabine and bevacizumab and capecitabine alone respectfully.” This is not clear, did some patients get oxaliplatin alone? Or bevacizumab alone? Please clarify.

6. Discussion: When discussing the shortcoming of the paper, there should be additional wording regarding the lack of elderly specific evaluation (comprehensive geriatric assessment).
Minor:
1. Abstract: the rate of male/female and colon/rectal is reported as ration (i.e. 21:15) this is not a typical way to present this data.
2. Introduction: page 6 line 7 – the OS state is 20m; the recent CALGB data should be used with OS closer to 30m.
3. Methods:
   b. Page 10 line 19 – CA19-9 was tested? Is this correct? Not clear why this would be included in a mCRC study.
   c. Page 11 line 10-13 – the authors added a list of factors that were evaluated in this elderly population (CCR, ASA score, age, BMI, etc) in this paragraph it says that the association was tested with discontinuation of therapy. However, in the results section the association is listed with toxicity. This needs to be clarified.
   d. Page 11 line 15-17 - The authors added a definition of TTF. This definition should be included in the section where PFS and OS are described.
4. Results:
   a. Page 13, line 1: change the ratio reporting to the typical way of reports.
   b. Page 13, line 4 – this line read median of 8 cycles of treatment. However the following line reports a median of 5 cycles, this is not clear.
   c. Page 14, line 14 – when discussing efficacy – should there be ref to table #3?
5. Discussion:
   a. Page 18 line 16: “studies in general population” – wording should be changed since this is not a general population.
   b. Page 19 line 13-14 – “Oxaliplatin is easier than cisplatin” – This is irrelevant since cisplatin is not used in management of CRC.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I do not have any conflicts.