

## Peer Review File

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### Reviewer A

1. Abstract-no changes suggested

Reply 1: We are very much thankful for all the positive and encouraging remarks on our review. No changes were made in the Abstract.

2. Introduction-while surgery followed by chemotherapy may be one of the approaches of treating localized gastric cancer, in other parts of the world, neoadjuvant chemotherapy followed by surgery and adjuvant chemotherapy is also another approach to treatment.

Reply 2: Thanks for this useful suggestion and in response we now have modified our text as advised (see Page 3, line 46-49).

3. Methods-kindly state the exact start dates of literature search ex 10-July 2017 till 12, August 2022.

Reply 3: Thanks for the great suggestion. We confirmed that the exact start dates of literature search ex January 11, 2017 till August 12, 2022 (see Page 5, line 95-96).

4. Methods-Keynote 59,61,62 kindly state OS findings in addition to response rate findings with pembrolizumab and MSI-high tumors as it is very important in context to your paper.

Reply 4: Thank you for the comment and suggestion. Among MSI-High patients, the median overall survival was not reached (NR) for pembrolizumab in KEYNOTE-059, KEYNOTE-061, and KEYNOTE-062. We now have modified our text as advised (see Page 12, line 241-243).

5. For checkmate 32, kindly state exact figure of OS with p value for immunotherapy and MSI high tumor.

Reply 5: We thank the reviewer for this important suggestion and have modified the text (see Page 12, line 252-255).

6. Discussion section needs to be more elaborate. It is very limited.

Reply 6: We thank the reviewer for this comment. As suggested, we have revised the Discussion section.

### Reviewer B

The authors performed literature search to review microsatellite instability (MSI) and immunotherapy in gastric cancer. The manuscript is important to acquire knowledge of clinical trials. Some significant randomized control trials are shown in the text and table. There are a few queries to improve this review.

Reply: We thank the reviewer for his/her very encouraging note on the significance of our study.

1. Table 2 can include more clinical trials that are mentioned in the text, e.g. CHECKMATE-649, and KEYNOTE-061, -062.

Reply 1: This is an excellent suggestion, that we have implemented (see Page 20-22, Table 1 in revised manuscript).

2. Additional information of clinical trials, such as lines of chemotherapy and number of the participants, should be shown in Table 2.

Reply 2: We have made modifications to the current Table 1 in revised manuscript according to your suggestions.

3. As the author indicated, MSI-H gastric cancer is caused by epigenetic silencing of hMLH1. Immunohistochemical pattern of MMR deficiency caused by promoter methylation of MLH1 can be described as well as genetic mutations.

Reply 3: Thanks for your comments. We have revised relative information in the revised manuscript (see Page 8, line 151-155).

4. Table 1 should be supplementary material.

Reply 4: Thanks for your suggestions. We have moved Table 1 to the supplementary material as Table S1 in revised manuscript.

### **Reviewer C**

Duan and Xu submitted a narrative review somehow addressing the prognostic and predictive value of microsatellite instability (MSI) in gastric cancer. The topic is of general interest for readers of Precision Medicine. However, there are major concerns.

Reply: We greatly appreciate the reviewer for his/her positive and encouraging remarks.

1) The authors state that a literature review was performed. However, neither selection of article nor focus (clinical/therapeutic/pathological) is clear and the whole review is a more or less loose assembly of different topics. The authors cite publications focusing on colorectal cancer and not gastric cancer (Acta Biomed 2018;89:97-101). In this respect, table 1 makes no sense and is useless.

Reply 1: Thanks for your constructive suggestion. As you and reviewer B pointed out, we have moved Table 1 to the supplementary material in revised manuscript.

2) Some topics are really very basic, such as explaining the mechanisms of MSI, and neither timely nor necessary.

Reply 2: We appreciate the reviewer's constructive comments. As suggested, we modified the relevant sections.

3) The whole manuscript really needs a very thorough proof reading.

Reply 3: Thank you very much for the critical reading of our manuscript. We completely agree with the comment of the reviewer. We have revised the text accordingly.

Again, we are very grateful to all of you for taking the time to review our manuscript. We sincerely hope that this revised manuscript has now addressed most of your concerns and meet with approval.