

Peer Review File

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Reviewer A

Comment 1: please consider to indicate the treatment outcomes in the title.

Reply 1: Thank you for reviewer's suggestion, we have revised in the title part of the manuscript as: "Camrelizumab and apatinib combined with chemotherapy in perioperative effective therapy for advanced gastric carcinoma with peritoneal metastasis: a case report (**Page 1, line 3**)".

Comment 2: the abstract is not adequate. The background needs to briefly describe the potential clinical significance of this case report. The case description needs more clinical information of this case such as health and nutritional status at admission, details of the chemotherapy, and oncological efficacy and safety outcomes. The conclusion seems to be overstated and please consider to tone down it.

Reply 2: Thank you for reviewer's suggestion, we have revised in the background part of the abstract as: "Peritoneal metastases (PMs) are the most frequent metastatic pattern with a very poor prognosis in stage IV gastric cancer (GC). An effective therapeutic option has yet to be established. Combination therapy of anti-angiogenesis therapy, immunotherapy and chemotherapy was first used in advanced GC for perioperative treatment in this case. (**Page 2, line 53-56**)". We further refined the patient's relevant clinical information, such as health and nutritional status on admission (**Page 2, line 57-59, Page 5, line 146,147**), chemotherapy details (**Page 2, line 59-65**), tumor efficacy (**Page 2, line 59-64**), and safety outcomes (**Page 2, line 66**).

Comment 3: in the introduction, the sentence "we conducted this prospective trial to investigate the efficacy and safety of camrelizumab plus apatinib" is misleading since this is a case report only. The authors need to review what has been known on the treatment strategies for advanced gastric carcinoma with peritoneal metastasis, including efficacy, long-term prognosis and safety. The authors need to analyze why camrelizumab and apatinib combined with chemotherapy is potentially effective. Please also indicate the clinical significance of this case report and analyze its unique clinical contribution. The last paragraph should not describe the findings from this case.

Reply 3: Thank you for reviewer's suggestion, I apologize that "we conducted this prospective trial to investigate the efficacy and safety of camrelizumab plus apatinib combined with chemotherapy as the front-line treatment for patients with GC." was not expressed accurately when I wrote the case at the time, we have revised as: "we investigated the efficacy and safety of camrelizumab plus apatinib combined with chemotherapy as the front-line treatment for patients with GC (**Page 4, line 119,120**)."

We analysed the reasons why combination chemotherapy with camrenizumab and apatinib may be effective (**Page 4, line 112-116**).

We have removed the description of the findings in this case in the last paragraph of the

introduction (**Page 4, line 127, 128**).

Comment 4: in the case presentation, please have more data on the clinical characteristics of this case such as smoking history and health and nutritional status, which are associated with the treatment outcomes.

Reply 4: Thank you for reviewer's suggestion, we described the clinical features of this case such as smoking history, health and nutritional status in the case presentation (**Page 5, line 132, 133, 146, 147, 148**).

Comment 5: in the discussion, the authors may consider to analyze the potential reasons for the relative good treatment response of this case.

Reply 5: Thank you for reviewer's suggestion, in fact in the introduction, we analyzed the possible reasons for the relatively good response to combination chemotherapy with camrenizumab and apatinib in this case (**Page 4, line 112-116**).

Comment 6: please consider to review and cite several related papers: 1. Shinkai M, Imano M. The clinical effect of conversion surgery for advanced gastric cancer patients with peritoneal metastasis. *J Gastrointest Oncol* 2022;13(5):2169-2177. doi: 10.21037/jgo-21-431. 2. Canbay E, Canbay Torun B, Cosarcan K, Altunal C, Gurbuz B, Bilgic C, Sezgin C, Kaban KK, Yilmaz S, Yazici Z. Surgery with hyperthermic intraperitoneal chemotherapy after response to induction chemotherapy in patients with peritoneal metastasis of gastric cancer. *J Gastrointest Oncol* 2021;12(Suppl 1):S47-S56. doi: 10.21037/jgo-20-121. 3. Pan L, Tian Y, Wang K, Tang J, Liu J, Zhang J, Wang M, Liu J, Xu H, Chen X. Low-dose apatinib combined with camrelizumab and the SOX regimen in the neoadjuvant treatment of locally advanced gastric/gastroesophageal junction adenocarcinoma (SPACE-neo): a protocol for an open-label, single-arm, clinical trial. *J Gastrointest Oncol* 2022;13(6):3300-3313. doi: 10.21037/jgo-22-1158.

Reply 6: Thank you for reviewer's suggestion, we have reviewed and cited these 3 relevant papers in this case: 1. Shinkai M, Imano M. The clinical effect of conversion surgery for advanced gastric cancer patients with peritoneal metastasis. *J Gastrointest Oncol* 2022;13(5):2169-2177 (**Page 12, line 347**). 2. Canbay E, Canbay Torun B, Cosarcan K, Altunal C, Gurbuz B, Bilgic C, Sezgin C, Kaban KK, Yilmaz S, Yazici Z. Surgery with hyperthermic intraperitoneal chemotherapy after response to induction chemotherapy in patients with peritoneal metastasis of gastric cancer. *J Gastrointest Oncol* 2021;12(Suppl 1):S47-S56 (**Page 12, line 349**). 3. Pan L, Tian Y, Wang K, Tang J, Liu J, Zhang J, Wang M, Liu J, Xu H, Chen X. Low-dose apatinib combined with camrelizumab and the SOX regimen in the neoadjuvant treatment of locally advanced gastric/gastroesophageal junction adenocarcinoma (SPACE-neo): a protocol for an open-label, single-arm, clinical trial. *J Gastrointest Oncol* 2022;13(6):3300-3313 (**Page 14, line 430**).

Reviewer B

The paper titled "Camrelizumab and apatinib combined with chemotherapy in perioperative therapy for advanced gastric carcinoma with peritoneal metastasis: a case report" is interesting. The incorporation may overcome resistance to treatment with therapy alone and can produce synergistic effects, indicating a promising treatment option in the clinic to gastric cancer with peritoneal metastasis. However, there are several minor issues that if addressed would

significantly improve the manuscript.

Comment 1: Compared with other chemotherapy regimens, what are the advantages of the treatment methods in this study? What is the most likely problem? It is recommended to add relevant content.

Reply 1: Thank you for reviewer's suggestion, the advantages and most likely problems of the treatments in this study have been described in the discussion (**Page 8, line 228-231; Page 9, line 268-269**).

Comment 2: There is only one patient in this study, which is limited and unrepresentative, so it is a little far-fetched to draw such a conclusion. It is suggested to increase the comparative analysis with the same or similar cases at home and abroad.

Reply 2: Thank you for reviewer's suggestion, unfortunately, at present there are no studies in the literature evaluating the efficacy and safety of camrelizumab and apatinib in combination with chemotherapy for the patients with peritoneal metastases from gastric cancer, and the references cited in this article primarily focus on investigations of the combination of camrelizumab and apatinib with chemotherapy for advanced gastric or gastroesophageal junction adenocarcinoma (**Page 8, line 235-240**).

Comment 3: In the introduction of the manuscript, it is necessary to clearly indicate the current treatment strategy for gastric carcinoma patients and the factors that affect the prognosis and recurrence.

Reply 3: Thank you for reviewer's suggestion, we have added to the introduction the current treatment strategies for patients with gastric cancer and the factors that influence prognosis and recurrence (**Page 3, line 83-86**).

Comment 4: What are the characteristics and evaluation criteria of apatinib? What are the effects of apatinib on tumor micrometastasis? It is recommended to add relevant content.

Reply 4: Thank you for reviewer's suggestion, apatinib is a novel oral tyrosine kinase inhibitor (TKI) that selectively targets vascular endothelial growth factor receptor 2 (VEGFR2) (**Page 4, line 103,104**), previous reports in the literature have focused on assessing the efficacy of apatinib in combination with immunotherapy and chemotherapy.

The effect of apatinib on tumour micrometastasis is described in the introduction section of the article (**Page 4, line 115,116**).

Comment 5: It is recommended to extend the follow-up time, and it may be more meaningful to observe the long-term effects of treatment.

Reply 5: Thank you for reviewer's suggestion, we have been continuously following up with the patient after surgery. This case was submitted after the writing was completed in 2021, so the follow-up time mentioned in the article corresponds to the time of the writing.

Comment 6: The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as "Efficacy, prognosis and safety analysis of anti-PD-1/PD-L1 inhibitor rechallenge in advanced lung cancer patients: a cohort study, Transl Lung Cancer Res, PMID: 35832441". It is recommended to quote this article.

Reply 6: Thank you for reviewer's suggestion, we have reviewed and cited this relevant paper in this case (**Page 12, line 364**).

Comment 7: What are the safety, activity and immune relevance of anti-PD-1 antibodies in cancer? It is recommended to add relevant content.

Reply 7: Thank you for reviewer's suggestion, we have added the content about the safety, activity and immune relevance of anti-PD-1 antibodies in cancer (**Page 4, line 101-103**).

Comment 8: With the discovery of new drug targets and the continuous emergence of new combination treatment options, what breakthroughs will there be in the treatment of advanced gastric carcinoma with peritoneal metastasis in the future? It is recommended to add relevant content.

Reply 8: Thank you for reviewer's suggestion, we have added the content related to the future treatment of advanced gastric carcinoma with peritoneal metastasis (**Page 10, line 281-284**).
