

Peer Review File

Article Information: <https://dx.doi.org/10.21037/jgo-23-511>

Reviewer A

First, please indicate the diagnosis of the two cases in the title. Second, the abstract needs some revisions.

Reply A-1: I acknowledge your comment. I added the diagnosis "gastric cancer" in the title
Change in the text: Title, page 1, line 1

The background needs to briefly describe the potential clinical significance of the current case report.

Reply A-2:

Thank you for your comment. I added the reason why this report is important.
Change in the text: Abstract, page 2, line 38

The case presentation needs to provide more clinical characteristics of the two cases including age, sex, disease length, treatment, and efficacy response.

Reply A-3:

Thank you for your comment.
I added some clinical information of the cases.
Change in the text: Background, Case Description, page 2, line 45

The conclusion needs some comments for the early prevention of drug-induced pneumonia.

Reply A-4:

Thank you for your comment. I added some additional comments of early intervention of irAE pneumonia.
Change in the text text Abstract, conclusion, page 3, line 64

Third, in the introduction of the main text, the authors need more review on what has been known on drug-induced pneumonia including the causes, treatment, and outcomes in real-world clinical settings.

Reply A-5a:

I added some general information on drug induced pneumonia.
Change in the text: introduction, page 4, line 1

The authors cannot review ATTRACTION-4 solely because this clinical trial's sample is highly

selective and its sample size is small, which cannot observe rare adverse events.

Reply A-5b: Thank you for your comment. I added latest retrospective study on ATTRACTION-4 regimen implying low incidence of pneumonitis.

Change in the text: Introduction, page 4, line 100

Please also clarify the potential clinical contribution of this report and what the unique characteristics of the two cases are.

Reply A-6:

Thank you for your comment.

I added some comments on clinical contribution and uniqueness in conclusion.

Change in the text: conclusion, page 11, line 267

Fourth, in the discussion of the main text, please also analyze the potential limitations or issues in the managing of the two cases, including lessons, for the failure in saving the two cases.

Reply A-7: Thank you for your comment. I added some comments on some issues on the two cases after the limitation of the study.

Change in the text: Discussion

Finally, please consider to review and cite several related papers: 1. Ma J, Xiao M, Li X, Zhao Q, Ji W, Ling Y, Yang Q. Analysis of the efficacy and safety of paclitaxel (albumin-bound) combined with S-1 and oxaliplatin combined with S-1 in the first-line treatment of advanced gastric cancer: a cohort study. *J Gastrointest Oncol* 2022;13(2):630-636. doi: 10.21037/jgo-22-279.

Reply A-8:

Thank you for your comment.

I added safety information of SOX without nivolumab.

Change in the text:

Discussion, page 8, line 197

2. Otsuka H, Sano A, Azuma Y, Sakai T, Koezuka S, Sugino K, Sakamoto S, Tochigi N, Homma S, Iyoda A. Surgical lung biopsy for interstitial lung diseases—a single center study of 129 patients. *J Thorac Dis* 2022;14(6):1972-1979. doi: 10.21037/jtd-21-1773.

Reply A-8:

Thank you for your comment.

I added the information of biopsy in the manuscript.

Change in the text: Discussion, page 11, line 260

3. Graur A, Montesi SB, Lanuti M, Fintelmann FJ. Treating lung cancer in patients with interstitial lung disease: what do we know? *J Thorac Dis* 2023;15(4):1555-1558. doi:

10.21037/jtd-23-316.

Reply A-8:

Thank you for your recommendation.

Patients with ILD can often be troublesome in cancer treatment. And I added the paper as reference of risk factor for ICI related pneumonitis.

Change: Discussion page 9, line 223

Reviewer B

The paper titled “Two autopsied cases of rare drug-induced pneumonia associated with nivolumab plus S-1 and oxaliplatin: A case report” is interesting. Patients undergoing this regimen (nivolumab plus S-1 and oxaliplatin) should be closely followed up with imaging, symptom evaluation, and serological marker analysis such as lactate dehydrogenase, C-reactive protein, and Krebs von den Lungen-6. However, there are several minor issues that if addressed would significantly improve the manuscript.

- 1) What is the tumour- and class-specific patterns of immune-related adverse events of immune checkpoint inhibitors? What adverse reactions are most likely to occur with the treatment regimen in this study? It is recommended to add relevant content.

Reply to B-1:

Thank you for your comment. I added some information on class-specific pattern and tumor-specific pattern of irAE.

Change in the text: Discussion, page 8, line 203

- 2) In the introduction of the manuscript, it is necessary to clearly indicate the knowledge gaps and limitations of prior study and the clinical significance of this study.

Reply to B-2:

Thank you for your comment.

I emphasized that limitation of prior study of the regimen and the significance of this report.

Change in the text: Introduction, page 4, line 102

- 3) What guidance can this research provide for the early identification and management of immune-related adverse events? How to provide treatment options for patients with advanced gastric cancer? It is recommended to add relevant content.

Reply B-3: Thank you for your comment.

I added some tips for early detection of pneumonia, in addition to some information.

Change in the text: Discussion, page 10, line 246

- 4) What are the key factors for the distant metastasis pattern and prognosis of patients with gastric cancer? It is recommended to add relevant content.

Reply B-4:

Thank you for your comment.

I added some information of prognosis factor of gastric cancer and discussed the effect of the treatment.

Change in the text: Discussion, page 10, line 239

- 5) In order to further verify the role of nivolumab plus S-1 and oxaliplatin, it is necessary to further accumulate clinical cases and conduct larger sample, multi-center, randomized, and controlled clinical trials.

Reply B-5:

Thank you for your reply. I added a phrase that you pointed out.

Change in the text: Discussion, page 10, line 251

- 6) Does immune therapy have long-term effects on other normal tissues? How to monitor the adverse reactions in the follow-up course? It is recommended to add relevant content.

Reply B-6: Thank you for your comment.

I added some information on endocrine irAE in the manuscript

Change in the text: Discussion, page 10, line 248

- 7) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as “Immune checkpoint inhibitor-related interstitial lung disease in patients with advanced non-small cell lung cancer: systematic review of characteristics, incidence, risk factors, and management, J Thorac Dis, PMID: 35693611”. It is recommended to quote the article.

Reply B-7:

Thank you for your reply. I added some information of pneumonia as irAE.

Change in the text: Introduction, page 4, line 84

- 8) What are the risk factors for nivolumab plus S-1 and oxaliplatin-induced pneumonia? It is recommended to add relevant content.

Reply B-8:

Thank you for your comment.

I cannot find specific risk factors for ATTRACTION-4 regimen, and I added general ones in the manuscript.

Change in the text: introduction, page 4, line 86