Response to Reviewer:

Reviewer Name: Anonymous

Review Date: 2022-11-27 20:59

1: Why was PD-L1 not tested after the whole exome sequencing to determine the suitability for PD-1 inhibitors more directly?

RESPONSE: Thank you very much for your question.When the patient was first admitted, routine blood tests showed that platelets were only $42*10^9$, which suggested that the patient was at risk of bleeding, so we did not perform a puncture to test for PD-L1.In response to this, we have added a sentence to the manuscript:" The patient's platelet count was $42*10^9$/L, suggesting a risk of bleeding, so the patient was not directly punctured to test the expression of PD-L1 on the surface of the tumour cells"(Page 5, line130-132, in red).

2: The key indicator affecting PD-1 inhibitors is whether the tumor cells express PD-L1 or not. Why put more emphasis on the expression of PD-1 in cervical cancer in the discussion section?

RESPONSE: Thank you for pointing out the mistakes in our article in time. In view of our mistakes, we make the following corrections:the sentence " In 2017, Angel Garcia-Diaz et al. discovered that interferon-γ could induce PD-L1 expression via the interferon-γ - JAK1/JAK2-STAT1/STAT2/STAT3-IRF1 axis in melanoma cells, leading to immune escape and cancer induction. Meanwhile, cervical cancer patients can also exhibit PD-1 expression. In 2018, Feng et al. reported that 46.97% of cervical cancer patients exhibited PD-1 expression. Additionally, the study confirmed that PD-1 in tumor-invasive lymphocytes (TILs) and PD-L1 and TILs in cancer cells together constitute the PD-1/PD-L1 pathway, and the balance of this pathway is one of the mechanisms of tumor one of the mechanisms of cellular immune escape. However, Meng et al. revealed that 60.82% of patients had PD-1 expression, and PD-1 overexpression was associated with vascular invasion and lymph node metastasis in cervical cancer"has been changed as "Cervical cancer patients can exhibit PD-L1 expression. In 2018, Feng et a reported that 59.1% of cervical cancer patients exhibited PD-L1 expression. Additionally, increased incidents of abortion and childbearing can also enhance PD-L1 expression in tumour cells. The study confirmed that PD-1 in tumour-invasive lymphocytes (TILs) and PD-L1 and TILs in cancer cells together constitute the PD-1/PD-L1 pathway, and the imbalance of this pathway is one of the mechanisms of tumour development and cellular immune escape. In addition, Meng et al revealed that 60.82% of patients had PD-L1 expression, and PD-L1 overexpression was associated with vascular invasion and lymph node metastasis in cervical cancer"(Page 6, line184-187, in red and Page 7, line188-192, in red).

Reviewer Name: **Anonymous**

Review Date: **2023-01-04 13:27**

1. Mild language editing required

RESPONSE: Thank you for your valuable advice.We have edited the article according to your suggestions.

2. To correct the numbers from figures to being spelled out in lines 75, 84 and 159.

RESPONSE: Thank you for advice on precise wording.We changed the number "3" to"three"and changed the number "6" to "six" and changed the number "1" to "one"(Page 3, line 80, in red,Page 4, line 90, in red and Page 6, line 175, in red)

3. All the figures and table lack legends that describe them and key indicators or arrows.

RESPONSE: Thank you very much for your precise advice.We have placed the figures and tables at the end of the manuscript and added the corresponding legends and explanations of the key indicators or arrows.(Page 13-15)

4. Figure 1: What is the H&E on tissue section showing?

RESPONSE: Thank you very much for your question. We have described the HE results of the patient's PJS. The details are as follows."The pathology of the polyp showed a dendritic extension of the mucosal muscle layer into the central part of the polyp, with the glands forming a villi-like structure. The surface of the polyp was covered with normal epithelium and the interstitium showed no obvious inflammatory lesions"(Page 12, line 373-376)

5. FINAL DIAGNOSIS Based on the patient's transoral single-balloon enterosocpy findings and the patient's surgical report, we diagnosed her with PJS combined with advanced cervical cancer However, the figure or data is not shown in this paper. I would think this information is crucial as it leads to a final diagnosis.

RESPONSE: Yes, thank you for your constructive comments.We have inserted in Figure 1 the pathological result of this patient's post-operative cervical cancer and described the result accordingly. The details are as follows."Pathological findings of cervical cancer revealed a highly differentiated adenocarcinoma of the cervix, partly with microscopic adenocarcinomatous changes, infiltrating into the deep mesenchymal layer near the outer membrane with visible vascular tumour plugs and metastases or infiltrations in the right external iliac lymph nodes".(Page 12, line 376-379)

6. Page 7: Considering that JAK2 can promote PD-L1 expression, the patient was treated for the first time with a PD-1 inhibitor (sindilizumab 200 mg, 21 days per cycle) in combination with the CD chemotherapy regimen. JAK2 promote PD-L1 in cancer cells (to cite the original reference)

RESPONSE: Thank you for your valuable advice. We have added the corresponding original reference.The details are as follows.:"The patient was then treated for the first time with a PD-1 inhibitor (sindilizumab 200 mg, 21 days per cycle) in combination with the CD chemotherapy regimen[12].(Page 5, line 135-137, in red and Page 9, line 290-294)

7. OUTCOME AND FOLLOW-UP After two months of follow-up, the patient''s vital signs (what exactly?)were stable. The patient also suffered no significant adverse effects and the tumor markers were within the normal ranges (Table?). It would help if the authors elaborate further on the vital signs/ adverse effects and tumor markers and refer to the table.

RESPONSE: Yes, appreciate reviewer's comments.We have supplemented the specific results

of the patient's vital signs and the changes in tumour markers (Table 2) and we have also discussed the results.The details are as follows."Studies have found that sindilizumab-treated patients often suffer from adverse effects such as fever(38%), anaemia (74.1%) and elevated aspartate aminotransferase (41%) and alanine aminotransferase (40.6%) . At the same time, carcinoma embryonic antigen（CEA）,CA199 and cancer antigen-125（CA125） are useful markers for detecting cervical cancer and monitoring the clinical course. In particular, CA199 and CA125 have been shown to be particularly useful in patients with adenocarcinoma[15]. In our case, after two months of follow-up, the patient's temperature, heart rate, respiratory rate, blood pressure, WBC, haemoglobin concentration, liver function and tumour markers(including CA199,CA125 and CEA) were within the normal ranges（Table 2）".

(Page 5, line 144-152, in red and Page 15, line 413-414, in red)

8. Line 159: 5-hemouracil - spelling error?

RESPONSE: Thank you for advice on precise wording. We changed the word "5-hemouracil" to "5-fluorouracil". (Page 6, line 173, in red)

9. Line 188: We performed whole-exome sequencing and identified the relevant causative genes (results not shown and discussed in this paper)

RESPONSE: Thank you very much for your careful advice. We have added the whole-exome sequencing results and discussed the results in the manuscript. The details are as follows."In addition, considering that the patient had both PJS and cervical cancer, whole exome sequencing (WES) was performed on the patient's blood and showed a mild correlation between Janus kinase-2 (JAK2) and the development of the disease" and "JAK2 is a nonreceptor tyrosine kinase that plays key roles as the intracellular signalling effector of the cytokine receptor. JAK2 was also found to regulate the expression of PD-L1. In 2016, Seiichi Ikeda et al found that the PD-L1 protein is upregulated by the simultaneous amplification of the PD-L1 and JAK2 genes through JAK-STAT signalling in non-small cell lung cancer (NCSLC). In 2017, Angel Garcia-Diaz et al discovered that interferon-γ could induce PD-L1 expression via the interferon-γ-JAK1/JAK2-STAT1/STAT2/STAT3-IRF1 axis in tumour cells, leading to immune escape and cancer induction". (Page 5, line 132-135, in red and Page 7, line 193-200, in red)