Peer Review File

Article information: https://dx.doi.org/10.21037/tcr-22-1679

Reviewer A

In this Case Report, Yang et al. presented a patient with SMARCA4-dificient undifferentiated tumor successfully treated by tislelizumab plus etoposide and carboplatin. The authors claimed that an immune checkpoint inhibitor (ICI) plus conventional chemotherapeutics may be useful patients with SMARCA4-dificient undifferentiated tumor. Additionally, co-existence genomic alterations of KEAP1 and TP53 may contribute to good clinical outcome by ICI.
This report included an important message for physicians to treat patients with SMARCA4-dificient undifferentiated tumor. However, there are major and minor criticisms which should be addressed.

Major comments

1. Figure 1 and 2 were reversed. Figure 1 (e) was not PD-L1 stain. What is an (f) in Figure 1. Those were critical data in this case report. Please correct them.
The authors should explain pathological features precisely. Did lymphocytes infiltrate into the tumor? Tumor microenvironment (TME) is one of predictive marker of ICI responses. In addition, please discuss TME and refer the manuscript (Gantzer J, et al. Oncologist 2022).
Reply1: The pathology image ‘e’ is CD34 stain, it is positive. The pathology image ‘f’ is PD-L1 stain, it is negative. The TME discussion has been added to the article.(see Page3, line 101-107). Thank you very much for your advice.

Minor comments

1. There are a lot of typos. Please correct them. (for example, STKII→STK11, extron→exon?)
Reply : we have modified our text as advised. Thanks.

2. Please correct ‘Professor Xu Shun’. It was not suitable for this journal. Please cite the manuscript.
Reply : we have modified our text as advised. Thanks.

3.This article should be reviewed by an experienced medical editor whose first language is English.
Reply: This article was reviewed by an experienced medical editor whose first language was English. Thanks.

Reviewer B

This manuscript describes the possibility that tislelizumab, etoposide and carboplatin may be effective for SMARCA4-UT. The topic addressed is interesting and deserves a constructive discussion. There are several points that need to be corrected in this manuscript.

1)Maybe, figure number 1 and 2 are reversed.

Reply 1): we have modified our text as advised. Thanks.

2)If pathology image 'e' is PD-L1 stain, it is positive. In the manuscript, PD-L1 expression is none.

Reply 2): The pathology image 'e' is CD34 stain, it is positive.

3)There is no legend for pathology images 'f'.

Reply 3): The pathology image 'f' is PD-L1 stain, it is negative.

4)It should specifically mention about all ten genes related to lung cancer on line 64.

Reply 4):we added some data in the text. (see Page2, line 52-53).Thank you very much for your advice.

5)Doses per body surface area of first and second chemotherapy regimen should be mentioned on line 66-68 and 77.

Reply 5): we added some data in the text. (see Page2, line 56-58and 68-70).Thank you very much for your advice.

6) KEAP1 should be capitalized.

Reply 6): we have modified our text as advised. Thanks.

Reviewer C

1.The wording and grammar is not well edited

2. The figures and manuscript are not compatible

3. I suggest authors to check the figures again and sent the manuscript to professional English editing.

Reply: we have modified our text as advised. Thanks very much.

Reviewer D

In the manuscript "Tislelizumab with Etoposide, carboplatin 1 was effective for 2 patients with Thoracic SMARCA4-deficient undifferentiated tumor: a 3 case report", Yang and colleagues extensively describe a case of thoracic SMARCA4-UT with a high tumor mutation burden (TMB) successfully treated with carboplatin, etoposide, and tislelizumab (TEC). Overall the manuscript provides a detailed clinical case description. I only have a few minor concerns regarding the content in the Discussion section and the Figures. Please see points below and incorporate into the manuscript:

1 Non-small cell lung cancers (NSCLC) are known to display a high TMB. Among the major drivers of NSCLC, loss of either KEAP1 or STK11 have been shown to induce an increase in TMB as demonstrated in the following studies (PMD: 34963055; PMID: 34142094). Since somatic mutations generate neoantigens, high TMB is expected to induce an anti-tumor response and, in fact, it represents a biomarker predicting favorable responses to ICB (PMID: 30775030; PMID: 30309915; PMID: 31470674). However, despite the significant survival benefit of ICB for a subset of patients with advanced NSCLC, the majority of patients exhibiting primary resistance (PMID: 31470674; PMID: 30505707; PMID: 29567705). All these mechanisms should be discussed and cited accordingly.

Reply1: we added some data in the text. (see Page 3, line 89-101).Thank you very much for your advice.

2 Labelling of Figure 1 and 2 should be consistent.

Reply2 : we have modified our text as advised. Thanks.