Peer Review File

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Reviewer A

Comment 1: Results: it would be interesting to know the results by PD-L1 subgroups given the implications of the results on immunotherapy treatments.

Reply 1: Thank you for your comments to our study. Ujiieet al. identified an association between high PD-L1 expression and LUAD-SC, suggesting that this subtype may have a superior benefit in immunotherapy and greater opportunities for ICI treatment. We found that the expression of PD-L1 in cluster 2 was the lowest.

Changes in the text: Page 7, line 207-208, Figure 2D.

Comment 2: Results: it is necessary to add a table with the general characteristics of the sample being studied.

Reply 2: We really appreciate your advice. we have modified our text as advised.

Changes in the text: Page 4, line 117-118, Table 1.

Comment 3: Title: the title is the conclusion of the study, it should be modified to make it a correct title.

Reply 3: We really appreciate your advice. we have modified our text as advised.

Changes in the text: Page 1, line 1-2.

Comment 4: Genes should be in italics.

Reply 4: We really appreciate your advice. we have modified our text as advised.

Changes in the text: Both of the text.

Comment 5: Abstract: I think it would be useful to add some more data in the background of the abstract.

Reply 5: We really appreciate your advice. we have modified our text as advised.

Changes in the text: Page 1, line 25-30.

Comment 6: Abstract: line 30-33 should go in the subject and methods section.

Reply 6: We really appreciate your advice. we have modified our text as advised.

Changes in the text: Page 1-2, line 34-37.

Comment 7: Introduction and discussion: it would also be useful to talk about iPARPs in addition to immunotherapy.

Reply 7: We really appreciate your advice. It is emerging that modulation of ADP-ribosylation signalling can alter the efficacy of clinical PARPi therapy. Identification of biomarkers which would modulate PARPi sensitivity will be essential for efficient treatment with PARPi but development of new inhibitors for ADP-ribosylation factors could have big clinical implications. We added some iPARPs content to the discussion.

Changes in the text: Page 13, line 369-373.

Comment 8: Introduction, line 88: this part of the introduction should go in the discussion.

Reply 8: We really appreciate your advice. we have modified our text as advised.

Changes in the text: Page 12, line 346-349.

Comment 9: Methods: indicate the centre where the study was conducted and the

duration of the study.
Reply 9: We really appreciate your advice. we have modified our text as advised.
Changes in the text: Page 4, line 118.
Comment 10: Methods: state more clearly the objectives of the study.
Reply10: We really appreciate your advice. we have modified our text as advised.
Changes in the text: Page 1-2, line 32-37, 39-41.

Reviewer B

1. The author mentioned in the following sentence is inconsistent with that in the corresponding reference, please check and revise.
   - Scielzo et al. found that in chronic lymphocytic leukemia, the level of HS1 phosphorylation in leukemic cells was associated with clinical prognosis, whereas HS1 hyperphosphorylation was associated with poor prognosis [13].
   - 13. Bray, F., et al., *Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries.* CA Cancer J Clin, 2018. **68**(6): p. 394-424.

   Reply 1: I noticed a confusion in the position of the references, so I reinserted the references for the entire text.

2. The numbers below in Table 1 don't match with your main text. 453+49=502, not 522. Please check whether the numbers are correct.

Table 1 The detailed information of included datasets.

ID	Series	Platform	Tumor	Control	Publication
1	TCGA-LUAD	TCGA	453	49	TCGA, (2022)

The normalized RNA-sequencing datasets (N = 522) and clinically relevant information of LUAD samples (N = 522) were retrieved from The Cancer Genome Atlas (TCGA) database

Reply 2: The number of normalized RNA-sequencing samples from TCGA is 502, including tumors (N=453), control (N=49). The number of clinically relevant information of LUAD samples is 522. The table 1 shows the number of normalized RNA-sequencing samples, not clinically information of LUAD samples.