

## Peer Review File

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### Reviewer A

**Comment 1:** This is a case report of a CD5+DLBCL that was evaluated using a large panel of genes by NGS. It is a case of personalized medicine. The case report is well written, it is easy to read, and to understand. More details of the NGS procedure and results would improve the report.

**Reply 1:** Thanks for the comments. We added and cited a recent published paper on our NGS procedure. In addition, we added more details of the NGS results inside (see Page 10, line 151-152; see supplementary table 1).

**Comment 2:** In the introduction, could you please explain why BTK inhibitors are recommended in the MCD subtype of DLBCL with CD79B and MYD88L265P mutation?

**Reply 2:** Thanks and we included the *in vitro* mechanism study which showed that cell lines of *CD79A/B* and *MYD88L265P* mutations confers ibrutinib sensitivity (see Page 7, line 93-95).

**Comment 3:** In the introduction, what is the pathological mechanism associated with the use of PD-1 inhibitor (torepalimab)? Why is PD-1 inhibition recommended in DLBCL?

**Reply 3:** We added the pathological mechanism of torepalimab in the introduction part (see Page 8, line 108-110). One publication for recommending PD-1 inhibition in DLBCL has also been cited, which showed that elevated PD-1 expression is associated with poor prognosis and the *in vitro* study showed that PD-1 blockade could restore the T cell function (see Page 8, line 114-117).

**Comment 4:** For Mum-1, please also mention the name IRF4.

**Reply 4:** Thank for your comments, we have revised this word into interferon regulatory factor 4 /multiple myeloma oncogene-1 (IRF4/MUM-1, diffusely positive) (see Page 10, line 145)

**Comment 5:** Please define "starry sky phenomenon".

**Reply 5:** We have added more details for the "starry sky" phenomenon, which was characterized by uniform, medium-sized lymphoma cells with multiple basophilic small, inconspicuous, centrally located nucleoli, and basophilic cytoplasm (see Page 10, line 139-142)

**Comment 6:** Could you please provide more information regarding the 689 gene panel?

**Reply 6:** Sorry that the panel should be 688 genes and we have cited a previous publication, which showed the included 688 genes and more detailed information on this panel (see Page 10, line 151-152).

**Comment 7:** The different mutated genes are shown, including the VAF, but is it possible to include the detailed description of the mutations? I imagine the mutations were annotated using anovar, and later the high confidence calls were identified using a series of parameters.

chr, start, end, ref, alt, func.ref.gene, etc. etc...

**Reply 7:** Thanks for your suggestions. We added the detailed description of the mutations inside and attached another file with the mutation details inside (see supplementary Table 1)

**Comment 8:** Line 197. Could you please confirm "glaucoma"?

**Reply 8:** Yes, we have confirmed that variants in the *CDKN2B/CDKN2B-AS1* gene have been reported to influence the risk of developing glaucoma in multiple genome-wide association studies conducted on diverse populations (see Page 14, line 214).

**Comment 9:** Is it correct to evaluate the TMB using this panel of genes?

**Reply 9:** Thanks for the valuable comments, we have included relevant articles that shows the advantages of evaluate the TMB using this panel of genes (see Page 16, line 248-252).

**Comment 10:** Do you have access to histological images, including the immunohistochemistry?

**Reply 10:** Thanks for your suggestions and we have provided the histological images, including the hematoxylin-eosin (HE) staining and part of the immunohistochemical staining results (see supplementary Figure 1).

#### **Reviewer B**

**Comment 1:** As suggested by the CARE reporting checklist, "case report" should be included in the keywords.

**Reply 1:** Thanks for the comments. We added the "case report" in the keywords and modified this section (Page 4, line 55-56).

**Comment 2:** The item #12 of CARE checklist should be "N/A" if the patient's perspective was not mentioned in the text. Please add it to the manuscript or revise the checklist.

**Reply 2:** Thanks for the comments. We revised the checklist and changed it to "N/A" for item #12 in CARE checklist (see CARE reporting checklist).

**Comment 3:** You refer to "studies" with only one literature citation couple times in the text. Please check and revise.

**Reply 3:** Thanks for the comments. We have modified the citation and added ref 21 (Quan L, et al), which is a citation in the original ref 20 (see Page 9, line 120; see Page 23, line 374-376).

**Comment 4:** Subfigures should be cited consecutively.

**Reply 4:** Thanks for the comments. We revised and cited the subfigures consecutively according to the figure details (see Page 10, line 146-151).

**Comment 5:** Provide an overview caption for Figure 2, 3, and S2.

**Reply 5:** Thanks for the comments. We added the overview caption for Figure 2, 3, S1 and S2 as suggested (see Page 27, line 427-438; see supplementary figure 1/2).

**Comment 6:** Add age units where necessary in the main text of the manuscript.

**Reply 6:** Thanks so much for the suggestions. We added the age units in the main text as advised (see Page 8, line 100/103/104; Page 17, line 272).

**Comment 7:** All abbreviations should be spelled out on first occurrence in Abstract/ Highlight Box/ Main Text/ Figure/ Table.

**Reply 7:** Thanks for the comments. We spelled out all the abbreviations on first occurrence in Abstract / Highlight Box / Main Text / Figure / Table (see Page 3, line 42/45; see Page 5, line 58; see Page 6, line 74-78; see Page 17, line 263; see Page 27, line 433; see supplementary figures and tables)

**Comment 8:** Indicate which time is correct.

232 In August 2022, the patient became “less talkative” and the Magnetic Resonance  
233 Imaging (MRI) results suggested a central recurrence with diffuse and nodular  
234 gray matter swelling with perilesional edema (measuring 28x20 mm) in left  
235 frontal lobe (Figure 3A-B). Afterwards, she was administrated four courses of

455 **Figure 3.** Magnetic Resonance Imaging of the brain for the patient. Magnetic  
456 Resonance Imaging with relapse in September 2022 (A,B); Magnetic Resonance

**Reply 8:** Thanks so much for the comments and we have confirmed that the time should be September 2022 (Page 8, line 239).

**Comment 9:** Check whether this time should be June 2023.

467 **Supplementary Figure 2.** Computed tomography of the lung for the patient.  
468 Computed tomography after toripalimab and rituximab treatment in March 2023  
469 (A-D); Computed tomography of progressive disease in July 2023 (E-H).←

**Reply 9:** Thanks so much for the comments and we have confirmed that the time should be June 2023 (Page 15, line 477).