

Peer Review File

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Reviewer A

Here are a few suggestions to consider:

1. I suggest that the title of the manuscript be reworded to: Review of recent data concerning the symptoms and toxicity free time for patients with relapsed/refractory Large B-Cell Lymphoma receiving CART cell therapy.

- Thank you for your suggestion to reword the title of the manuscript. We appreciate your input and have carefully considered your recommendation. "Comparing Axi-Cel and SOC in Relapsed/Refractory Large B-Cell Lymphoma: Q-TWiST, Survival Insights, and CAR-T Therapy Considerations" was found to effectively encapsulate the core focus and scope of our study, allowing readers to quickly grasp the essence of our editorial.

2. I suggest a major revision of the first paragraph of the manuscript:

2A) Follicular lymphoma should be added to the list of indications for CD19 CART therapies.

- Thank you for your suggestion. We have revised the first paragraph of the manuscript to include follicular lymphoma in the list of indications for CD19 CAR-T therapies, as per your recommendation.

2B) The authors should re-evaluate the statement "In Europe, tisagenlecleucel axicabtagene ciloleucel (Yescarta™) is approved for the treatment of R/R high-grade B-cell lymphoma" Tisagenlecleucel (Kymriah by Novartis) and Axicabtagene ciloleucel (Yescarta by Kite) are 2 different CART products. I wonder if the authors forgot to put the word "and" between tisagenlecleucel and axicabtagene ciloleucel. If that was the authors' intent, then the sentence should be revised accordingly. Once the sentence is revised, then the appropriate indications for the products should be listed.

- Thank you for your observation. You are absolutely correct. The sentence was revised to reflect the two distinct CAR-T products and their respective indications in the 1st paragraph.

3. I suggest that the authors should stay consistent on the use of "immune-chemotherapy" and "chemo-immunotherapy". Either of them is correct but the authors should use the same format throughout the manuscript.

- Thank you for your observation regarding the consistency in terminology. We ensured that a consistent format is used throughout the manuscript with the following: "chemo-immunotherapy".

4. I suggest that the authors define the chemotherapy regimens first prior to using the abbreviations: R-CHOP, R-CARBO-DHAP, R-ICE. While many hematologists would understand what the abbreviations stand for, non-hematologists may not. Alternatively, a list

of abbreviations should be provided as a supplement to the article.

5. I suggest that the authors reword the 3rd paragraph (lines 35-38) to read: “The standard of care (SOC) for relapsed DLBCL patients had previously been salvage chemoimmunotherapy, such as R-CARBO-DHAP, R-ICE or similar regimens, followed by autologous stem cell transplantation where appropriate. Recently, CAR-T cell therapies have demonstrated improved response rates and improved survival in patients with R/R DLBCL.

- Your suggestion incorporated. We have revised both the second and third paragraphs in alignment with your recommendations regarding abbreviations, and subsequently merged them, as they addressed the same subject matter.

6. I suggest that the authors should first define Q-TWiST and then use the abbreviation subsequently. That way, all readers can be familiar with what Q-TWiST means. Alternatively, a list of abbreviations should be provided with the manuscript.

- Thank you for your suggestion. We have noted your recommendation in the 3rd paragraph and ensured that the abbreviation "Q-TWiST" is mentioned and we initially defined it in the manuscript too.

7. I suggest that in the 4th paragraph (lines 39-46), the authors should first inform the readers that they are about to pivot to discussing the article by Kersten et al [Transplant Cell Ther. 2023 126 May;29(5):335.e1-335.e8. doi: 10.1016/j.jtct.2023.01.008]. Without that gentle introduction, the reader is lost as regards which Q-TWiST analysis is being referred to. I personally had to search several times in the manuscript to know which Q-TWiST analysis was being referred to.

- We made the necessary revisions to the 3rd paragraph to introduce the transition and context for the upcoming discussion, ensuring that readers can readily identify the relevant Q-TWiST analysis.

8. The word “value” should be added after utility in Line 44 as follows: method, state specific QoL utility value (U, ranging from 0 to 1), assuming a base case

- The following was implemented in the 3rd paragraph

9. The points raised by the authors from lines 49-86 are reasonable, and well presented.

- Thank you for your positive feedback on our manuscript. We appreciate your acknowledgment of the points we raised in lines 49-86

Reviewer B

1. Paragraph 1: CAR T cell therapy is also approved for treatment of r/r follicular lymphoma.

- Thank you for your suggestion. We have revised the first paragraph of the manuscript to include follicular lymphoma in the list of indications for CD19 CAR-T therapies, as per your recommendation.

2. Paragraph 2: please note that Pola-R-CHP is also approved as a first line therapy, please mention briefly and include citation.

- Thank you for providing this additional information. We will make the necessary revision to the second paragraph to include the mention of Pola-R-CHP as a first-line therapy and provide the appropriate citation

3. Paragraph 3: when comparing SOC to CAR T in second line, should probably cite Zuma 7 and the study leading to approval for liso-cel in this setting as well.

- Thank you for your suggestion. We have incorporated the relevant citations for the ZUMA-7 trial and TRANSFORM Trial, as well as their respective findings in the paragraph.

4. Line 63: I agree that longer term OS data is needed in second line setting, but it already is available in the third line setting for axi-cel and is compelling. Could mention that here

- We appreciate your input. We have addressed this point in the manuscript. We have mentioned the availability of long-term OS data for axi-cel in the third-line setting from the ZUMA-1 trial, and we have reported the findings of this trial in the same paragraph

5. Paragraph starting on Line 72: Is there any available data on PROs, functional status, etc. and how they relate to CAR T outcomes in the literature? I believe there are for at least one available CAR T product, and can be mentioned here to strengthen your argument.

- Thank you for your suggestion. We have incorporated two recent studies, Balitsky et al. (2022) and Sidana et al. (2022), to the manuscript to improve our argument in the same paragraph

6. Since the toxicity and efficacy appear similar but not exactly the same for each of the available CAR T agents, this could be mentioned as something that could also be evaluated.

- Thank you for this important suggestion, the following was incorporated in the last paragraph of the manuscript.

7. Last paragraph: there are publications regarding the cost effectiveness of CAR T in the third line setting that could be mentioned briefly to strengthen your point here, I believe.

- Thank you for your comment regarding the last paragraph. We incorporated this relevant information into our manuscript to enhance the strength in the last paragraph