

Peer Review File

Article information: <http://dx.doi.org/10.21037/atm-20-5546>

Reviewer A: The review reports the existing data on the efficacy and safety of CAR T-cell therapies in mature lymphoid malignancies (lymphomas, chronic lymphocytic leukemia, and multiple myeloma), with an in-depth scenario of the challenges posed by CAR T-cell therapeutics. The manuscript is well written and well organized, and in my opinion is suitable for publication.

Comment 1: Please check the text formatting and the lack of some spaces, especially between the references in brackets and the text.

Response 1: We thank the reviewer for the positive review. We have ensured that all spaces are uniform throughout the manuscript.

Reviewer B: The review article focuses on the applications of CAR-T therapy in mature lymphoid malignancies, with an in-depth discussion on challenges and suggestions of such approach. The review provides a good overview of the topic from a clinical perspective, although certain sections may need revision:

Comment 1: Introduction and Section 2 can be shortened and combined together. There are a lot of reviews available on structure of CARs, which can be referenced to shorten this section, and the information could be delivered via adding more detail to Figure 1 and a comprehensive figure legend.

Response 1: We thank the reviewer for the suggestion. We have shortened and combined the two sections as per reviewer suggestions and have added more detail to the Figure 1 and legend.

Comment 2: Introduction would benefit from a description of current clinical challenges linked to mature lymphoid malignancies, and why CAR-T is an advantageous treatment option, as they are not immediately mentioned in the initial presentation of the review.

Response 2: We thank the reviewer for this constructive feedback and have added some information pertaining to challenges in mature lymphoid

malignancies, especially in DLBCL, in the introduction section.

Comment 3: The review would benefit from a section summarising the biology and possible targets of mature lymphoid malignancies, and explaining the choice of focus on these malignancies, e.g. the difference with other lymphoid malignancies (e.g. acute lymphoblastic leukaemias).

Response 3: We appreciate the reviewer's comment and agree that it is important to highlight why certain targets are chosen for CAR T-cell therapy. Since mature lymphoid neoplasms are a large and heterogeneous group of disorders, we have discussed the biology of targets in each section and added more information (3.2- 3.4) instead of creating a separate section. This would also allow the reader to find all pertinent information within a particular lymphoid neoplasm section. We hope that the reviewer finds this alternative solution acceptable.

Comment 4: Figures 2, 3 and 4 need more detailed labelling and explanation in figure legends. Also Figures 3 and 4 can be combined in one and their differences better explained in figure legends.

Response 4: We have added more detailed labeling and explanation in figure legends for the figures. We have also combined Figure 3 and 4 into one figure.

Comment 5: The title could be further refined to highlight the focus on mature lymphoid malignancies, and perhaps specify "clinical opportunities and challenges"

Response 5: We have edited the title according to reviewer suggestions.