Peer Review File

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Reviewer A

This editoral commentary is for original report by Schultz et al. which has been published in JCO, "Outcomes After Nonresponse and Relapse Post-Tisagenlecleucel in Children, Adolescents, and Young Adults With B-Cell Acute Lymphoblastic Leukemia".

We thank the reviewer for the thorough examination and the favorable summary of our paper. Please find below a detailed response addressing each comment and how we have incorporated them into the revised manuscript.

Comment 1: >5% bone marrow blasts.

- it is incorrect. ≥5% bone marrow blasts is correct as the crtiteria for high disease burden.

Reply 1: Thank you for this correction.

Changes in the text: See line 51 and 79 of the revised manuscript.

Comment 2. 41% (22 of 52) of relapsed patients had loss.

- 41% should be incorrect. 42% is correct.

Reply 2: While we do agree with the author, that the correct percentage would be 42%, the number 41% is given in the original manuscript by Schultz et al. and was therefore used in our discussion.

Changes in the text: /

Comment 3: Loss of CD19 was associated with significantly decreased overall survival rates,

- Loss of CD19 is not accurate description. Loss or downregulation of CD19 should be precise.

Reply 3: We agree with the reviewer that “loss or downregulation” is the more precise description and have changed the text accordingly.

Changes in the text: See line 66, 68, 70, 73, 88, 137 of the revised manuscript.

Comment 4. highlighting109 the feasibility of subsequent CAR infusions to reinstate remission. However, overall survival analysis after second CAR-infusions can not be unequivocally.

- Please unify the term, CAR infusions or CAR-infusions,

Reply 4 and changes in the text: Has been corrected in line 118 of the revised manuscript.

Comment 5. antigen loss and CD19-negative relapse are

- antigen loss and CD19 downregulation relapse should be accurate.

Reply 5: Has been specified in the revised version.

Changes in the text: see line 137-138:

“Schultz et al. emphasized that relapse with antigen loss or downregulation of CD19 are associated with an even worse overall survival…”

Reviewer B

Comment 1: This is a very nice editorial on the manuscript by Schultz et al; I only recommend that the authors are consistent with their nomenclature; for example, they use at least three different versions for 'CD19-CAR T-cell therapy' (CD19-CAR therapy, CD19-CAR-T therapy, CD19-CAR-T-cell therapy).

Reply 1: We thank the reviewer for this endorsement and addressing the nomenclature have revised the manuscript using only “CD19-CAR-T cell therapy” or “CD19-CAR therapy”.

Changes in the text: see line 31, 39, 57, 82, 105, 113, 115, 125, 146

Reviewer C

Comment1: This editorial is a very good commentary on the article by Schultz et al and highlights the relevant findings of the cohort of patients treated with tisa-cel in the real-world setting, the achievements and the pitfalls.

Reply 1: We thank the reviewer for this favourable assessment of our manuscript.