

Peer Review File

Article information: <https://dx.doi.org/10.21037/tp-22-656>

Comment 1: Line 93: Delete "We also" as it was used in the sentence above and change to "including "American Society of Hematology" and cross referenced the references..."

Reply 1: Thank you for the observation of this redundancy.

Changes in the text: Methods section inserted from side document to make line numbers coincide with draft sent with review. "We also" was removed and the closing sentence of the methods was concatenated to the previous sentence in lines 93-94.

Comment 2: Line 96: Change "Molecular targeted" to "Molecularly targeted"

Reply 2: Thank you for the recommendation.

Changes in the text: Changed to molecularly in line 96.

Comment 3: Line 105" This statement makes it seem that all TALL can be effectively targeted with ABL1 inhibitors. Please edit to describe which TALL should ABL1 inhibitors be considered.

Reply 3: Appreciate the recognition of this lack of clarity in the language.

Changes in the text: The statement is updated per your suggestion specifying the type of TALL and additional reference provided.

Comment 4: Line 107: imatinib was initially used as a single agent in Ph+ CML and then came to R/R Ph+ ALL as a single agent.

Reply 4: Thank you for bringing historical context to this discussion.

Changes in the text: Lines 107-108 - The initial treatment of Ph+ CML was corrected to the initial use of imatinib, and the subsequent use of imatinib to treat r/r Ph+ ALL as referenced by the article cited. Additional reference of imatinib use in CML provided.

Comment 5: Line 115: What is the even better 5-yr EFS better than? The 3-yr was 80% and 5-yr drops to 70% Please edit to clarify this statement.

Reply 5: Thank you for recognizing this lack of clarification.

Changes in the text: The statement was edited and the language adjusted to avoid confusion.

Comment 6: Line 123: A problem with the Shen data you reference is the outcomes in the imatinib arm is significantly lower than what COG has published and thus makes the dasatinib data look even better. The COG dasatinib and imatinib 5-yr data in Ph+ BALL are not different. You need to make this clearer to the reader.

Reply 6: Thank you for identifying this study dichotomy regarding outcomes.

Changes in the text: Lines 129-131- The additional clarification of the outcomes of AALL0622 has been included and the additional outcomes study has been cited. Lines 143-144- Additionally since similar outcomes were mentioned briefly in the section below, the sentence structure was simplified. Sourcing was added.

Comment 7: Line 138: The COG AALL1131 trial is not ongoing but has closed after completion

Reply 7: Thank you for pointing out the current accrual state of the trial.

Changes in the text: Lines 138 – Language for the current study status has been adjusted.

Comment 8: Line 142: What % of relapses after dasatinib have T315I mutations? I believe these are very rare in peds, even in the relapse setting.

Reply 8: Thank you for this interesting question.

Changes in the text: No data was able to be found on the % of T315I mutation in peds. The reference was actually cited from an adult study. The statement was revised to reflect information taken from adult studies.

Comment 9: Line 144/145: You state the COG and BFM imatinib/dasatinib trials report similar outcomes so how do you rectify the Shen results? Which is accurate? This should be discussed.

Reply 9: Thank you for pointing out the discrepancy in the presented data.

Changes in the text: Elaboration was added in the preceding lines of the paragraph to clarify the above point regarding the two trials. This portion is outlining the similar outcomes between AALL0031 and AALL0622.

Comment 10: Line 189/190: FDA was already described so you don't need to spell it out again but can use the acronym FDA here. Chronic lymphocytic? What is chronic lymphocytic?

Reply 10: Thank you for pointing out the redundancy and lack of clarity on the disease discussed.

Changes in the text: Line 189-190, explicit FDA language removed in favor of abbreviation. Disease meant to be noted is chronic lymphocytic leukemia, language adjusted. Also, added the full description at the first used term.

Comment 11: Line 227: The COG study AALL1521 is not currently open but has completed accrual and closed. You could change it to "A recently completed phase II study".

Reply 11: Thank you for pointing out the lack of clarity in the study status.

Changes in the text: Line 227 – language adjusted as suggested above.

Comment 12: Line 253: The COG bortezomib was NOT a placebo study. There was no placebo so please remove. Bortezomib was compared to the control arm which had the same chemotherapy but without bortezomib.

Reply 12: Thank you for pointing out the incorrect statement regarding control arm.  
Changes in the text: Line 253- language adjusted to reflect above.

Comment 13: Line 259: carfilzomib is not a new drug and has completed a phase 1 trial in pediatric R/R ALL (see Burke M et al. PBC 2022; PMID: 36215217)

Reply 13: Thank you for the additional information to include regarding carfilzomib.  
Changes in the text: Line 259-260, added reference to above mentioned study as well as reference to completion of phase 1b study.

Comment 14: Line 284-287: this paragraph does not flow with the one above and ETP is not defined for the reader to follow what you are talking about. What does this paragraph add to the paper? Please edit

Reply 14: Thank you for pointing out this discrepancy. We agree with you, the paragraph does not seem to add any significant information here.

Changes in the text: The paragraph was removed to maintain the fluency of the sections of the manuscript.

Please note that reference #86 was removed as part of this editing. In the clean version of the edited manuscript, provided as an additional/supplementary document, the bibliography and references appear in the correct updated manner.

Comment 15: Line 310: This trial has closed

Reply 15: Thank you for clarifying the trial status.

Changes in the text: Line 310- study status has been adjusted and results from ASH (2022) added with additional reference.

Comment 16: You should reference data in ped AML using HMA (PMID: 29339403; PMID: 35726868; PMID: 35180323)

Reply 16: Thank you for pointing out these publications as corroborating data on pediatric AML.  
Changes in the text: References have been included and mention of their results was also included.

Comment 17: Line 381: The COG study AALL1821 was closed due to inferior outcomes in both study arms.

Reply 17: Thank you for pointing out the status of AALL1821.

Changes in the text: Line 381- explanation of study closing noted and language adjusted.