Peer Review File

Article Information: https://dx.doi.org/10.21037/tp-23-567

Review Comments

Comment 1: L47-38 Does 60% cases positive for EOI MRD? Please clarify.

Reply 1: The text has been clarified to reflect 60% of patients were EOI MRD negative.

Changes in the text: Page 3, lines 59-61: Text changed to, "For comparison, *KMT2A-r* infants treated on Interfant-06 achieved CR1 91% of the time with 60% EOI MRD negative, and 85% of patients achieved an M1 marrow with 68% EOI MRD negative on the MLL-10 study."

Comment 2: L88 ziftomenib (KO-539) is another menin inhibitor. Please clarify.

Reply 2: The text notes that the KOMET-007 trial utilizes ziftomenib. The authors believe this wording appropriately indicates that data are being reviewed that utilizes a different menin inhibitor as the text initially was written, but additional clarifying language has been added.

Changes in the text: Page 5, line 103: The words, "another menin inhibitor" have been added before ziftomenib for additional clarification.

Comment 3: Please cite JPLSG MLL10 study

Reply 3: Incorporation of this citation improves the manuscript by adding an important infantile ALL patient cohort.

Changes in the text: Page 3, lines 59-61 and page 4 lines 78-81: The data from the MLL10 study have been summarized with appropriate citations added.

Comment 4: The reviewer has requested a table with open menin inhibitor clinical trials or a figure showing the mechanism of action of these drugs

Reply 4: The authors have added a table outlining menin inhibitors undergoing clinical trial investigation.

Changes in text: See Table 1 Active and pending clinical trials utilizing menin inhibitors

Comment 5: The reviewer notes that the authors should comment on the TINI 2 trial being active and enrolling

Reply 5: The authors have added reference to this enrolling study.

Changes in text: See both Table 1 and page 5, lines 105-106 for reference to the TINI 2 trial

Comment 6: The reviewer has requested the additions of the KMT2A translocation breakpoints upon first mention in the text

Reply 6: The authors agree that incorporation of the translocation breakpoints and resulting gene fusions would enhance the manuscript.

Changes in text: See page 3, lines 50-58 for incorporation of full translocation breakpoint annotation among the discussed KMT2A translocations.

Comment 7: The review notes that text was not dedicated to the excellent outcomes seen in t(11;19)(q23;p13.3)/KMT2A::MLLT1-positive T-ALL

Reply 7: Treatment response for these patients initially was not noted in the editorial commentary given the focus on the overall poor response of KMT2A-rearranged ALL patients to chemotherapy. The authors agree that incorporating this data adds completeness and strengthens the manuscript.

Changes in text: Page 3, lines 56-59 discuss the favorable response to therapy of the t(11;19)(q23;p13.3)/KMT2A::MLLT1-positive T-ALL patients and compare to the dismal response of t(9;11) T-ALL patients.

Comment 8: In line 20, I would replace "lysine methyltransferase 2A (mixed lineage leukemia, KMT2A)" with "lysine methyltransferase 2A (KMT2A, formerly mixed lineage leukemia, MLL).

Reply 8: The authors thank the reviewer for this attention to detail and have made the recommended change.

Changes in text: Page 2, lines 23-24 now state "lysine methyltransferase 2A (KMT2A, formerly mixed lineage leukemia, MLL)"

Comment 9: References supporting a statement concerning the prognostic value of the KMT2A rearrangement partners in pediatric AML (lines 54-56) could also include a recent, very large study by the International Berlin-Frankfurt-Münster Study Group (van Weelderen et al. J Clin Oncol. 2023;41(16):2963-74).

Reply 9: The authors are appreciative of this suggestion and agree that adding this reference adds additional completeness to the citation.

Changes in text: Page 3, line 68. This citation has been added.

Comment 10: References no. 15 (Hodder et al.) and no. 22 (Stein et al.) are incomplete. Please provide year of publication and doi for the former, prepublished paper, and a journal name, year of publication, volume and page numbers for the latter article.

Reply 10: The authors appreciate this comment and apologize for incompleteness of the initial citation.

Changes in text: Please see updated references 17 (Hodder et al.) and 24 (Stein et al.).

Comment 11: "Event-free" and "disease-free" should be hyphenated.

Reply 11: The authors agree with this grammatical correction.

Changes in text: All instances of "event-free" and "disease-free" now include the needed hyphen.