



March 2017

Dear Dr. Kong

Please find enclosed our revised submission of the manuscript 33493 entitled "Lymphocyte Recovery is an Independent Predictor of Relapse in Allogeneic HCT Recipients for Acute Leukemia"

The following cover letter is in response to the reviewer's comments. The response follows each comment and the corresponding changes in the text (if applicable) have been highlighted in bold.

Reviewer #1

Comments to the authors: Moussab Damlaj et al report a retrospective study on the value of lymphocyte recovery in predicting the outcome of leukemic patients receiving an allogeneic transplant. The work is well designed and performed, and the interpretation of the results supports previous papers. The authors admit the intrinsic limitations of this type of retrospective analysis. Minor comments:

1. Abstract: Check wording, recovery is repeated?

Response: Thank you for your comment. The redundancy has been removed.

2. What type of allogeneic donors were used? Related, unrelated, haplo? This should be clarified in the patients section.

Response: Thank you for your comment. This information was included in table I and for added clarity, we incorporated this information in the results section, under "patient and transplant characteristics".

3. It appears that all transplants were performed using mobilised peripheral blood grafts. This should be also clarified in the patient section.

Response: Thank you for your comment. All patients received grafts from peripherally mobilized stem cells and in fact, bone marrow or cord blood grafts were excluded as they result in different immune reconstitution kinetics. This was previously illustrated in the methods section. For added clarity, we included a statement in the results section under “patient and transplant characteristics”, as well as in the first paragraph of the discussion section.

4. Progression Free Survival (PFS) was calculated from the time of transplant until death of any cause or relapse. It should be time to relapse.

Response: Thank you for your comment. We used a standard definition for PFS in which death from any cause or relapse of disease is considered an event, whichever comes first. This is the standard definition used in BMT and BBMT journals. (For example; Bone Marrow Transplant 2001; 28: 909-915).

5. Regimens containing TBI were more common in the DLR group at 63% vs. 33% (p = .019). This finding deserves a comment on the discussion section.

Response: Thank you for your comment. We acknowledge that TBI was used more frequently in the DLR group however we did not see an impact on relapse on the use of TBI in the univariate stage with the hazard ratio and p-value almost approaching 1. A statement to this effect was included in the first paragraph of the discussion section.

Reviewer #2

This is an interesting study, demonstrating lymphocyte recovery as Independent predictor for relapse in allogenic hematopoietic stem cell Transplantation for acute leukemia. Comments:

- 1. In Table 1 the authors described favorable, intermediate and high risk cytogenetics. Please add references to show which criteria they used.**

Response: Thank you for your comment. The definitions of cytogenetic risk status was highlighted in the materials and methods under “patient selection” subsection. Reference 15 indicates the definition used to indicate cytogenetic risk status in AML patients, whereas references 16-20 were used to highlight high risk status in ALL patients. This information was included in the original submission.

- 2. The authors demonstrated ELR as a protective factor from disease relapse in acute leukemia. But PFS and OS were not significantly improved. The authors should discuss this point in more details.**

Response: Thank you for your comment. This point was discussed further in the first paragraph of the discussion section and changes highlighted in bold. We observed a higher incidence of cGVHD and cGVHD related deaths which may rationalize why no difference of PFS and OS was seen.

We hope you find the responses above and the revised manuscript to be acceptable for publication. Thank you for your consideration.

Moussab Damlaj, MD (on behalf of the co-authors)