ANSWERING REVIEWERS

Dear Editor,

We would like to thank the reviewers for their review and comments. Following your advice we are now submitting a revised manuscript, which has taken into account the comments of the reviewers. Changes from the previous manuscript are underlined. The specific changes in response to the reviewers' comments are described below.

Title: Advances and perspectives on cellular therapy in acquired bone marrow failure diseases

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Name of Journal: *World Journal of Hematology*

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Reviewer 1 comment:

1. **"The authors included AA, MDS and PNH in one category, but recent therapies differ for each of these diseases. Since the introduction of eclizumab and azacitidine, treatments of PNH and MDS have changed significantly, no more depending on SCT."**

   Answer: This mini-review of ABMFD is to cover the three most prevalent disorders that compose ABMFD. Though AA is the most prevalent form of ABMFD, discussion of AA only as a representation of all ABMFD disorders is incomplete. Eculizumab, as the first drug approved by FDA to specifically treat PNH, significantly changed landscape of PNH treatment, but SCT still is the only existing treatment that can cure PNH. Azacitidine and decitabine as two hypomethylating agents have shown effectiveness in treating not only MDS, but also other malignant diseases as well. However, SCT is still a gold standard treatment for MDS with unfavorable prognosis as per NCCN guidelines.

2. **"To convince the readers about the efficacy and usefulness of stem cell therapy, actual therapeutic data to date should be included".**

   Answer: We would like to thank the reviewer for his/her thoughtful comment. However, this is an invited mini-review to particularly discuss the current status and future prospects of ABMFD managements. We consider preparing a meta-analysis review on the efficacy and usefulness of current available stem cell therapies for ABMFD based on this mini-review in the near future.

3. **"in America or worldwide how many patients with AA were actually treated with non-SCT (IST alone) and with SCT and what were the comparative outcomes for OS or EFS between these two groups? Also, how many patients with AA received PBSCT, BMSCT, UCBT and Novel SCT? What were the actual outcomes among those patients? Also, to date, how many patients received**

haploidentical HSCT, amplified UCBSCT, and mesenchymal SCT? What were the actual outcomes among those patients?"

Answer: We would like to thank the reviewer for this excellent epidemiological question regarding AA managements and outcomes. We provided some epidemiological information at the section of "Clinical Presentation and Current Management Options" in this manuscript. Briefly, AA is an extremely rare disease with an incidence rate of 2 case per million people in Europe and 4 to 6 cases per million people in Asia. Because of the rarity of this disease, there is lack of statistics data on managements and outcomes.

4. **"Minor points: (1) Incidences of MDS and PNH were in America, while that of AA was worldwide? No data on AA in America? (2) It is stated that platelet transfusion should be avoided if it is possible. More specifically, how to cope with such situation needs to be commented. (3) More clear statements are required about the importance of allogeneic SCT rather than auto-SCT for ABMFD."**

Answer: (1) As per data form AA &MDS International Foundation, 12,000 to 15,000 people are diagnosed with MDS, 600 to 900 people are diagnosed with aplastic anemia, and about 500 people are diagnosed with PNH each year in the United States.
(2) The sentence "platelet transfusion should be avoided if it is possible" was intended to avoid unnecessary transfusion and to reduce the risk of transfusion related infection. We edited this sentence in the manuscript to make it a more clear statement. There is nothing for patient to cope under such situation.
(3) The patients with ABMFD lack of hematopoietic stem cells themselves. Autologous stem cell transplantation is not an option for this group of patients. We edited the sentence in the manuscript make it a more clear statement.

<u>Reviewer 2</u>:

We thank reviewer 2 for enjoying reading this paper, grading it as excellent and accepting its' publication as its current format.

<u>Reviewer 3</u>:

"to change the word thrombocytes for platelets"

Answer: We thank the reviewer for acknowledging the paper as a very updated, precise and concise article that will be of great interest for the hematological community readers. The reviewer's specific concerns are now addressed. We changed thrombocytes for platelets on pages 3, 4, 11and 12.

<u>Reviewer 4</u>:

"Although transfusion and HSCT are used for the treatment for the ABMFD, the authors should emphasize the points that are more specific or relevant to ABMFD."

Answer: We thank the reviewer for acknowledging the manuscript as a well written manuscript and easy to follow. The reviewer's specific concern is now addressed. This article is a mini-review with a word limitation, thus we cannot make it an extensive or detailed review. We are preparing a meta-analysis review that will provide more detailed discussion on therapy impacts on individual ABMFD.

Reviewer 5:

"the authors could highlight along of the revised text more about the novelty and importance of their paper."

Answer: We would like to thank this reviewer for his nice comments. Following this reviewer's advice, we add the sentence ".Currently, there is a lack of literature that offers insight into ABMFD as a class of disorders. This review offers a comprehensive overview of many of the standard and novel treatment options." at the end of introduction section.