

Responses to reviewers' comments:

Reviewer #1:

- This mini-review on the use of stem cells for the treatment of perianal IBD/Crohn's disease describes the current literature on autologous and allogeneic adipose and bone marrow derived stem cells. This is an area of interest given the efficacy of published studies and the article is structured so that it is easy to follow. While the authors describe several relevant studies, my major concern is that the aim of the study and inclusion/exclusion of studies are not clearly listed. As a result, the article acts more as a brief description of some of the previous studies rather than something more substantial which would be of greater benefit to clinicians. There are substantial differences in the outcomes reported in the various studies and hence further details or descriptions of why this may be the case would help explain the apparent differences in results to readers across the trials and what the future direction of study would be (beyond stating that randomized study are necessary, more details on techniques of delivering stem cells the dose that is more efficacious and any preparation techniques that have been particularly promising). - Would you expect there to be a difference between the different types of stem cells and what would be the basis of this? Based on the available studies do you believe one type is superior or shows more promise compared to the others or are further studies required?
 - Thank you! This article was written as a mini-review, with the primary goal of summarizing the major and recent clinical trials evaluating stem cell therapies for perianal IBD. Certainly, there is a need also for systematic reviews and meta-analysis evaluating the all-inclusive utility of these treatments; however, our main goal was to provide a mini-review summarizing the major studies on this topic of growing interest.
- When did the search for articles for the review finish? For example, there is an article in Gastroenterology by Dietz et al. Autologous Mesenchymal Stem Cells, Applied in a Bioabsorbable Matrix, for Treatment of Perianal Fistulas in Patients With Crohn's Disease. This article was not included in your review, but it seems it should have been. Why? –

- The search for articles ended in 2017. This study was relatively small, particularly for a trial done recently, so it was not originally included. I have now added this article to our review.
- More details are required in the table describing the differences in techniques used to administer the stem cells as this would allow readers to understand the differences in response rates – method of administration, number of treatments, amount of stem cells administered, concurrent therapies (e.g. infliximab), inclusion criteria (such as disease severity, if stated), duration of study and definition of primary end point should all be included so readers will not have to revert to the text for these details.
 - The table has been updated with the above information; I intentionally held off including all the inclusion and exclusion criteria, but I did add the most unique and trial-specific aspects of the different studies' details to the tables
- Minor comments: The last sentence in the first paragraph explains that the article reviews hematopoietic stem cells but it focuses on mesenchymal stem cells which as the authors say are non-hematopoietic. Please correct or clarify.
 - I corrected this. Thank you.
- Consider removing “promising” from the title.
 - We will keep it in the title for now but are flexible to remove it.
- The use of frustrating in the first line of the conclusion is a bit emotive, consider changing it e.g. to problematic.
 - Changed to problematic

Reviewer #2:

- Well done. Would consider more appropriate for World Journal of Gastroenterology. Would include more details on largest study and mention current phase 3 in US.
 - Thank you! I have now included more details on largest study and mentioned its phase 3 status.