

## 3251 – Answering reviewers

We would like to thank the journal and the reviewers for giving their precious time and making valuable comments on the manuscript.

### Reviewer #1:

No changes required

### Reviewer #2:

No changes required

### Reviewer #3:

*1. "This manuscript is lacking in sufficient introduction of the current progress about diagnosis and therapy of perianal CD. More information about deep remission of perianal Crohn's disease should be involved because the definition is still controversial. Defining deep remission as the association of clinical remission and healing on MRI may not be completely reasonable. Mucosal lesion under endoscopy should be considered. This reviewer considers that deep remission should be defined as an integrated assessment of clinical remission and mucosal heal. Then the correlation between deep remission and MR image should be analyzed to explore the predictors of deep remission".*

AU: Thank you for these comments.

First, we agree that the field of perianal disease diagnosis and treatment is changing fast. Improvements in MR technique including 3 Tesla imaging and serial MR examination have emerged as standard to prepare, to guide and finally to gauge the success of treatment (Sheedy SP, Bruining DH, Dozois EJ, Faubion WA, Fletcher JG. MR Imaging of Perianal Crohn Disease. *Radiology* 2017;282(3):628-645). We have modified the introduction section to emphasize these innovations.

Second, recent innovative procedures have been published. If plug insertion in fistula tract failed to achieve significant improvement for patients, activation of expanded allogeneic adipose-derived mesenchymal stem cells, was recently proved to be effective as reported by Panés et al in the Lancet (Panés J, García-Olmo D, Van Assche G, Colombel JF, Reinisch W, Baumgart DC, Dignass A, Nachury M, Ferrante M, Kazemi-Shirazi L, Grimaud JC, de la Portilla F, Goldin E, Richard MP, Leselbaum A, Danese S, for the ADMIRE CD Study Group Collaborators. Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial. *Lancet* 2016;388:1281-1290). We have included these promising results in the introduction section of the manuscript. Also we would like to draw the reviewer's attention to our definition of deep remission, including complete clinical response and MR normalization, which is in accordance with the approach developed in Panés' paper and is adapted to perianal lesions. However, we agree that the absence of ulceration in the anal canal should also be part of the definition of deep remission (as in luminal CD) and accordingly we have changed the definition in our revised version. Please note that none of the patients fulfilling the criteria for clinical remission and normal MR had ulcers on anal canal in endoscopy. We did not perform complete endoscopy in this study. As a consequence we can not provide the results of colonoscopy concerning the entire colon.

2. *“There are some minor spell mistakes in the manuscript. For example, “reportedfollow-up at line 1 paragraph 3 of the discussion section,” and “.” at line 3 paragraph 5 of the discussion section”.*

AU: We thank the reviewer for drawing our attention to these typographical errors and apologize for this oversight. The mistakes have now been corrected as suggested.

3. *“Language - Grade C: A great deal of language polishing*

AU: We are grateful for the reviewer’s remark. The paper has been extensively edited for accuracy of language and clarity of expression by Rouen University Hospital’s native English speaking Medical Editor.