Author’s response to reviews

Title: Evaluation of dose reduction vs. standard dosing for maintenance of remission in patients with spondyloarthritis and clinical remission with anti-TNF (REDES-TNF): study protocol for a randomized controlled trial

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Author’s response to reviews: see over
Dear Sirs/Madams,

Please find attached below the answer to the second reviewer and editor comments to the manuscript with reference MS:6429041331585359, entitled "Evaluation of dose reduction vs. standard dosing for maintenance of remission in patients with spondyloarthritis and clinical remission with anti-TNF (REDES-TNF): study protocol for a randomized controlled trial", whose authors are Caridad Pontes, Jordi Gratacós, Ferran Torres, Cristina Avendaño, Jesús Sanz, Antoni Vallano, Xavier Juanola, Eugenio de Miguel, Raimon Sanmartí and Gonzalo Calvo, and for which I am the corresponding author.

On behalf of the author’s please find a new version of the manuscript edited accordingly, as well as a point-by-point response to the concerns raised by the reviewer, which we feel have been all addressed. We would very much appreciate if you could re-consider the publication of this new version of the manuscript.

Please don’t hesitate to contact me for any questions or clarifications.

With best wishes,

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**Summary of changes:**

**Last paragraph of page 10 (Inferential analysis)**
The principal and key secondary end-points will be assessed by estimating the between-treatment risk differences after 1 year of randomization and checking these against the pre-defined non-inferiority margin (delta (δ)) of 17%. If the remission rate of dose reduction is lower than that of full dose, the lower bound of the confidence interval in the full dose arm has to be above 60% to conclude non-inferiority, to ensure that the control treatment has been reasonably effective. Rates and risk differences will be estimated using a log-binomial regression model including the treatment and the factor used to stratify the assignment. In the event that the model does not fit, the Poisson link distribution function with robust variance will be used instead [34-38].

**First paragraph of page 15 (discussion)**
“there is no data on their value in predicting the clinical result”

**ACKNOWLEDGEMENTS (Page 18)**
We have combined the two Acknowledgements sections into one section.

**Detailed responses to the Reviewer**

According to the letter detailing the responses, the article is much improved; however, there are a number of incomplete editing aspects.

a) Although the letter says a sentence beginning with “If the remission rate of dose reduction …” has been added in the Statistical Analysis / Inferential Analysis on p 9 (appears to be p 10 of the revised draft), I cannot find it in the revised draft. I assume this was just an oversight. Please ensure that this is corrected. This should be considered a compulsory revision but should be easily corrected.

**Response:** We apologise for this important oversight, which has now been corrected by adding the text in last paragraph of page 10.

b) Regarding the added paragraph (which is on pp14-15 of the revised draft) beginning with “The study has a number of potential limitations...”: I think this paragraph is a valuable addition to the discussion. Note about 2/3 of the way into the paragraph a redundant use of language: “their predictive value in predicting”.

**Response:** We have deleted the word “predictive” in the corresponding sentence of the first paragraph in page 15, to avoid redundancy.

**Otherwise, the responses and text changes are all satisfactory.**

**Response:** We thank very much the reviewer for the thorough review and relevant commentaries raised.
Detailed responses to the Editorial requests

1. Please combine the two Acknowledgements sections into one section.

Response: We have combined the two Acknowledgements sections into one section.