Author’s response to reviews

Title: The efficacy of a cyclin dependent kinase 9 (CDK9) inhibitor, FIT039, on verruca vulgaris: study protocol for a randomized controlled trial

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Response to comments by the Reviewer and the Associate Editor

We greatly appreciate for the precious comments by the Editor and the Reviewer.

Comment 1: In your response you mentioned that an ITT analysis is being done. Generally this means that all subjects who were randomized would need to be in the analysis, and thus a plan for missing data is needed to specify how to handle the potentially missing outcomes of any individuals who drop out. The Spirit Guidelines provided by the authors imply (20c) there is not a plan for missing data, suggesting a complete case analysis instead is planned. Please clarify in the protocol this apparent contradiction and if an ITT analysis is planned, how any missing outcomes of randomized individuals who drop out will be handled in the analysis.
Response to Comment 1: Accordingly, we have clarified how to handle missing data in lines 311 to 314 (underlined) of the revised manuscript.

Lines 311-314: For patients who drop out of this trial regarding the efficacy primary endpoint of disappearance of warts in the efficacy primary analysis, the missing data are imputed as the failure of disappearance of warts (baseline observation carried forward approach). For the other efficacy analyses, missing data are not imputed.

Relating to this comment, we correct a typographic error found in line 326 as follows:

Before correction: … patients who drop out of this trial and who fail to include the full analysis set…

After correction: … patients who drop out of this trial or who fail to include the full analysis set…

With regard to the 20c of the Spirit Guidelines we provided, we agree to the discrepancy the Reviewer raised. We accordingly filled the page number (page 18) where our plan for missing data is described. We appreciate for the Reviewer's suggestion.

Comment 2: There still seems to be problems with the page numbers listed in the current Spirit Guidelines do not always match where the corresponding content is in the manuscript, for example allocation, sample size, and statistical methods. Please correct accordingly.

Response to Comment 2: We apologize for the discrepancies between the Spirit Guidelines and our manuscript. We have corrected them accordingly.

Additionally, we would like to remove the following lines to avoid too speculative descriptions:

Lines 49-50 (Abstract): …as well as HPV-mediated malignant and premalignant diseases, such as oral florid papillomatosis, Bowenoid papulosis, and cervical cancer.

Lines 378-381: …that can cure HPV-mediated malignant and premalignant diseases, such as oral florid papillomatosis, recurrent respiratory papillomatosis, Bowenoid papulosis, and epidermodysplasia verruciformis, all of which are difficult to control with treatment strategies.

Furthermore, according to a request from the Editorial Office, we have removed the below listed files from the submission.

Ethical Approval Document

Funding Documentation