LETTER

Comment on “A Randomized, Double-Blind, Non-inferiority Study of Febuxostat Versus Allopurinol in Hyperuricemic Chinese Subjects with or Without Gout”

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With interest we read the article of Zhang et al. on the efficacy of febuxostat in the treatment of hyperuricemia [1]. The authors reported that febuxostat 40 mg/day did not meet the primary endpoint of non-inferiority versus allopurinol 300 mg/day, but superiority was demonstrated for febuxostat 60 and 80 mg/day. We compliment the authors on the performance of this randomized controlled trial, however we would like to address two considerations regarding the design of the study.

Firstly, the selection process, which we find to be unclear. How were the participants recruited? And what was the applied definition of “a history of gout”? The gold standard is the identification of monosodium urate (MSU) crystals in synovial fluid. Information on these items is important for the generalizability of the results.

Secondly, the data analysis. To determine the primary endpoint the authors performed a per-protocol analysis that included only 472 of

the 599 randomized participants. However, a sample of 474 participants was required, and so the results of that analysis are underpowered (although minimally). The authors then compared the results of this pre-protocol analysis with those from what they called the full analysis set. However, the full analysis set comprises only those subjects with a serum uric acid level of > 7.0 mg/dl at randomization and who had taken at least one dose of the randomized treatment; this still excluded 46 participants, therefore insufficiently ruling out confounding and attrition bias. We would suggest that the authors additionally perform an intention-to-treat analysis that includes all 599 randomized participants. In such an analysis, the effect of febuxostat would possibly be diluted, but the analysis would at least more certainty provide a true effect with sufficient power.

In conclusion, based on these considerations we look forward to a more thorough description of the selection process and the results of the intention-to-treat analysis, with the aim to improve the robustness of the found effect of febuxostat.

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

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REFERENCE

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