To the Editor: We read the study on the efficacy and safety of tenapanor in Japan with interest.1 We present a few concerns.

Our first concern is about the reason for the withdrawal of patients from the study in the 60 mg per day titration group. In the discussion, the stated reason for these withdrawals was diarrhea. In the 60 mg per day dose-titration group, the dose was adjusted according to the gastrointestinal symptoms. Therefore, we think that a factor other than diarrhea may have caused the withdrawals in the 60 mg per day dose-titration group. We believe that further clarification and investigation into the reason for these withdrawals could help to reduce the number of withdrawals in clinical practice.

Our second concern is about the appropriateness of the minimum dose. In a previous study conducted in the United States, the efficacy was confirmed in the 6 mg per day group.2 This would suggest that perhaps a lower dose than the minimum dose used in this study1 would have been a better choice.

Finally, our third concern is about a typographical error. In Table 1, the number of people taking vitamin D in the placebo group ought to be 33, and not 3.

1. Inaba M, Une Y, Ikejiri K, Kanda H, Fukagawa M, Akizawa T. Dose-response of Tenapanor in patients with hyperphosphatemia undergoing hemodialysis in Japan—a phase 2 randomized trial. Kidney Int Rep. 2021;7:177–188. https://doi.org/10.1016/j.ekir.2021.11.008

2. Block GA, Rosenbaum DP, Yan A, Chertow GM. Efficacy and safety of tenapanor in patients with hyperphosphatemia receiving maintenance hemodialysis: a randomized phase 3 trial. J Am Soc Nephrol. 2019;30:641–652. https://doi.org/10.1681/ASN.2018080832

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NCT04766385, NCT04766398, and NCT04767581), a dosage regimen of dose-up titration from the minimum dose was adopted based on the results of this phase 2 study.

Regarding the second point, the efficacy and safety of a daily dose of 6 mg were confirmed in a previous study in the United States of America, as Drs. Aoki and Kataoka indicated. In addition, the safety of daily doses of 30 mg, 60 mg, 120 mg, and 180 mg was confirmed in the phase 1 study with healthy Japanese volunteers, and a daily dose of 6 to 30 mg is expected to be safe in Japanese patients. Based on those results, the minimum study drug dose in our study was set at 10 mg per day.

Finally, regarding the third issue identified about the number of patients taking vitamin D in the placebo group in Table 1, this was indeed a typographical error, which we will correct in an erratum.

1. Block GA, Rosenbaum DP, Yan A, Chertow GM. Efficacy and safety of tenapanor in patients with hyperphosphatemia receiving maintenance hemodialysis: a randomized phase 3 trial. *J Am Soc Nephrol*. 2019;30:641–652. https://doi.org/10.1681/ASN.2018080832

2. Johansson S, Rosenbaum DP, Knutsson M, Leonsson-Zachrisson M. A phase 1 study of the safety, tolerability, pharmacodynamics, and pharmacokinetics of tenapanor in healthy Japanese volunteers. *Clin Exp Nephrol*. 2017;21:407–416. https://doi.org/10.1007/s10157-016-1302-8

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