

ber of concerns. It is not surprising that casopitant with ondansetron was superior to ondansetron alone; this certainly would not be a proof of efficacy unless one could compare ondansetron alone with casopitant alone. If the authors had any questions regarding the efficacy of this drug, I am very curious as to why they decided not to analyze the data of the casopitant-alone arm. Because the authors did explain why their study did not include a placebo-only arm, I believe that they also owe an explanation for why the casopitant-only arm was not included in the efficacy analysis. I do not believe that there are enough data on casopitant for the authors to assume primary efficacy of this drug and move on to look only at its efficacy when combined with a second drug. If the study's primary purpose was dose finding for the prevention of postoperative emesis in the first 24 h, it is concerning that the only data analyzed were the data where casopitant was given with another antiemetic.

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In Reply:

Ondansetron is currently generic, inexpensive, and considered by most to be safe with few side effects. Presently, consensus guidelines recommend that patients at high risk for

postoperative nausea and vomiting should receive combination therapy.¹ Therefore, this study was designed to examine the most likely clinical scenario (patients at high risk of postoperative nausea and vomiting receiving combination therapy). We do agree that a direct comparison between ondansetron and casopitant would provide valuable information. To that end, we did include the casopitant-only exploratory arm in the study. In fact, the article does already provide the 0- to 24-h complete response data (primary endpoint) for the casopitant-only arm. In this arm, 71 of 142 patients (50%) achieved the primary endpoint in contrast to 56 of 140 patients (40%) in the ondansetron-only arm. In the article, statistical tests were not performed on these data because the analysis would have been *post hoc* and violated our statistical plan.

As designed, the study was underpowered to evaluate single-agent casopitant *versus* ondansetron. However, a simple chi-square analysis comparing the casopitant-alone arm to the ondansetron-alone arm would have resulted in a *P* value of 0.09 favoring casopitant. This analysis has important methodologic flaws and as such inferences based on this *P* value should be drawn with care. Thank you for your letter; it raises an issue that was the subject of much discussion among the investigators during the design of the trial and the preparation of the manuscript.

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