Reviewer's report

Title: Palonosetron versus ondansetron as rescue medication for postoperative nausea and vomiting: a randomized, multicenter, open-label study

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Reviewer: David Hardman

Reviewer's report:

I have serious concerns about this manuscript, because it appears to be over-reaching to find something positive to say about palonosetron, especially given the potential for bias with two of the four authors having currently or previously worked for Eisai. This is of a particular concern given the open-label design of this trial.

Major compulsory revision:

Although neither the primary nor secondary endpoints showed any advantage to the use of palonosetron, the conclusions in the abstract and manuscript are trying to massage any possible advantage to the use of palonosetron, by referring to trends in emesis reduction that favor palonosetron, but are not statistically significant.

Why not comment that this work appears to confirm the earlier work of Canidotti showing no efficacy with rescue administration of 5-HT3 RA's after earlier prophylaxis for PONV with these same type of agents? Also, there should be more commentary in the discussion about the study design choosing to administer prophylactic ondansetron at the beginning of the case, rather than at the end of the case as per SAMBA PONV Guidelines. Giving ondansetron at the beginning of the case would potentially bias study results to favor palonosetron.

There needs to be more discussion about how the study was powered. Although I did not review their calculation, they indicate that the study was powered for descriptive purposes, but later on claim that it could have been underpowered and that's why there was no detectable difference in the primary or secondary endpoints. And yet the authors achieved the total number of patients treated with either palonosetron or ondansetron that they were trying to recruit (98 vs 100), which leads me to believe that the study was adequately powered for the primary endpoint.

What could further studies add to this topic? There appears to be no advantage in using palonosetron vs ondansetron for rescue anti-emetic therapy, after prophylactic treatment with a 5-HT3 RA. Even if a small, statistical difference could be eventually be proven, the clinical relevance is negligible, given the 300X cost differential, not to mention the availability of other cheaper pharmacologic alternatives that work via different receptor antagonists or mechanisms, and are efficacious.
Furthermore, these data are almost 5 years old. Why has it taken them so long to submit their work? But most seriously, the only piece of data that would potentially show any advantage to the use of palonosetron does not appear to be credible. Everything in their argument hinges in table 3 (secondary end points). Looking down the columns for palonosetron and ondansetron, and across the rows, "no-emesis," "0-72 hr," and "0-24 hr," the number of patients who received ondansetron and had no episodes of emesis was lower over the 0-72 hr time period than it was over the 0-24 hr time period. That simply does not make sense, and this is the only reason why the 0-72hr time period "approaches statistical significance," while the 0-24hr time periods, and 24-72hr time periods show no difference.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests below