Reviewer's report

Title: Comparison of vilanterol, a novel long-acting beta2 agonist, with placebo and a salmeterol reference arm in asthma uncontrolled by inhaled corticosteroids

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The primary aim of this study was to show that Vilanterol, a new ultralong acting beta 2 agonist was superior to Salmeterol and Placebo at 24 hour after dosing. 34 centers recruited 347 patients and 298 completed. As main inclusion criteria was patients with asthma, symptomatic and unstabel despite being treated with regular ICS.

The study fail to show superiority over placebo or salmeterol. The authors argue that this is because of a very significant placebo effect, probably due to improved ICS adherence after entering the study.

I miss information on patient demographics and evaluation of incusion criterias. In previous GSK studies evaluating the effect by LABA included patients usually have an FEV of 50-80% of predicted and a minimum reversibility of 15%. Patients in this study had a mean FEV at screening of 66.6% of predicted normal and a mean FEV reversibility of 26.2-30% All were on ICS treatment at baseline.

Real life feasability evaluation has shown that this type of very beta-2 responsive patients on regular ICS treatment are very rare. Consequently there is a risk for selection bias where centers having a large fraction of ICS non-adherent patients are being favorized.

This problem should be discussed more in detail.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.