Reviewer's report

Title: Real-life Effectiveness of Budesonide/Formoterol Maintenance and Reliever Therapy in Asthma Patients Across Asia: SMARTASIA study

Version: 2 Date: 4 October 2012

Reviewer: Sejal Saglani

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Major Comments to be addressed

I agree it is important to assess the efficacy of the SMART regimen in a real life clinical setting, but the outcomes assessed are very limited. Importantly, there is no record of acute exacerbations. This is an important outcome to assess since most of the clinical trials have reported the main impact of SMART on exacerbations and hospital visits.

It is also very difficult to work out the baseline severity of the subjects’ asthma. The treatment they were on before being changed onto the SMART regimen is not clearly documented anywhere.

In table 2, it appears that only 19 subjects were on ICS at entry. Does this mean almost all patients were not on any controller medication before inclusion? The usual management would be to introduce ICS alone in all patients as an initial step-up from just as required SABA. Why was a combination device introduced before this initial step to achieve control. This study does not tell us the effect of stepping up to a combination device and SMART regimen, we may just be seeing the beneficial effect of regular ICS when added to mild uncontrolled asthma.

Were any patients already on a combination device before being included (so did some have a twice daily combination device plus SABA as required, and then changed to SMART?).

Did the patients have a SABA as well in case extra doses of the combined inhaler were ineffective? If so, was a record made of SABA use?

If this is a “real-life” setting study, then the use and completion of daily diary cards is likely to be unreliable. It is well recognized that even in clinical trials patients do not accurately record daily symptoms, therefore it is difficult to know in this scenario how accurately daily diary cards would have been completed.

How was adherence to medication recorded?

Although this is an open label study, and therefore a placebo arm cannot be expected, there is no comparator arm at all. For example if patients were being stepped up to combination therapy, it would be much more useful to have compared twice daily combination therapy alone to the SMART regimen. I feel
very uncertain whether the benefits seen here are actually from the SMART regimen, or simply from a step-up in medication from ICS to combination therapy, or from SABA to combination therapy. Therefore it is difficult to know what question is actually being answered.

Minor comments to be addressed
Figure 4 is not helpful. There are no error bars, and no markers of statistically significant differences / change. Why has FEV1 not been plotted longitudinally as a line graph in a similar manner to ACQ and AQLQ? The axes have also not been labeled, should they say FEV1 (L)?? There is no record of change in FVC this would also be useful to see.

The mean number of inhalations taken of the drug is not recorded. How many extra inhalations in addition to the twice daily inhalations were taken?

The ACQ score and AQLQ score have been stated in the text, in a table and in figures – the same data does not need to be shown in 3 different formats.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

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