Reviewer's report

Title: Efficacy and safety of inhaled formoterol 4.5 and 9 microg twice daily in Japanese and European COPD patients: Phase III study results

Version: 1 Date: 21 June 2011

Reviewer: Gabriele Nicolini

Reviewer’s report:

Major compulsory revisions:

1) abstract background actually is not a background and states the study included moderate to severe patients but there is no lower limit for FEV1 in inclusion and from table 1 FEV1% range it is clear that patients with less than 30% were included. This patients are considered very severe in the GOLD guidelines.

2) Among safety outcomes, hematology, ECG and vital signs were measured but are not reported in the results.

3) The sample size was calculated to show a difference between treatments of 0.06 L that is less than what is considered a clinically relevant difference. Especially when evaluating the 60 min post dose effect that is nearly the maximum effect of formoterol. How can this choice be justified?

4) the primary outcome is reported only as % change from baseline that is not fully clear, can absolute values be shown?

5) In the tolerability results the number of patients that discontinued treatment for adverse events is not consistent (1 unit greater) when compared with that reported in figure 1 for any group

6) table 2 reports ratios between groups but would be more clear and useful for interpretation if reporting absolute values

Minor essential revisions

1) In the background there is a reference to studies with budesonide/formoterol but the references [5-8] include the TORCH study that was made with fluticasone/formoterol.

2) in the methods is reported that patients were required to have at least 2 points of a symptom score, it would be useful to know which scale was used and the range

3) figure 4 lacks information about the measure (puffs/day?)

4) in the discussion numbers and p values related to reliever medication use and SGRQ score are the same repoted in the results, it would be better to discuss the
results and not repeat the numbers and p values in the discussion section

5) the part of the discussion focusing on the comparison of LABA and anticholinergics in COPD (Salpeter and Rodrigo) is repeated from the introduction

6) check reference 10

7) in the safety results two deaths are reported of which one for unknown causes

8) the primary outcome shows an increase of 113% vs baseline in both groups but in figure 2 the column of formoterol 9 is higher than formoterol 4,5

discretionary revisions

the title focuses the study was done in Japanese and European patients but no info is given in the results or in the discussion between these subgroups, were analyses made?

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

Quality of written English: Acceptable

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

Declaration of competing interests:

I am employee of a multinational Pharmaceutical Company named Chiesi Farmaceutici S.p.A. with headquarters in Italy