Author's response to reviews

Title: Phase IV non-inferiority trials and additional claims of benefit

Authors:

Rosemarie DLC Bernabe (R.Bernabe@umcutrecht.nl)
Grace Wangge (g.wangge@uu.nl)
Mirjam J Knol (mirjam.knol@rivm.nl)
Olaf H Klungel (O.H.Klungel@uu.nl)
Johannes JM van Delden (j.j.m.vandelden@umcutrecht.nl)
Anthonius de Boer (a.deboer@uu.nl)
Arno W Hoes (A.W.Hoes@umcutrecht.nl)
Jan AM Raaijmakers (jan.a.raaijmakers@gsk.com)
Ghislaine JMW van Thiel (g.j.m.w.vanthiel@umcutrecht.nl)

Version: 6 Date: 26 April 2013

Author's response to reviews:

Dear Editor,

Thank you for your comment. Below is a description of our revision.

Associate Editor’s comment:

The authors could have been more responsive regarding Comment 5 by the Reviewer. I think we should ask them to include their response regarding this point in the discussion section of the paper to reflect critically on potential problems with their literature search.

(Comment #5: In my opinion it is helpful to include the additional reference on the article in the discussion. A way forward would indeed be adding an objective to show superiority for a relevant endpoint to the objective to show non-inferiority for another endpoint of interest. The concern of my original comment was that phase IV trials could be described as superiority trials in PUBMED and the (subordinate) non-inferiority objective may not have been mentioned in the abstract. These studies are then consequently not included in the analysis presented by the authors, which is acceptable, but could be mentioned briefly in the discussion.)

We added the following sentences in the discussion section (in the paragraph that discussed limitation of the study) to further accommodate the revisions described in comment #5:

“There may be concerns that phase IV trials could be described as superiority trials in PUBMED and the (subordinate) non-inferiority objective may not have been mentioned in the abstract. However, a trial is referred to as superiority or non-inferiority based on its primary objective and not on its
secondary/subordinate objective. Hence, we believe we did not miss any phase IV NI trial given our search strategy. To include trials that are not explicitly stated as NI trials, in our opinion, would be extremely difficult. Our analysis was done based on published reports in PUBMED. We did not include trials databases, such as the clinicaltrials.gov, since data included in these databases are not suitable for our in-depth analysis (for example, data on NI margin and how it was determined are missing from such a database)."

We hope this is sufficient for our manuscript to be accepted for publication in BMC Medical Research Methodology.

For the co-authors,
Kind regards,
Rosemarie Bernabe