Author's response to reviews

Title: Comparison of efficacy between different incretin-based therapies; GLP-1 agonists and DPP-4 inhibitors in type 2 diabetes mellitus:

Authors:

Kaustubh Nisal (knisal@gmail.com)
Ram Kela (drramkela@doctors.org.uk)
Kamlesh Khunti (kk22@le.ac.uk)
Melanie Davies (melanie.davies@uhl-tr.nhs.uk)

Version: 2 Date: 16 July 2012

Author's response to reviews: see over
Dear Editor,

Please find the attached revised manuscript, “Comparison of efficacy between different incretin-based therapies; GLP-1 agonists and DPP-4 inhibitors”. Authors would like to sincerely thank the editorial board and the reviewers for their time. Authors would like to resubmit the article, revised as per the suggestions. Following are the suggestions and the revisions.

Reviewer 1 (Baptist Gallwitz)

Major Comments-

1. Introduction: please cite the novel diabetes prevalence data of the IDF published in fall 2011 and update reference 1 in the reference list.

   \textit{The IDF data has been updated and appropriate reference is now cited (introduction- page 5, line 2)}

2. Page 6: Here, the authors explain that the diminished incretin effect is partly due to a reduced post-prandial GLP-1 response, (Refs. 14, 15) and a reduced insulinotropic response (Ref. 16). Data regarding that are heterogeneous. Please change the wording accordingly and cite Nauck et al, Diabetologia 2011.

   \textit{We have reviewed the data regarding GLP response in patients with type 2 diabetes mellitus. We accept the data are heterogeneous and has cited the appropriate reference (Page 6 –physiology of incretins, last 3 lines)}

3. Page 8: vildagliptin was the second DPP-4 inhibitor available in many European countries.

   \textit{Corrected (page 8- 3\textsuperscript{rd} and 4\textsuperscript{th} line from top)}
4. Page 17 bottom: the large outcome studies (LEADER, EXCEL, TECOS etc) could also be mentioned in a separate paragraph on cardiovascular outcome studies. These studies are powered for cardiovascular outcome and will of course also come up with data on safety regarding pancreatitis and cancer; for these two events, the studies are not powered, however

_The large outcome studies have been mentioned in the para reviewing Cardiovascular outcome (Page 19 para- Cardiovascular outcomes)_

Minor comments:

1. General: terminology exenatide LAR in the manuscript. Since the formulation of long-acting exenatide was changed and the DURATION studies were mostly performed with the novel formulation, the term exenatide QW (for once weekly) should be used

_We have corrected the terminology throught the paper and have used exenatide QW term_

2. Page 7 line 2: long-acting engineered GLP-1 agonists
3. Page 11 para 2, line 1: ....there appear to be ... differences...
4. Page 12 line 2: in the T-Emerge trial....
5. Page 13 para 2: in the T-Emerge trial....

_These minor grammatical errors have been corrected._

Reviewer 2 Sten Madsbad

1. The major point is that so many reviews have been written about the GLP-1 receptor agonist and the DPP-4 inhibitors, also reviews discussion differences between the incretin based therapies. Not quoted in the present review. One may ask, whether it is necessarily to write a review based on two mechanistic studies, and only two published clinical controlled trials.

_There are review articles published comparing various incretin based therapies. There has been great enthusiasm about these newer therapies. The present review however has been written to compare these 2 classes of agents based on head on comparative trials. Inspite of several published trials there are only handful of head on comparative trials. We have acknowledge some important review articles on this subject which have been published recently (page 5- introduction- last 3 lines)_

2. Maybe a major part of the first 8 page, which is without any new information, can be shorten.
We have edited and shorted the first 8 pages

3. Regarding Duration 4, if the present reviewer remember correctly it has been published as an abstract (poster presentation) at ADA or EASD.

Since this article was submitted to BMC Medicine, results of the DURATION 4 trials have been published. The article text has been amended and the data from Duration 4 has been included.

4. Page 19, can be rewritten. Many figures for differences in treatment satisfaction is given, but a difference of, i.e. 1.39 (line3) will not make any sense for most readers.

We have amended the text (treatment satisfaction page 20)

Also the title of the article has been amended as per the suggestions to make it more general and reflecting the condition being investigated. The new title is

Comparison of efficacy between different incretin-based therapies; GLP-1 agonists and DPP-4 inhibitors in type 2 diabetes mellitus:

Once again many thanks for the review.

Yours sincerely

Kaustubh Nisal

University Hospitals of Leicester
Leicester Royal Infirmary
Leicester LE1 5WW
knisal@gmail.com