Author’s response to reviews

Title: Exenatide Once Weekly Treatment Maintained Improvements in Glycemic Control and Weight Loss Over 2 Years

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Author’s response to reviews:

28 February, 2011
Re: MS 1343862011464658

Dear Dr. Shipley,

The manuscript “Exenatide Once Weekly Treatment Maintained Improvements in Glycemic Control and Weight Loss Over 2 Years” has been revised according to the reviewer’s report. The list below addresses the changes made that were associated with each of the reviewer’s comments.

Major Compulsory Revisions

Comment: The authors focus only on the completer population which in itself overestimates the effects from the ITT population. Fortunately the authors mistakenly left in a few references to the results for the ITT population which is what they should be reporting (along with the completers’ results for a more clear understanding of the data). It is especially important to include the ITT results when describing the changes from baseline to week 104. The completers’ analysis provides information also but it should be interpreted in the context of the ITT results.

Revision: Results of the ITT analyses were added to the text (Results) and figures wherever they were not previously included. These revisions include the addition of ITT results for:

# Demographic characteristics
# Change in A1C over time (Figure 2A)
# Percentage of patients who achieved target glycemic goals (Figure 2B)
# Change in fasting plasma glucose over time (Figure 2C)
# Changes in systolic blood pressure (Figure 3C) and diastolic blood pressure
Changes in serum lipid concentrations (Figure 3D)

An expanded description of the last observation carried forward (LOCF) method was also added to the Methods.

Comment: Plus they continually focus on the effect from baseline to week 104, when the true focus of this article should be on the change from week 52 to 104. Alternatively they could report BL, week 30, week 52 and week 104 to provide a true overall picture of what happens with 2 years of treatment with exenatide QW. (This would be very valuable for Figure 1, in which one wonders what were the numbers and reasons for discontinuation at 1 year.).

Revision: Figure 1 was revised to include the disposition of patients at 52 weeks.

Explanation: To best describe the long-term effects of exenatide once weekly treatment in patients with type 2 diabetes, this manuscript focuses on the effect of treatment from baseline to week 104. Interim analyses at week 30 and week 52 have been published previously using both the completer and ITT populations at week 30 (Drucker DJ, et al. Lancet 2008, 372(9645):1240-1250) and 52-week completer population (Buse JB, et al. Diabetes Care 2010, 33(6):1255-1261). We now report data from the 2-year completer and ITT populations over time for change in A1C and FPG; however, it would be potentially confusing to focus on 52-week data from a 2-year completer population as it would differ from the published 52-week data in the 52-week completer population. Additionally, we present differences in adverse events from weeks 0-30 and weeks 30-104 (Table).

Comment: Plus the presentation in Figure 3a is the method in which all the data in 3c and 3d should be presented too.

Revision: Figures 2A-C, 3C, and 3D were revised to include the results of ITT analyses.

Minor essential revision

Comment: In the limitations section, they should discuss the limitations of completers’ analyses.

Revision: A paragraph was added to the end of the Discussion section that discusses the limitations of both a completer analysis and an ITT analysis.

Discretionary revision

Comment: Additionally, the doses of the drug should be mentioned in the abstract.

Revision: Drug doses were added to the first sentence of the methods in the abstract.
Comment: The authors should add at the beginning of the manuscript an abbreviations section.

Revision: A list of abbreviations was added to the beginning of the manuscript, to be placed in the article at the discretion of the editor. Abbreviations are defined at first use in the text of the manuscript.

Please contact me with any additional questions or issues.

Sincerely,
Kate Gurney