Reviewer’s report

Title: Two-year assessment of the efficacy and safety of sitagliptin in elderly patients with type 2 diabetes: Post hoc analysis of the ASSET-K study

Version: 2 Date: 14 March 2015

Reviewer: Yoshifumi Saisho

Reviewer’s report:

This is a post hoc age-stratified analysis of patients receiving sitagliptin therapy for 2 years to evaluate its efficacy and safety in elderly patients with T2DM. A total of 831 patients were divided into three age groups (<65 years, 65-75 years and >=75 years old). They found a significant improvement of glycemic control in each group with no significant difference in adverse events among the groups. The authors concluded that efficacy and safety of sitagliptin treatment was comparable among all three age groups and sitagliptin is also useful for elderly patients with T2DM.

The strength of the study is a relatively large sample size conducted in Japanese population. However, there are a number of issues to be addressed.

Major compulsory

1. The authors concluded that the similar efficacy of sitagliptin was observed in each group. However, there is no comparison among the groups. Comparison among the groups should be conducted.

2. In their previous report, they reported that high HbA1c, short duration of diabetes and low BMI, but not age, are factors associated with the reduction of HbA1c by sitagliptin. So that the similar efficacy among the three age groups is not surprising. Achieving glycemic target without hypoglycemia may be more important to assess efficacy of anti-diabetic medication in elderly population. Thus it will be better if the authors assess the efficacy of sitagliptin by not only reduction of HbA1c but rather the proportion of patients who achieved glycemic goal without hypoglycemia.

3. P values should be added in table 1. Also, the comparison between the patients who received sitagliptin for 24 months and those who did not (n = 496?) should be added in table 1.

4. Standard deviation of each data point should be added in all figures. Comparison among the groups also should be conducted and indicated in figures.

5. HbA1c and FBG seems higher in the group of age <65 years, while PBG seems comparable among the three groups during the study. This point should be discussed. Also, the method to assess postprandial blood glucose should be described in the Methods.
6. The definition of hypoglycemia and methods to assess hypoglycemia are unclear. Hypoglycemia was confirmed by measuring blood glucose? If not, as the authors mentioned, asymptomatic hypoglycemia occurs more often in the elderly population so that the authors might not be able to detect hypoglycemia in the elder population. This point needs to be mentioned and more carefully discussed. Also, hypoglycemia was expressed as %. This should be expressed as events/person month.

7. The rate of withdrawal due to adverse events is not described in the Results section.

8. The dose of SU in each group should be added in table 1. Also, change in medication during the study should be described. Is there any reduction in SU dose during the study?

9. Figure 5 also should be divided into the three age groups consistently.

Minor essential
1. The reference should be added in the end of first paragraph of the Background.

2. “Blood glucose” should be “plasma glucose”.

3. The first paragraph of the Results section is too redundant. This should be more concisely described.

4. Page 7, line 119, “protect the pancreas” should be “protect the beta cell” or “islet”.

5. Page 11, line 232, “cAMP”?

6. The results are presented repeatedly. The parameters shown in figures should be removed from table 2.

7. The numbers of x-axis scale are not distributed appropriately. The x-axis scale should be divided equally by 24.

8. eGFR is calculated by serum creatinine and the both parameters are essentially the same. One of the figures of figure 3 can be removed.

9. It is recommended that the manuscript is edited by a native English speaker.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

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

I declare that I have no competing interest.