Author’s response to reviews

Title: Effect of sitagliptin on blood glucose control in patients with type 2 diabetes mellitus who are treatment naive or poorly responsive to existing antidiabetic drugs: The JAMP Study

Authors:

Hiroshi Sakura (jamp@n-place.co.jp; sakuragm@dnh.twmu.ac.jp)
Naotake Hashimoto (hasimoto@tymc.twmu.ac.jp)
Kazuo Sasamoto (kazuosasamoto@m.jcnnet.jp)
Hiroshi Ohashi (oechiro@nyc.odn.ne.jp)
Sumiko Hasumi (keiwa@teishinkai.or.jp)
Noriko Ujihara (ujihara.noriko@twmu.ac.jp)
Tadasu Kasahara (t.kasahara@johsai-hp.or.jp)
Osamu Tomonaga (boss@tomonaga-clinic.com)
Hideo Nunome (nunome-dm@umin.ac.jp)
Masashi Honda (mashonda@chime.ocn.ne.jp)
Yasuhiko Iwamoto (y-iwamoto@asahi-life.or.jp)

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Author’s response to reviews:

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Dear editors and reviewers,

Thank you very much for reviewing our manuscript.

I have revised our manuscript carefully and those changes are as follows.

If you have any questions about our manuscript, please contact JAMP Study office at the address shown below.
I am looking forward to your reply.

Yours sincerely,
JAMP STUDY (On behalf of Dr. Sakura)
Address: 4-1-28, Toranomon, Minato-ku. Tokyo, Japan 105-0001
Tel: +81-3-6680-2525
Fax: +81-3-6777-0033
Email: jamp@n-place.co.jp

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Requests from reviewers

Reviewer#1

> This reviewer feels that the authors did not adequately respond to the comment #1 and correct the manuscript appropriately.

According to the authors' response, it is now clear that sitagliptin was simply added on to the pre-existing therapy in this study.

Thus, low-dose and medium-dose glimepiride groups were not intended to be randomly assigned but rather classified retrospectively. Therefore, the comparison among the groups were posthoc analysis and the results should be less emphasized.

Thank you for your valuable comment. As you pointed out, this study was an observational study with sitagliptin added on, and not a randomized controlled study. However, this was a prospective study, as patients were divided into low- and medium-dose glimepiride groups and compared; this was clearly stated in the protocol. Nevertheless, we would like to address the issue by clearly stating, as limitations, that the present study was not performed by higher-accuracy methods such as a randomized controlled study, and that there were differences in patient baseline characteristics, including numbers of patients, between the groups. Moreover, in
the Abstract, we emphasized the results of the primary endpoint (change in HbA1c after 3 months), and clearly stated that comparisons between the groups were conducted by exploratory analysis.

Please see P.3 (Method) and P.12 (Study Limitations)

>Moreover, the description of methods section remains confusing. For example, lines 19-23, the sentence should be changed to "The patients were treated with glimepiride, biguanides, thiazolidinediones, alpha-glucosidase inhibitors or two or more of these drugs in combination".

Thank you for pointing this out.

We apologize for the confusing descriptions. They have been corrected.

Please see P.5 (Study Subjects)

>Also, if the patients treated with more than 2mg of glimepiride or other SUs were excluded from the study, this should be clearly stated as exclusion criteria.

Thank you for pointing this out. This was not stated in the exclusion criteria in the study protocol, so we did not mention this as exclusion criteria in the manuscript. However, those patients were actually not included in the efficacy analysis. Therefore, we have added the explanation in the manuscript.

Please see P.5 (Study Subjects)

>In this regard, the reviewer wonders why the patients treated with rapid-acting insulin secretagogues were excluded from the study?

Thank you for pointing this out. At the time when the study was started, concomitant use of rapid-acting insulin secretagogues was not allowed, thus, patients receiving treatment with rapid-acting insulin secretagogues were excluded. We have added the explanation in the manuscript.

Please see P.5 (Study Subjects)
>Likewise, lines 48-50. "The patients were treated with diet/exercise therapy … for at least 1 month during the observation period" does not make sense. This should be "The pre-existent therapy for type 2 diabetes were not changed during the observation period and entire study period".

Thank you for pointing this out. The text has been corrected according to your suggestion.

Please see P.5 (Treatments)

> If there was any change in anti-diabetic medication during the study, it should be clearly described in the manuscript.

Thank you for your suggestion. For the 585 patients who completed the study, we have summarized the changes in anti-diabetic medication during the study in a table 4.

Please see P.9 (Results) and Table 4.

> In abstract. Methods should be changed to "Sitagliptin (50 mg/day) was added on to the pre-existing therapy for type 2 diabetes and changes in the glycated hemoglobin (HbA1c) level after 3 months of treatment were compared with the baseline".

Thank you for pointing this out. This has been corrected according to your suggestion.

Please see P.3 (Method)

Reviewer#3

> The authors carried out clinical study to evaluate the efficacy and safety of sitagliptin in a practical clinical setting and they found that sitagliptin is effective in monotherapy or combination therapy. Their findings seem to be useful for clinical practitioners.
However, this manuscript still includes points to be corrected.

> The inclusion criteria of patients about glucose control are not clear.
> What does poorly controlled blood glucose' (written in line 12 of page 5) mean?
Is 'poorly controlled' used as the same meaning as inadequate blood glucose?

Thank you for pointing this out. These parts of the manuscript have been amended to make them clearer.

Please see P.5 (Study Subjects) and P9 (Discussion)

> Judging from figure 5, patients whose blood glucose was not inadequate were included in this study.

We have described about the inclusion criteria in the following sections.

(Study Subjects P.5)

The criterion for inadequate blood glucose control was set at a glycated hemoglobin (HbA1c) level of ≥6.9% (52mmol/mol) or a fasting blood glucose level of 130 mg/dL.

(Evaluation P.6)

According to Figure5, the proportion of patients whose HbA1c was <7.0% was 15.3% and that of those whose FBS was <130mg/dl was 21.1% at 0 month. Those who do not meet the inclusion criteria seem to be included in this study.

Thank you for your valuable comment. The inclusion criterion for inadequate blood glucose control was determined on the basis of either HbA1c <6.9 or fasting blood glucose <130 during the observation period. This is because, in some institutions, laboratory test results may not be available on the day specified as baseline, so patients who met the inclusion criteria on the baseline day or sometime during the observation period were included.
In the figure showing the percentage of patients achieving the target, values measured on the baseline day were used, which included data of patients who had actually achieved the target at baseline. We have added the explanation in the manuscript.

Please see P.8 (Results)