Reviewer’s report

**Title:** No increased risk of glucose metabolism disorders in adults with growth hormone deficiency undergoing long-term treatment with biosimilar somatropin (Omnitrope®): data from an observational, longitudinal study

**Version:** 0  **Date:** 04 Aug 2019

**Reviewer:** So Nagai

**Reviewer's report:**

This is a report on the occurrence of diabetes of a biosimilar rhGH in adult GHD patients. It is important to confirm whether biosimilars have the same effects as reference biological products and side effects. Considering the physiological actions of GH, in particular, it is significant to evaluate glucose metabolism. However, additional data and discussion is needed for accepting.

#1 The diagnosis of diabetes was made by OGTT or HbA1c. HbA1c is used in daily clinical practice, but in general, there are some reasons when OGTT is performed. If a large number of diabetes diagnoses are made by OGTT, it may be a bias in the rate of diabetes diagnosis. If you able to know the conditions under which OGTT was performed, please describe the reason. If you do not know, please describe the "potential selection bias" in the discussion part.

#2 Of the 21 diabetic patients, it is assumed that cortisone has been administered to 14 patients. Is there any report that low dose cortisone causes glucose intolerance in patients with hypopituitarism?

#3 Table 2 and the discussion describe whether cortisone or statin is given in patients with diabetes. However, with regard to these medications, when these medication rate in patients without diabetes is unknown, it can not be described the contribution to impaired glucose tolerance in patients with diabetes. On the contrary, it emphasizes the impression that progress to diabetes is not due to GH treatment. Please note whether these medications were given before the start of GH treatment. Also, please state your point of view in the discussion part.

#4 In Table 2, the body weight and HbA1c before GH treatment are described, but neither is showed at AE onset. It is better to describe comparable metabolic parameters before and after GH administration.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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