Reviewer's report

Title: Treatment with PBI-4050 in patients with Alström syndrome: study protocol for a Phase 2, single-centre, single-arm, open-label trial

Version: 1 Date: 13 Sep 2018

Reviewer: J. H. de Vries

Reviewer's report:

This study will investigate the actions of PBI-4050 in patients with Alström syndrome. The study is well designed. With recruitment of 2/3 of the anticipated number of patients now completed, there is of course only limited opportunity to further improve the study design.

My recommendations are the following.

Please adhere to the most recent consensus definitions of hypoglycemia as given by the International Hypoglycaemia Study Group, Diabetes Care 2017;40:155-7.

Please specify which HOMA you will use (HOMA-B?).

The use of Bonferroni seems too strict to me given the small sample size which is limited by the rareness of the disease, making a proper power calculation a futile exercise. Significance might sometimes be hard to achieve despite clear apparent differences. And in the end the 95% CI around the point estimate tells the reader all there is to know.

I would recommend that clamp quality is reported, according to Benesch J Diabetes Sci Technol 2015;9:792-800.

Typo: Background line 19. patients not patient's.
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.

Unable to assess

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

Unable to assess

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.

I am able to assess the statistics

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

Acceptable

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