Reviewer’s report

Title: A randomised, open-label study of insulin glargine or neutral protamine Hagedorn insulin in Chinese paediatric patients with type 1 diabetes mellitus

Version: 0 Date: 07 Jun 2016

Reviewer: Kednapa Thavorn

Reviewer's report:

Summary

The manuscript reports the results of the open-label randomized controlled trial of insulin glargine compared to NPH insulin in paediatric Chinese patients with type 1 diabetes. The authors use the absolute change in glycated haemoglobin from baseline to week 24 as a primary endpoint. The trial is found to be novel in that it compares the use of insulin glargine to NPH insulin in paediatric population in developing countries who may have different characteristics or disease profiles from those living in the North American or European countries.

Major comments

1. In the abstract, the conclusion is not entirely correct, and the message may be misleading given that the trial did not have enough statistical power to detect any statistically different in effectiveness and safety data. Please revise.

2. The major limitation of this study is a small sample size due to recruitment failure. Since the trial did not have enough power to assess the difference in outcomes across arms, the objective should be revised from "...to assess the safety and efficacy of …" to "...to describe the safety and efficacy of…".

3. Why the authors chose to conduct an open label as opposed to single or double blinded trial? Why a randomized 2:1 design was used? Please provide the justification under the methods section.

4. It is unclear how patients were randomized. How the randomization sequence was generated? Was the allocation concealed? What was the unit of allocation? Please describe allocation process.

5. On Page 4, Line 5-11, why NPH insulin was used by investigator's discretion. Why its use was not guided by local clinical practice guidelines?
6. Under the enrollment section, clearer justification for the decision to reduce the sample size from 366 to 150 patients should be added. As well, original sample size should be included.

7. Page 4, Line 46 should be study outcomes instead of study objectives. This section should also describe how the primary outcome was measured. Detailed descriptions of outcome measures in the supplementary information should be moved to this section.

8. Page 5, Line 53, why minimum and maximum values were used to represent the dispersion of median as opposed to an interquartile range?

9. How many patients did not have outcome data at Week 24? Given that LOCF ignores whether the participant's condition was improving or deteriorating at the time of dropout, this technique may inappropriately stop the increase in glycemic measures or artificially stabilize glucose level in those who dropout. This may introduce bias to the trial's results. The use of LOCF should be discussed as one of the limitation. In addition, Table 1 should present data for Week 24 WITH and WITHOUT LOCF.

10. On Page 11, the authors clams that there is no competing interest; however, two co-authors (LS and XLD) are employers of Sanofi, the company that produces and sells insulin glargine. Both authors also contributed to the analysis and interpretation of the data. Competing interest section should be revised.

Minor comments

1. Page 6, Line 20-21, the authors indicate that demographic and baseline characteristics were shown in Table 1, but they were included as a supplementary information. Please verify.

2. Page 6, Line 57, please delete an extra word (between) at the end of Line 57.

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.

No
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

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