Reviewer’s report

Title: The efficacy and safety of insulin-sensitizing drugs in HIV-associated lipodystrophy syndrome: a meta-analysis of randomized trials

Version: 2 Date: 15 January 2010

Reviewer: Shelley Salpeter

Reviewer’s report:

Comments for the authors

1. Is the question posed by the authors well defined?
   - Yes.

2. Are the methods appropriate and well described?
   - Yes

3. Are the data sound?
   - Yes

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   - Yes. I have some minor suggestions.
     - The inclusion criteria allowed for comparison with placebo or no treatment, but this is not consistently reported. For example, in the abstract, methods, results, and figures, it states the comparisons were rosiglitazone versus placebo, etc. Please go through the manuscript and correct these to “placebo or no treatment”. Alternatively, the control group could be defined as placebo or no treatment, and results could be compared with “control”.
     - The revised manuscript has taken out most of the reports of nonsignificant results, but not all. For example, in the section on rosiglitazone versus placebo, it states that there was a small decline in fasting glucose that did not achieve statistical significance. This should be changed to “no significant effect on fasting glucose”. In addition, the discussion states that pioglitazone had minimal impact on fasting insulin or glucose. This should be changed to “no significant effect”. Alternatively, in the discussion, it could be appropriate to discuss nonsignificant trends in results, but this should be clarified and consistent for all agents.
     - In the section on rosiglitazone compared with metformin, it states that there were “significant” reductions in HDL, and “clinically relevant” reductions in LDL and TG. Please clarify whether these were all statistically significant, and what the definition of clinically relevant is. I suggest that the clinically relevant results be reported in the discussion.
- In the heterogeneity section, please clarify the statement that 5 summary tests did not pass their respective tests for heterogeneity means. Does this mean that there was evidence for potential heterogeneity?

5. Are the discussion and conclusions well balanced and adequately supported by the data?

- Yes. I have some minor suggestions for improvements in the introduction and discussion.

- In the introduction, please add a reference to the statement that recent data have raised safety concerns about the use of thiazolidinediones in the non-HIV populations. For example, the meta-analysis by Nissen et al should be presented.

- In the discussion, the statement that “head-to-head trials reinforced findings of placebo-controlled trials” could be clarified. For example, it could be stated that metformin had statistically significant reductions in all three areas of interest, compared with placebo. In addition, metformin demonstrated superiority in improving lipids and body fat redistribution, compared with rosiglitazone.

- In the discussion, please provide references for the statement that these findings are consistent with a growing safety concerns surrounding the use of thiazolidinediones and the risk for cardiovascular events.

6. Are limitations of the work clearly stated?

- Yes.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?

- Yes.

8. Do the title and abstract accurately convey what has been found?

- Yes.

9. Is the writing acceptable?

- Yes.

Please divide your comments into the following categories:

- Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)
- Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
- Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

No conflicts of interest.