Reviewer's report

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

Version: 1 Date: 22 August 2009

Reviewer: Cresio C Alves

Reviewer's report:

1. Major compulsory revisions (the author must respond to these before a decision on publication can be reached).
   - None

2. Minor essential revisions (the author can be trusted to correct).
   - None.

3. Discretionary revisions (recommendations for improvement which the author can choose to ignore).
   - Although the authors present, in some extent, the limitations of their work, I think it would be important, to include, in more detail, the following aspects in their discussion: (1) Since the study subjects were predominantly males in their forties the data cannot be generalized to children, adolescents and young adults. This is important due to the variability in insulin sensitivity, especially when comparing pre-puberal and puberal children; (2) As stated, the wide range of HIV-associated lypodystrophic syndrome (HALS) population, do not allow to precisely assess the impact of its individual components on the response to the insulin sensitizing agents; (3) Only measures of central obesity (body mass index [BMI], waist to hip ratio [WHR]), visceral abdominal fat [VAF]) were analyzed. The assessment of peripheral wasting could not be assessed. This does not allow the clinical practitioner, to verify if their current use of metformin for the lypohypertrophic pattern and thiazolidinediones for the lypoatrophic pattern has scientific validity; (4) The type and dose of the ART (e.g., NRTIs and PIs) could not be adequately assessed, therefore it was not possible to evaluate the impact of these drugs in the insulin resistance; (5) Although the standardization of the measures of insulin sensitivity (e.g., euglycemic clamp, HOMA [homeostasis model assessment]) could be important, in clinical practice the fasting insulin and fasting glucose are the parameters more frequently used. Therefore they have some clinical validity; (6) If possible, information of the impact of leptin in insulin sensitivity would be important due to the known association of hypoleptinemia and insulin resistance and due to the ongoing trials using leptin to improve this metabolic derangement; (7) Although the short term effect of the insulin sensitizing drugs are described, their long term effects on cardiovascular risk still needs to be evaluated.
**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.