Reviewer's report

Title: Randomized, controlled, parallel-group prospective study to investigate the clinical effectiveness of early insulin treatment in patients with latent autoimmune diabetes in adults.

Version: 1 Date: 18 December 2007

Reviewer: amalia gastaldelli

Reviewer's report:

The protocol is interesting, particularly because one of the aim is preservation of beta cell function.

However, I have a few comments:

1. Among treatments, insulin vs metformin/rosiglitazone and sulfonylurea (the last one is not clear if accepted only at entry, see below comments) were contemplated. DPP-IV inhibitors or GLP-1 (exenatide for example) have been proposed in impaired beta cell function. What was the reason not to choose them? (ie not on the market, too expensive, etcâ#) I think this should be discussed.

2. What is the expected change in c-peptide with different treatments? Are data available on C-peptide in LADA in the considered population vs Japan? I expect an ethnic difference

3. The authors stated â”As the power calculation is based on patients in Japan, we will re-calculate the sample size based on the standard deviation of the first 60 patients recruited in our studyâ”

What is the expected drop out rate in each group? How the authors expect to handle this in the randomization and after the analysis of the first 60 recruited patients?

4. statistical analysis seems naïf or not well described. The authors should performed 2 way ANOVA for repeated measurements, with account for cofactors when variables are normally distributed. Otherwise, log transformation or non parametric tests should be employed

Figure 1:
â€¢ An algorithm on initial dose of insulin should be reported. This figure only report information on dose adjustment. Usually initial dose of insulin is given based on pre-prandial glycemia and or BMI.

Figure 2.
â€¢ Sulfonylurea at baseline entry should be discontinued and substituted with another treatment. This is sort of reported at page 6, but should be made clear in this figure if this is the intention (another decision seems unethical based on the
results of sulfonylurea reported in the introduction)

â Although rosiglitazone is still on the market, it can increase risk of heart failure and myocardial infarction. Thus, cardiac as well as renal evaluation should be performed before putting a subject on rosiglitazone. Excluding criteria on renal function and presence of heart failure cannot exclude the risk.

â Pioglitazone does not seem to be as harmful as rosiglitazone: an explanation should be reported on why rosiglitazone, vs general TZD, was chosen.

â Second part of figure 2 (page 19): sulfonylurea disappeared and rosiglitazone with/without metformin is present. Where rosiglitazone alone has been introduced at baseline?

Figure 3

â Only fasting C-peptide was used in the screening. Most of these patients have low/normal C-peptide but impaired postprandial response. This should be checked as well and could be also a good endpoint.

What next?: Accept after minor essential revisions

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:

I declare that I have no competing interests