Reviewer’s report

Title: Variation of C peptide decay rate in autoimmune diabetes: better discrimination with initial fasting C peptide

Version: 1 Date: 19 November 2012

Reviewer: Christiane Hampe

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Major Compulsory Revisions:

1) The criteria used to categorize patients into T1D and LADA are unusual and need to be explained. Ketosis is usually not used for the classification as not every patient with T1D experienced ketoacidosis at clinical onset. Inclusion of only GADA for classification of autoimmune diabetes is not sufficient. Especially young T1D patients may be GADA negative, but positive for IAA and/or IA-2Ab.

2) The statement that GADA are the most widely used and valuable markers for autoimmune diabetes needs to be rephrased. Positivity for GADA or any of the other islet cell autoantibodies alone is not used as autoimmune markers for prediction or diagnosis of T1D. In T1D other autoantibodies (IAA and IA-2Ab) are in fact often more prevalent as they correlated inversely with age at onset, while GADA correlate directly with age at onset. Positivity for GADA is used as a predictor only in LADA.

3) The authors argue that the initial FCP level may be a predictor of beta cell function failure. Judging from the presented figure, it would be important to calculate the loss of c-peptide level over time. Both cohorts appear to loose c-peptide over time.

Minor Essential Revisions

1) The argument that the authors make when comparing decline in beta cell function in group 1 and 2 is not clear. The authors state that patients in group 2 (longitudinal loss of FCP) had higher FCP at onset. However, this is evident by their own categorization of group 1 of being FCP negative at onset and therefore does not need to be stated.

2) It would be of interest to know what is the percentage of T1D and LADA in Groups 1-3.

The similar age in groups 1 and 2 suggests that the traditional T1D and LADA forms of autoimmune diabetes overlap in this cohort.

3) The authors refer to a paper by Maldonado, using autoantibody positivity and beta cell functions to differentiate four forms of ketosis-prone diabetes. It needs to be emphasized that the Maldonado paper refers only to patients with ketosis-prone diabetes.

4) Some published work was not cited. Other publications already show that FCP at onset predict loss of beta cell function in T1D (Jensen RA et al 2007), the
authors site only some of the publications on prediction of beta cell loss in autoimmune diabetes.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**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.