Reviewer's report

Title: Personalized medicine in psoriasis: developing a genomic classifier to predict response to Alefacept

Version: 4 Date: 23 August 2009

Reviewer: Erna Snellman

Reviewer's report:

Discretionary revisions:
Should the acknowledgement be completed?

Minor essential revisions:
None

Major compulsory revisions:
Methods should be given more carefully so that also a reader, who has not possibility to go to previous publications, can get an idea, how the patients were recruited, what was the initial aim of the study in 2003, the description of the methods used - at least the main points.

The limitations of the tiny cohort should be stressed further as well as the possibility of miss-interpretations. The risk of multible publication bias of a tiny study should be considered.

Reviewers detailed further comments to the authors

1. Background information and the question posed are well defined and open the question well. The item is important and interesting.

2. Some major problems are found in description of methods.
   a. The study is based on old material rooting form a study completed in 2003. Almost all data is already presented in pieces in at least three earlier published studies. These are referred and included in the list of references (n:o 5 Haider AS et al. 2005, n:o 14 Chamian F, Lowes MA et al. 2007 and n:o Chamian F, Lin SL et al 2007).
   b. In the present manuscripts almost no data about the patients or their psoriasis is given. The referred earlier works either don’t tell all details. How the 22 patients were recruited in the study, from where they came, and what was the initial aim of the recruitment? Was it a pharmacy industry paid study for the efficacy of Alefacept?
   c. As regards the soundness of the data the authors conclude already in 2005 in an other published paper that this is a preliminary study and based on a small cohort of only 22 patients, and that in future it is necessary to perform studies in a larger cohort to confirm the findings.
a. I am a little worried that, despite of their previous conclusions, the same data is used again. Background description of the patients is negligible and using the same data many times may increase the risk of publication bias.

b. The situation becomes even more uncertain as the classifier mis-identified two of the patients as reponders although they were histological non-responders.

c. The only new data in study seems to be the more detailed description and classification of the selected genes according to response and non-response. In addition the data on only 9 reponders and 7 non-responders were available.

4. The over-all picture of the manuscript is that it refers too much on previous studies of the authors assuming that the readers have all these studies available. Without reading the other manuscripts it is almost impossible to say if any standards are followed. Accordingly, the reader cannot be sure of the quality of the study.

5. The discussion in reasonable and interesting. The results show that it is possible to try to predict a response e.g. to Alefacept in advance. Prediction of the response could be valuable in choosing a medication for patient and in avoiding unnecessary cost and health risks.

6. The uncertainties due to tiny groups of patients and miss-classifications should be pointed out more clearly. In addition, the description of the selection and demographic of patients as well as methods in general is too minimal and relies too much on reading of other previous papers.

7. No one of the writers announces in the author contributions to have participated in the care of the patients in 2003, or in the blood or biopsy samplings. Should they be included in the author list or mentioned at least in the acknowledgements? Did the patients know this study including their files continue this long and that new researchers are involved?

8. The title seems adequate and it gives an idea of the content. However, the abstract doesn’t convince.

9. Writing is OK.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests