Reviewer’s report

Title: Skin-impedance in Fabry Disease: A prospective, controlled, non-randomized clinical study

Version: 2 Date: 21 February 2008

Reviewer: Carla C Hollak

Reviewer’s report:

- Major Compulsory Revisions

1. A large proportion of readers may not be familiar with the DDIM System. A short description of its validation as an instrument that reliably measures skin moisture should be added, including a reference. Also, a reference should be provided that supports the statement that the Force compensated moisture parameter is the most reliable parameter.

2. The main observation in this study is that skin impedance is decreased in Fabry patients compared to controls. ERT does not seem to affect the skin moisture using the DDIM System. The authors suggest that recording of skin-moisture values at 24-hour intervals from day two to day 13 may eventually reveal a difference. It is unclear why they would expect such a difference. Also, it is highly speculative to argue at this point that these serial measurements may determine the frequency of the ERT needed for its optimum response in Fabry disease. For the same reason, the last sentence of the abstract is not supported by data. In their conclusions, the authors make a different recommendation, suggesting that measurement of skin moisture may prove to be a very good screening instrument. The specificity of this instrument is, however, not tested.

3. The authors state that GALA enzyme levels in subjects very closely mirrored patient group membership and were statistically related. Was there a significant correlation between skin moisture and residual GALA activity? Was there a relationship with renal involvement (since sweating may become impaired in end-stage renal failure; see Krishnan et al, Muscle Nerve 2007 Mar;35(3):273-90 Uremic neuropathy: clinical features and new pathophysiological insights.) When there is a relation with renal failure, this might also explain the lack of response to ERT.

4. What are the units for Skin moisture? These should be given (y-axis in figs 2 and 3)

- Minor Essential Revisions

Abstract: healthy 22 controls should be 22 healthy controls

Introduction: i.e. Below 50 years should be i.e. below 50 years
- Discretionary Revisions
   The authors may consider to leave table 3 out.

What next?
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- Unable to decide on acceptance or rejection until the authors have responded
to the major compulsory revisions

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

Quality of written English
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- Acceptable

Statistical review
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Is it essential that this manuscript be seen by an expert statistician?
- Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests
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I received reimbursement of expenses and honoraria for lectures on the
management of lysosomal storage diseases, including Fabry disease, from
Genzyme Corporation, Shire and Actelion. All honoraria are donated to the
Gaucher Stichting, a national foundation that supports research in the field of
lysosomal storage disorders.