Reviewer's report

**Title:** Frequency of Fabry disease in male and female haemodialysis patients in Spain

**Version:** 3 **Date:** 2 October 2009

**Reviewer:** Soumeya Bekri

Reviewer's report:

This manuscript describes a screening program for Fabry disease (FD) in patients undergoing hemodialysis in Spain. This screening approach permitted to identify 7 (8?) patients with GLA mutations.

Such screening program in this 'at-risk' population (many of these patients do not have a clear renal diagnosis) is relevant and there is a clear need of precise diagnosis to adjust the treatment. Thus, the yield is potentially significant and of possible benefit to the relatives of affected cases.

There are few limitations that need to be clarified.

The screening strategy chosen for this study do not permit to diagnose FD in all affected female patients. Molecular genetic testing is the most reliable method to screen for females with Fabry disease, but due to its high cost this approach could be ruled out. This point is not discuss in the “discussion” section but is inappropriately and briefly mentioned in “material and method” section. This important limitation should be clearly described and discussed.

There are a number of small typing errors throughout the text that required attention.

Specific comments:

**Abstract:**

The authors should correct the number of the patients with Fabry disease. Indeed, in the abstract, it is written that “Seven unrelated patients with GLA alteration were found…” while in the result section it is stated that “the #-GAL A activity in the eight patients with FD…” and in the discussion it is written that “two patients were related”.

**Introduction**

It is not clear that the observed cardiomyopathy in FD is due solely to Gb3 deposition in cardiomyocytes.

**Results**

The relevance of the chosen cut-off in female patient is not obvious. Bona fide FD may be associated to normal #-GAL A activity in female.

The percentage of residual activity of #-GAL A and of the GLA mutation frequency should be recalculated (for instance R118C represents 50% of the identified mutations).
The potential causality of D313Y mutation should not be discussed in this section.

Table 1

The mutations should be named following the current nomenclature rules. The reference of the sequenced used for the designation of the variation should be mentioned.

Some results are not expressed as percentage. No clinical data is given for patient 8.

This table should be presented in a concise shape.

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

**Declaration of competing interests:**

We have received funding from Shire HGT, Genzyme, OrphanEurope, Biominin.