Reviewer's report

Title: Quality of Life (QoL) assessment in a cohort of Phenylketonuria patients

Version: 5

Date: 23 September 2014

Reviewer: Nicola Longo

Reviewer's report:

This manuscript reports quality of life assessment in patients with phenylketonuria receiving different types of therapy. The manuscript is interesting given the new tools utilized, but would benefit from further clarification of the results.

CRITIQUE

1. Line 118: Current guidelines do not restrict BH4 use. A trial is actually recommended in all patients with PKU. Patients with milder forms of PKU are more likely to respond to BH4 treatments.

2. Table 1: please add the control value for QOL in unaffected people with relative reference.

3. Table 2: please make the average ± SD of concomitant phe values and mean phe values and comment in the text on whether the values differ statistically among groups.

4. Unclear what was actually done in table 3 and 4. Was a regression performed between values of behavioral testing and the different variables? What are the variables (age, school, treatment length, BH4)? Was linear regression done for each variable and then combined with other variables? Which one were the combinations used in the multivariate analysis?

5. Was there any correlation of scores with average Phe levels in groups?

6. It seems that in some cases a group comparison was used (males), but it is unclear what was the comparison group (was this the normal controls?).

7. The tables need to be corrected to clarify the points above and the text corrected accordingly.

Level of interest: An article of outstanding merit and interest in its field.

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:
Grants and consulting from BioMarin (all paid to my Institution)
No stocks, patents or other interest.