Reviewer's report

Title: A multi-center, open-label trial to compare the efficacy and pharmacokinetics of Artemether-Lumefantrine in children with severe acute malnutrition versus children without severe acute malnutrition: Study protocol for the MAL-NUT study

Version: 2 Date: 9 February 2015

Reviewer: Ina Danquah

Reviewer's report:

Minor essential revisions:

1) Background
The authors cite reference 18 which contains also information on the relationship between malnutrition and malaria. This information might be included in the respective background paragraph.

Also, in the last paragraph the authors suggest that anti-malaria medication could improve nutritional status as reflected by anthropometric measures. This has not been observed in other highly endemic areas, a fact that could help to undermine the importance of the proposed study.

2) Terminology
SAM: For the ease of understanding, the authors have introduced the terminus sever acute malnutrition (SAM). The main objective of the proposed trial is to compare the efficacy of SAM children and non-SAM children. This terminology should be contained throughout the manuscript to avoid misinterpretations of the case definitions and analytical procedures. For instance, the following terms are also used: severely malnourished children (page 12), each group (page 21), malnourished children (page 22).

Hemoglobin: “Hemoglobin” alone can mean genetic variants of hemoglobin or hemoglobin concentration. Please, refer to hemoglobin concentrations as such. The use of “hemoglobin levels” should be avoided.

3) Pharmacokinetic profile
The authors describe the reasons for testing only the PK profile of lumefantrine late in the manuscript (page 16). It may be wise to shortly address this earlier in the paper, possibly in the paragraph “Hypothesis and aims”.

4) Eligibility criteria
Is history of fever during the previous 24 hours reported by the parents/caretakers or documented by hospital personnel?

5) Randomization of PK sampling times
The authors claim a “random allocation sequence of PK sampling times will be
computer-generated by Excel" (page 16). What randomization technique will be applied to generate this sequence?

6) Adverse events
Are there typical adverse events that are expected by the study team?

Discretionary revisions:

1) Please correct on page 4 “weight for height z-score below -2 standard deviations (SD)” and “Z-score under -3 SD” to “weight-for-height z-score <-2” and “z-score <-3”

2) Please, correct the typos and orthographic errors.

3) To contrast the enrolment of malaria cases in SAM versus non-SAM children, the authors may wish to review the first paragraph on page 12. A short word of introduction will help to understand that this paragraph describes the enrolment of non-SAM children. Also, the last sentence of this paragraph appears to be redundant.

**Level of interest:** An article of importance 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:**

I declare that I have no competing interests.