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: Michèle Dramaix-Wilmet

Reviewer's report:

Minor Essential Revisions

Sample size
I have checked the sample size with STATA 12 and I found a smaller sample size: 480 subjects (120 SAM & 260 non-SAM), using the same specifications as those indicated in the paper (87% vs 95%, significance level 0.05, power 0.8 and two-sided test). Did you increase sample size to account for children lost to follow-up?

How did you choose the percentages you used to compute sample size: percentage in non-SAM and hypothesized difference?

Settings
Could you give the references of the studies from which the prevalence of malnutrition in Koulikoro and Maradi regions were obtained?
It would perhaps be useful to write in full the abbreviation “MoH” the first time it appears in the text.

Eligibility
Is it not a problem to include children with moderate malnutrition in non-SAM children? Do you have elements that suggest that the outcomes for these children are similar to those in children with z-score # -2 and MUAC # 125 mm?

Screening
The study was planned during two malaria seasons in Mali and one malaria season in Niger; were these periods long enough to recruit 540 children? What was the expected number of SAM and non-SAM children with malaria in the two sites where the study was conducted? Will the SAM children meeting the inclusion criteria be consecutively enrolled till the needed sample size is reached or will a systematic sampling be used?

It would be important to know the percentage of children not included because of refusal to participate in the study or is it generally low in that kind of study and in these settings?
Pharmacokinetics

Can you give more details about the choice of the sample size (150 SAM and 150 non-SAM) “To achieve adequate precision in the estimation of PK parameters”? Did you perform some sample size calculation on the basis of confidence intervals for some parameters? Can you clarify?

Statistical considerations

p. 21, 1st paragraph, you write “patients enrolled, randomized..” but there was no randomization.

Estimation of parasite clearance

You say the “Parasite clearance will be compared between groups of SAM and non-Sam children on a regular basis…”. Does it mean that you planned to do interim analyzes? Should it be the case, did you planned to apply some corrections to the P-values?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests