Reviewer’s report

Title: Association of non-synonymous mutations in the Plasmodium falciparum kelch13 gene (PF3D7_1343700) with parasite clearance rates after artemisinin-based treatments - a WWARN individual patient data meta-analysis

Version: 0 Date: 23 Jun 2018

Reviewer: Liwang Cui

Reviewer's report:

Overall, this is a nice comprehensive meta-analysis of association between K13 mutations and delayed parasite clearance after ACT treatment from clinical studies conducted mostly in SE Asia (including a couple of African studies). The authors identified strong association of 24 mutations with longer PC1/2. The manuscript is well written, I only have the following minor or editorial comments.

* I would suggest that the authors include all the wild type amino acids when mentioning mutations so that the readers can immediately know which types of mutations they are (for example C580Y instead of 580Y) - like in Table 7. Also in Figures 3, 4.

* Be consistent with either US or UK spelling: for example in most places the authors used "parasitaemia, haemoglobin, haematocrit", whereas they also use "analyzed, neighboring" throughout the manuscript.

* Page 3: Southern Yunnan Province, China - remove "Southern". The study sites are actually in western Yunnan.

* Page 4, line 4-5: the statement that "these mutations are common in GMS" is true for three of the mutations, but not for M597I - since this mutation was not detected in the GMS (or at least not common in GMS). So reference 43 needs to be removed from here.

* Page 11, line 1: "Although a mutation"

* Table 3, 4, 5: Specify the mutations: e.g., F446I.

* Page 13: first line: > 5.5 hours (also make sure you either abbreviate hours as h or use hours throughout).

* Table 7: Is xPC1/2 stands for fold increase? If yes, revise the footnote (to be consistent with that in Table 3).
* Page 15: Since P1/2 in different places seem to vary, what about the ratio of mutant K13 vs WT K13 in the two studies mentioned in Myanmar and Vietnam (given most analysis compared their ratios - e.g. Table 3)?

* Page 22: "northwestern" as one word.

* When discussing E252Q allele, it would be nice to mention that this mutation is also present in the China-Myanmar border (see Wang Z. et al. 2015 Malaria Journal).

* Page 23: The description of increased prevalence of certain mutations in Africa needs to include a follow-up sentence to indicate that these are from small sample sizes (e.g., 31, 26, 29), and thus may not represent the true scenarios.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
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Yes

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