Reviewer's report

Title: Genetic polymorphisms in MDR1, CYP3A4 and CYP3A5 genes in a Ghanaian population and their relevance on response to ivermectin treatment

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Reviewer: Dave Bartley

Reviewer's report:

The manuscript still contains a large number of grammatical errors.

Page 5
* The authors state “Although the host and the parasite do have MDR1 and CYP3A genes, we anticipated that genetic polymorphisms of MDR1 and CYP3A genes within the host may provide an explanation for the suboptimal response phenotype observed by Awadzi and colleagues in the use of IVM for the control of onchocerciasis [26, 27].” Do they believe that the parasites play a role in the of apparent drug inefficacy? This should be addressed

Page 8
* “Haplotypes 1 (*1B/*1/*1/*1) and 2 (*1/*1/*1/*1) may be associated with normal expression of CYP3A proteins while haplotypes 3, 4 and 5 may be linked to the reduced CYP3A protein expression. This may be due to the presence of CYP3A5*3 variant allele.” These sentences need further explanation.

Abstract
* “compared the data with that of those from ivermectin treated patients.”
* “CYP3A5*6 alleles were detected at varied varying”
* “responders in a small size group of 42 patients”

Background
Page 3
* “P-glycoprotein (P-gp), a product of the multidrug resistance”
* “and prevents the accumulation of drugs”
* “an also be substrates for Cytochrome P450”

Page 4
* “be acting synergistically as a barrier for its oral drug absorption [24].”

Page 5
* “high microfilariae loads after many years of treatment [26].”
* “To examine the influence of genetic variations within MDR1, CYP3A4 and
CYP3A5 genes on response of patients

Page 6
* “Aliquots of the blood sample (500 µL) was were spotted and preserved”
* “A P-value # 5 was considered significant.” Was this 5%?

Page 8
* “CYP3A5 allele frequency distribution profiles for”
* “variant was the only allele significantly different allele among”

Page 9
* “Although haplotype data for the MDR1 polymorphism did not demonstrate a statistically significant difference between responders and suboptimal responders (p = 0.127, FET), individuals with (C-G-T) haplotype were more likely to be a suboptimal responders.”
* “or suboptimal responders respectively”
* “However a significant difference was observed between”

Page 9
* “This These data is are also similar to the incidence levels”

Page 11
* “Whilst some studies have indicated the possibility of the parasite genes being involved in the suboptimal response”. Needs a reference also.
* “analysed in the Ghanaian population (POP), responders (RES) and suboptimal responder (SOR) subjects”
* “in a representative Ghanaian population were comparable”

Table 2
* Needs Ghanaian population (POP), responders (RES) and suboptimal responder (SOR)

Figure 1B
* Why do the figures not add up to 100%?

Declaration of competing interests:

I declare that I have no competing interests'