Reviewer's report

Title: The public health impact of malaria vaccine RTS,S in malaria endemic Africa: country-specific predictions using 18 month follow-up Phase III data and simulation models

Version: 2
Date: 4 June 2015
Reviewer: Steffen Borrmann

Reviewer's report:

The authors’ responses are mostly adequate. A few remaining minor points:

1) “Due to availability of site- and time-specific data from Phase II, we restrict trial data to Phase III sites using adjuvant AS01”.
   Should be: “Due to an absence of …”?

2) "Repeated malaria infections induces natural, but not complete, immunity in the host to all stages of the parasite life-cycle, including the blood stage causing clinical disease."
   This is a potential controversial statement. Whether or not, even partial immunity (i.e., protective immune response) against liver stages is being induced by natural infections remains an open question. I recommend to rephrase slightly to emphasise the massive evidence for partial immunity against blood stages.

3) Fig. SM1a, right panel: “Burden in cohort with no vaccine"
   Remove one ‘with’

 Also, I’m not sure whether I understand what the red blocks labeled “vaccine modified burden…” on an age vs time plot are supposed to indicate...

4) Fig. SM1b: why is the number of total events AVERTED including the burden in non-vaccinated ages over time? Are the authors referring to a potential excess burden in the non-vaccinated groups?

5) "We didn’t address co-administration, interaction with hep b explicitly, but did briefly address maternal immunity."

This left me wondering whether my question was unclear… my original point has been to provide an elegant explanation for the differential effects in the 6-12 week vs 5 to 17 months cohort. The authors repeatedly mention the ‘age shifting of susceptibility’ … predicting that vaccine induced protection is more difficult to prove in children who are in the process of acquiring partial immunity. Now, 6-12 week old infants are ‘natural recipients’ of maternally transmitted antibodies (that are slowly decaying over the first year of life) and so represent a mirror-image of the immunological situation of children slowly acquiring immune responses… extending (or rather, reversing?) the ‘age shifting of susceptibility’ paradigm to the younger cohort may therefore be useful.

None of this, however, is essential for rapid publication.
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I have no competing interests.