RTS,S MEDICAL AND SCIENTIFIC QUESTIONS & ANSWERS

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Disclaimer

The primary focus of this resource is to be an internal training tool for RTS,S malaria vaccine candidate, containing related data in the format of a Q&A for Medical Affairs personnel. Information presented here is not for external distribution.

Whilst this document can be inspirational for reactive responses to experts or medical enquiries, local regulations, the GSK Code of Practice, scientific engagement principles and/or medical information processes should be followed appropriately.

Please Note

- For media enquiries, please refer to the specific reactive Q&A for Media Enquiries and notify the Global Pipeline Communications team before you respond to a request for an interview so that they can help you to prepare (contact person: Aoife Pauley at aoife.x.pauley@gsk.com).
- The vaccine RTS,S/AS01 has completed phase 3 clinical program and positive regulatory assessment from the European Medicines Agency, but is not yet authorized for marketing in any country. The RTS,S vaccine is being developed in Public Private Partnership with PATH-MVI, as an additional tool to be added to the currently available malaria preventive interventions and for implementation through the national immunization programs in malaria endemic regions in sub-Saharan African countries.
- When referencing clinical data on RTS,S any statements should be prefaced by "In this study...", to make it clear that it is too early to make any general statement on the vaccine profile outside the context of the ongoing clinical trails.
- Have you found what you were looking for? If you have any suggestions for information which should be included in this tool please contact us at the following address: Carys Calvert at carys.calvert@gsk.com.

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Why do you use different case definitions e.g. for vaccine efficacy and cases averted?

The phase III study protocol includes multiple case definitions to ensure balance between specificity and sensitivity[a]. The case definitions have been selected to be consistent with research practice wherever possible to allow generalizability of trial findings and comparability with other interventions. Where applicable for fuller interpretation of the data, multiple case definitions for a given endpoint have been used.

For the evaluation of efficacy, the most specific case definition is used. A specific case definition is one that only captures the true cases. In this case we specify that the child is brought into health care facility and has a temperature of 37.5°C or more when seen and has a high number of parasites in the blood (*P. falciparum* asexual parasitemia (>5000 parasites per cubic millimeter) in order to be sure that these were true malaria cases and not another febrile illness in a child that happened to have concomitant malaria parasites in his blood. Efficacy calculated using the specific case definition was not different from other case definitions used in the trial. [b,c,d].

Cases averted are calculated based upon a secondary case definition which is more sensitive. It includes any child that is brought to a health centre and has any parasites at all in the blood and even if they do not have a measured fever when seen is still included if the carer says that he/she observed a fever within the previous 24 hours. This is appropriate because this is closer to the reality of real life practice all such children would require treatment for malaria. Therefore this is used to assess the public health impact of vaccination. By looking at cases prevented by vaccination with a malaria vaccine, one can have reasonable certainty that these cases are true malaria cases ("vaccine probe" approach).

a. *Leach A, et al. Malaria Journal 2011; 10: 224.*

b. *The RTS,S Clinical Trial Partnership. NEJM 2011, 365: 1863-75.*

c. *The RTS,S Clinical Trial Partnership. NEJM 2012, 367: 2284-95.*

d. *RTS,S Clinical Trial Partnership. PloS Medicine 2014; doi/10.1371/journal.pmed.1001685*