

RTS,S MEDICAL AND SCIENTIFIC QUESTIONS & ANSWERS

For internal use only - NOT FOR DISTRIBUTION

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 trials.
- 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.

RTS,S MEDICAL AND SCIENTIFIC QUESTIONS & ANSWERS

For internal use only - NOT FOR DISTRIBUTION

What data was included in the file submission to the European Medicines Agency?

Data from the Phase III vaccine trials programme conducted at 13 African research centres in eight African countries (Burkina Faso, Gabon, Ghana, Kenya, Tanzania, Mozambique, Malawi and Nigeria) including over 16,000 infants and young children have been included to support the filing. This includes data from the pivotal efficacy trial, safety in HIV+ children and infants, and co-administration of the RTS,S vaccine candidate with other paediatric vaccines. Data and reports from the clinical development including phase I and phase II trials are also presented in the application, as relevant for the assessment of the claimed indications of prevention of malaria and hepatitis-B diseases.

Quality data from commercial manufacturing of RTS,S, and a substantial amount of nonclinical data were also included.

The main clinical study is the phase III efficacy study Malaria-055. Malaria-055 is a large controlled, randomized, observer-blind, multi-centre study aiming to evaluate, in over 15,000 infants and children, the efficacy, safety and immunogenicity of RTS,S/AS01_E against malaria disease caused by *P. falciparum* infection, across diverse malaria transmission settings in SSA ^(a). Study results including co-primary endpoints and efficacy and safety over 3-4 years and the effect of a booster dose have been published ^(b,c,d,e). Three centres of the Malaria-055 will follow-up children to further evaluate efficacy and safety over an additional 3 years in the Malaria-076, an open-label study (January 2014 to December 2016) ^(f)

The concomitant use with other vaccines was evaluated in two other studies besides the Malaria-055:

- Malaria-050: safety, immunogenicity and efficacy when given with DTPw-HepB/Hib, measles and yellow fever vaccines ^(g)
- Malaria-063: safety/immunogenicity when given with *Infanrix* /Hib + OPV, *Synflorix* and *Rotarix* ^(h)
- The characterization of immune responses to the candidate vaccine was mainly done in phase II trials; vaccine lot-to-lot consistency was evaluated in two phase III trials:
- Malaria-061 lot-to-lot consistency with respect of the anti-CS response in children 5-17 months ⁽ⁱ⁾
- Malaria-063 lot-to-lot consistency with respect of the anti-HBs response in infants 6-12 weeks ^(h)

Safety and immunogenicity in special populations have been assessed in:

- Malaria-055: subgroup analysis in HIV seropositive children, low-for-weight children and pre-term infants
- Malaria-058 trial ^(j), 200 children 6 weeks to 17 months with a known HIV seropositive status.

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

e. *RTS,S Clinical Trial Partnership, The Lancet*, 2015. dx.doi.org/10.1016/S0140-6736(15)60721-8

f. GSK study ID 200599; clinicaltrials.gov NCT number NCT02207816

g. Agnandji ST, et al. *J Infect Dis* 2010;202:1076-87

h. *Malaria-063, study ID 113681; NCT01345240*

i. *Malaria-061, study ID 113398; NCT01323972*

j. *Malaria-058, study ID 112745; NCT01148459*