# 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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**Are the phase 2 results published by Olotu and Bejon in line with the phase III results?**

Previous PhII results[a,b] are aligned with the Phase III, Malaria-055 results.[c]

Olotu A. *et al*[a], studied children who had previously been randomized at 5-17 months of age to receive three doses of RTS,S or rabies vaccine. Vaccine efficacy over the four year follow-up period was 16.8% resulting in 650 clinical malaria cases averted per 1,000 vaccinees, over the entire follow-up period. Efficacy fell over time, from 43.6% in the first year of follow-up to zero in the fourth year after vaccination, with a stronger decline when malaria exposure was more intense. Vaccine efficacy seemed to be lower with high malaria exposure (16% compared to 45% in children with less than average exposure to malaria), the number of malaria cases averted was actually higher in children with high malaria exposure (780 per 1,000 children compared to 620 per 1,000 vaccinees among children with less than average exposure to malaria), due to the higher malaria incidence in children with more intense malaria exposure. The authors propose that waning of vaccine-induced immunity as well as more rapid acquisition of natural immunity in children in the control group may both have contributed to the observed effect over time.

Bejon P. *et al*[b], reported the results of a sophisticated multivariate statistical analysis using pooled data from 7 clinical trials, performed at 11 sites in sub-Saharan Africa, in an attempt to better understand what elements might influence the efficacy of the RTS,S malaria vaccine candidate. Results indicate that vaccine efficacy appeared to be influenced by 1) time since vaccination (waning of efficacy over time), 2) malaria transmission intensity (higher efficacy in areas with lower malaria transmission intensity), 3) Adjuvant System used (higher efficacy for more recent trials with RTS,S/AS01 compared to earlier trials with RTS,S/AS02). The analysis indicated that vaccine efficacy varied significantly according to time since vaccination from 36% to zero per cent after 3 years across different transmission settings and adjuvants used.


a. Olotu A. *et al*. NEJM 2013; 368:1111-20

b. Bejon P. *et al*. Lancet ID 2013; 13: 319–27

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