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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What are the key safety results of the Phase III (Malaria-055) study?

Safety is carefully monitored by the investigators and closely reviewed by an Independent Data Monitoring Committee (IDMC), GSK and MVI, as well as public health authorities and ethics review committees with whom important safety information is shared.

Side effects following vaccination included mainly **local reactions** (such as pain or swelling at the site of injection) and **fever**, that were observed more frequently following RTS,S immunisation as compared to the licensed rabies or meningococcal C comparator vaccines. Very few of these reactions were of severe intensity[a,b] except for fever >39°C which occurred in 5.3% of children following a booster dose of RTS,S[d]. In the infant 6-12 week age category, the rates of local injection site reactions following RTS,S vaccination were lower compared to those observed at the injection site of the co-administered routine DTPw-HepB/Hib vaccine[b].

Over the entire 3-4 years of the study, the overall reporting of **serious adverse events** (SAEs) in this trial was similar (24-28%) between the RTS,S candidate vaccine recipients and those receiving a comparator vaccine, but only 0.3% were considered as vaccine related[c,d]. Apart from malaria, the other most frequently reported SAEs were **pneumonia** and **gastroenteritis** (known to be common in infants and children of this age in sub-Saharan Africa) which both occurred in comparable rates in RTS,S and comparator vaccine recipients[a,b].

Differences in the rates of some individual SAEs were observed **in the 5-17 months age category** between the vaccine groups for two specific events: **febrile convulsions** and **meningitis**, both reported more frequently in the malaria vaccine group[a].

The increase in febrile convulsions was considered to be related to the increase in fever following RTS,S vaccination in children over 5 months of age and is therefore now reflected in the core safety information of the RTS,S malaria vaccine candidate as an uncommon adverse reaction (between 1/1000 and 1/100).

During the study, a statistically significant imbalance in reported cases of **meningitis** was reported in older children[c,d] . No obvious explanation for this association has been found, a temporal relationship to vaccination is lacking and biological plausibility is low. A **causal relationship cannot be confirmed or excluded at this point**. This safety signal will be further evaluated in the planned post-marketing studies.

Final assessment of the benefits and risks will be part of the review by regulatory authorities before the vaccine can be made available to the public.

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

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

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

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