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 is the overall safety profile of RTS,S across the Phase II and Phase III programme?

More than 11,000 children have been vaccinated with RTS,S/AS01 in the Phase II and Phase III trials and, to date, the vaccine was shown to have an overall acceptable tolerability and safety profile[a,b,c,d].

The most commonly reported adverse reactions were fever (27%), irritability (14%) and injection site reactions such as pain (16%) and swelling (7%)

- Very few of these reactions were of severe intensity.

The most serious adverse reaction was febrile convulsions (within 7 days post-vaccination) (0.1%)

- Within 7 days after the first 3 doses,the incidence of febrile convulsion per 1000 doses was:
  - in the children category (aged 5-17 months at time of first dose):1.04 in the RTS,S group and 0.57 in the control, for a risk ratio of 1.8 (95% CI, 0.6 to 4.9)
  - In the infants category (aged 6-12 weeks at time of first dose): no increased risk of febrile convulsion was observed after the 3 first doses, which is coherent with the peak of incidence of febrile convulsion (18 months of age)
- Within the 7 days after the 4th dose, the incidence of febrile convulsions per 1000 doses was:
  - in the children category: 2.5 in the R3R group, 1.2 in the R3C group, and 0.4 in the C3C group
  - in the infants category: 2.2 in the R3R group, 0.0 in the R3C group, and 0.5 in the C3C group
  - Over 30 days post vaccination, the overall rates of febrile convulsions were similar between groups
  - Adverse reactions reported are listed according to the following frequency[e]:
    - Very common ≥ 1/10
    - Common ≥ 1/100 to < 1/10
    - Uncommon ≥ 1/1000 to < 1/100

System Organ Class	Frequency	Adverse reactions
Metabolism and nutrition disorders	Common (very common following booster)	decreased appetite
Psychiatric disorders	Very common	irritability
Nervous system disorders	Common	somnolence
	Uncommon	febrile convulsions (within 7 days post-vaccination)
Gastrointestinal disorders	Common	diarrhoea
	Uncommon	vomiting
General disorders and administration site conditions	Very common	fever, injection site reactions (including swelling, erythema and pain)
	Uncommon	injection site induration

Clinical data in more than 4200 children who received a booster dose of Mosquirix shows that, following booster vaccination, decreased appetite was reported more frequently (very common) compared to the rates observed during primary vaccination.

a. *Vekemans J, et al. Human Vaccines 2011; 7: 1309-16.*

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

e. *Mosquirix SmPC July 2015; European Medicines Agency, ema.europa.eu/ema/.*