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 data has been generated on RTS,S in HIV-infected children?

Limited data are available from use of Mosquirix™ in HIV-infected children. [c]

Data from clinical studies suggest that HIV-infected children are more likely to experience local and systemic reactogenicity (injection site pain and injection site erythema, fever, somnolence, irritability, decreased appetite) [a] compared to the general population of children vaccinated [b]. Over the entire follow-up period, incidences of SAEs and deaths and viral load were similar in HIV-infected children vaccinated with RTS,S/AS01 or a control licensed vaccine.

No significant effect of RTS,S was observed on growth parameters, CD4+ T-cell percentage, absolute CD4 + T-cell counts, HIV viral load and WHO AIDS clinical classification.

Immunogenicity, safety and efficacy of RTS,S was evaluated in children aged 6 weeks to 17 months diagnosed with HIV (WHO stage 1 and 2) in two phase III studies, Malaria-055[a] and Malaria-058[b],

In **Malaria-055**, children with known HIV/AIDS disease stage I and II (WHO AIDS staging) were eligible. It should be noted that HIV testing was not a study procedure; this analysis included therefore all children known to be HIV infected at enrolment or subsequently diagnosed on clinical suspicion, with the limitation that HIV testing practices differed from one centre to another. A first sub-analysis of safety and immunogenicity of a primary course of RTS,S/AS01$_E$ in HIV-infected children was conducted in 2012 [a]. At study end, 1.0% of the children and infants had a confirmed HIV positive status and a few additional children and infants (9 in total) had an SAE coded as retroviral infection that was not confirmed by PCR or HIV antibody test (suspected HIV positive status). Six children were known to be HIV infected at enrolment, the others were identified HIV-infected during study conduct. Therefore, most of the children included in this analysis were not under treatment at the time of RTS,S/AS01$_E$ vaccination. The adherence to treatment during the length of the study is unknown.

- Based on 125 children with confirmed HIV-infection, RTS,S elicited a lower anti-CS antibody response in HIV-infected children (GMC=193 EU/ml) as compared to children of unknown HIV infection status (GMC=492 EU/ml). [c]
- The overall safety information from dose 1 to study end showed that HIV-infected children in the three groups R3R, R3C and C3C experienced similar incidence of SAEs (92%, 85% and 88% respectively) and fatal SAEs (29%, 28% and 31% respectively).

Malaria-058, enrolled 200 children in Kenya, aged 6 weeks to 17 months, who were diagnosed with WHO stage 1 or 2 HIV disease in the context of high treatment coverage (anti-retrovirals and co-trimoxazole). These children were randomized to receive RTS,S/AS01 (99 children) or rabies control vaccine(101 children). This study looked specifically at safety of the vaccine in these children in terms of both reporting of safety events and monitoring of disease progression markers. The study also evaluated vaccine efficacy against clinical and severe malaria.

- The anti-CS antibody GMC was 329 EU/mL, one month after the third dose of RTS,S.
- The incidence of SAEs was similar (41% in the RTS,S group and 37% in the rabies vaccine group) over 14 months post dose 1.There were 9 fatal SAEs, 5 in the RTS,S group and 4 in the rabies vaccine group.
- Over one year of follow-up, the VE of RTS,S against all episodes of clinical malaria was 37% (95% CI: -27; 69).

a. *Malaria-055, ClinicalTrials.gov NCT00866619 (GSK study ID 110021)*

b. *Malaria-058, ClinicalTrials.gov NCT01148459 (GSK study ID 112745)*

c. *Mosquirix European SmPC 2015; ema.europa.eu*