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 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.

RTS,S MEDICAL AND SCIENTIFIC QUESTIONS & ANSWERS

For internal use only - NOT FOR DISTRIBUTION

Why was the efficacy lower in infants 6-12 weeks of age than in children 5-17 months of age?

Although no correlate of protection has been demonstrated, a likely explanation for the difference in efficacy against clinical and severe malaria between 6-12 weeks old infants and 5-17 months old young children is the difference in anti-CS antibody titre between both age-categories (being 3-fold lower in 6-12 week olds). Similar differences in immune responses were however seen previously in Phase II studies, without impacting on the vaccine efficacy measures.

The analysis after 18 months of follow-up of the Phase III efficacy trial [(a)] has provided some clues as to why young infants respond less effectively to RTS,S/AS01 than children. Maternal antibodies are likely to have played a role as young infants with detectable anti-CS antibodies at enrollment had a lower post-vaccination anti-CS response than young infants without and a high post-vaccination anti-CS antibody titer was associated with VE in young infants. However, maternal antibodies cannot explain fully the lower anti-CS response in young infants as those without detectable maternally derived anti-CS antibodies still had a lower post-vaccination anti-CS GMT than did children. Immune interference due to administration of RTS,S/AS01 at the same time as EPI vaccines remains a possible factor. The fact that phase 2 trials showed that co-administration in one setting was associated with lower anti-CS responses when compared with staggered administration in another setting supports this hypothesis. A suppressive effect from exposure to malaria antigens in utero might be more marked in young infants than in older children who have had a longer period to acquire immunity. Finally the immature immune system of young infants may not respond as well as that of older children. In contrast with findings from a phase 2 trial, we found no evidence that priming with hepatitis B vaccine in children explained their enhanced anti-CS antibody response. Although we do not yet fully understand the reasons for the difference in efficacy observed between both age categories, these results confirm that the RTS,S malaria vaccine candidate allows to further reduce the malaria burden over and above the reduction achieved with existing interventions. This was observed in infants when the vaccine was co-administered with routine childhood vaccines, as well as in older children 5-17 months of age, when the vaccine was given alone. Given the significant public health burden of malaria and the major scientific challenge of developing the first ever vaccine against a human parasite, these results are a major achievement.

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