

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 trials.
- 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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How does RTS,S work?

The RTS,S malaria vaccine candidate aims to trigger the immune system to defend against the *P. falciparum* malaria parasite when it first enters the human host's bloodstream and/or when the parasite infects liver cells. This is the pre-erythrocytic part of the parasites lifecycle and explains why RTS,S is commonly referred to as a pre-erythrocytic vaccine. RTS,S is designed to prevent the parasite from infecting, maturing and multiplying in the liver, and from re-entering the bloodstream and invading red blood cells, at which point the infected person would begin to show symptoms of the disease^(a).

Although no correlate of protection has currently been established, both humoral and cellular immune responses are considered to contribute to protection against *P. falciparum*.^(b) To stimulate an immune response to the malaria parasite, a portion of the circumsporozoite protein (the surface protein that helps the malaria parasite invade human liver cells) was fused with the hepatitis B surface protein (HBsAg). This 'RTS' fusion protein is expressed together with 'free' HBsAg ('S') in yeast cells (*Saccharomyces cerevisiae*), allowing spontaneous formation of 'RTS,S' particles known to enhance immune responses to the antigen. The addition of one of GSK's proprietary Adjuvant Systems (AS01) aims to further improve the immune response to the antigen and thereby induce protection^(c,d).

a. Gordon et al. J Infect Dis 1995; 171:1576-85

b. White et al 2013 PLoS ONE 8(4): e61395

c. Cohen et al. Ann Pharm Françaises 2010;68:370-9

d. Cohen et al. in Parasitology, Springer-Verlag Berlin Heidelberg 2011, Chapter 7