Fact Sheet: RTS,S Malaria Vaccine Candidate

The RTS,S malaria vaccine candidate

Malaria kills close to 800,000 people a year worldwide and sickens tens of millions more, most of them children living in sub-Saharan Africa. A safe and effective vaccine would be an important component of a comprehensive malaria control programme and could potentially save hundreds of thousands of lives.

RTS,S is the most clinically advanced malaria vaccine candidate in the world today. In clinical trials, it was the first to demonstrate that it could help protect young children and infants in malaria-endemic areas against infection and clinical disease caused by *Plasmodium falciparum*, the most deadly species of the malaria parasite.[1,2]

How RTS,S works

RTS,S aims to trigger the immune system to defend against *P. falciparum* malaria parasite when it first enters the human host's bloodstream and/or when the parasite infects liver cells. It is designed to prevent the parasite from infecting, maturing and multiplying in the liver, and from re-entering the bloodstream and infecting red blood cells, at which point the affected person would begin to show symptoms of the disease.

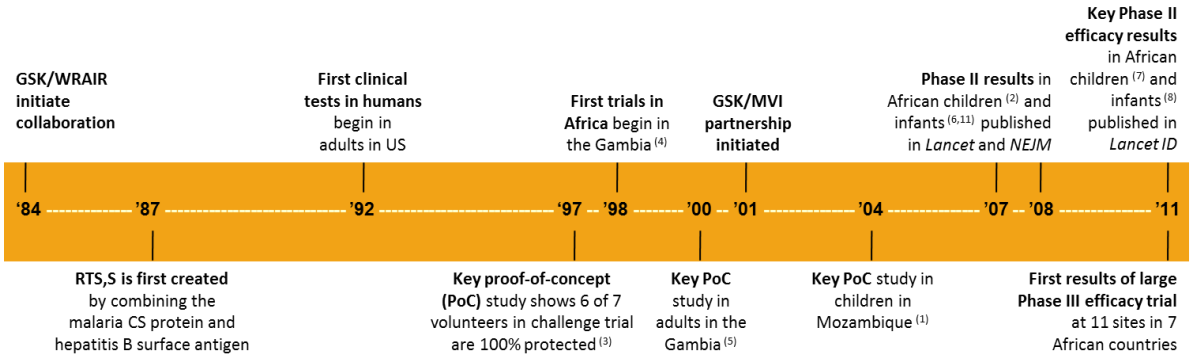
To stimulate an immune response to the malaria parasite, RTS,S fuses a circumsporozoite protein – the surface protein that helps the parasite invade human liver cells – with a protein found in GSK Biologicals' (GSK Bio) hepatitis B vaccine. The addition of GSK's proprietary Adjuvant Systems (AS) aims to further improve the immune response.

Early development of RTS,S

The RTS,S malaria vaccine candidate was created in 1987 by scientists working at GSK Bio's laboratories. Early development and clinical testing of the RTS,S malaria vaccine candidate was part of an ongoing collaboration between GSK Bio and the United States Walter Reed Army Institute of Research. The vaccine candidate was initially tested in healthy adults in the United States and Belgium in 1992, before the first study in Africa was conducted in adults living in The Gambia in 1998.

In January 2001, GSK and the PATH Malaria Vaccine Initiative (MVI), with grant monies from the Bill & Melinda Gates Foundation to MVI, entered into a public-private partnership to develop an RTS,S-based vaccine for infants and young children living in malaria-endemic regions in sub-Saharan Africa. Research centres were selected for their track record of conducting world-class research, fostering strong community relationships, and meeting the most rigorous ethical and regulatory standards. They coordinate their efforts and share information through a formal structure, the Clinical Trials Partnership Committee, which includes the research centres' Northern academic partners, MVI and GSK. The participating research centres also received support from the Malaria Clinical Trials Alliance.

RTS,S key milestones



RTS,S results to date

Results of a Phase II proof-of-concept trial in Mozambique were published in *The Lancet* in 2004 and demonstrated for the first time that it was possible to provide partial protection against malaria to children living in malaria-endemic regions of sub-Saharan Africa, and that the clinical benefit lasted for at least 42 months after the initial vaccination.[1,9] A study in children 5 to 17 months of age living in Kenya and Tanzania showed that the RTS,S malaria vaccine candidate had a promising safety and tolerability profile and reduced the risk of children experiencing clinical malaria by 39% over a 12-month follow-up period.[6,7]

Results of a study in Gabon, Ghana and Tanzania in 6 to 10 week-old infants showed that the RTS,S malaria vaccine candidate also has an acceptable safety profile when administered alongside standard infant vaccines that are part of existing African national immunisation programmes, called the World Health Organisation (WHO) Expanded Programme on Immunisation (EPI).[10] Recently published efficacy data from this study showed that the RTS,S malaria vaccine candidate reduced the risk of children experiencing clinical malaria by 62% over a 12-month period.[8]

Next steps in advancing RTS,S

Based on the successful trials to date, GSK, MVI and leading African research institutions are continuing clinical trials with infants and young children, the most vulnerable groups and those who would benefit most from an effective malaria vaccine.

The first results from the Phase III efficacy trial will be available by the end of 2011 (5 to 17 month-olds) with subsequent results to be reported in 2012 (6 to 12 week-olds) and 2014 (longer-term protection). The RTS,S malaria vaccine candidate is still under development and subject to the evaluation of its safety, quality and efficacy, as well as its benefits and risks, by the regulatory authorities before being made available. If the required public health information, including safety and efficacy data from the Phase III programme, is deemed satisfactory, the WHO has indicated that a policy recommendation for the RTS,S malaria vaccine candidate is possible as early as 2015, paving the way for decisions by African nations regarding large-scale implementation of the vaccine through their national immunisation programmes (EPI).

GSK and MVI are committed to making RTS,S—if approved for use—available to those who need it most: infants and young children in malaria-endemic regions of sub-Saharan Africa. In January 2010, GSK announced that the RTS,S pricing model will cover the cost of the vaccine together with a small return, which will be reinvested in research and development for second-generation malaria vaccines or vaccines against other neglected tropical diseases.

GlaxoSmithKline Biologicals (GSK Biologicals), GlaxoSmithKline's vaccines business, is one of the world's leading vaccine companies and a leader in innovation. The company is active in vaccine research, development, and production with over 30 vaccines approved for marketing and 20 more in development - both in the prophylactic and therapeutic fields. Headquartered in Belgium, GSK Biologicals has 14 manufacturing sites strategically positioned around the globe. In 2010, GSK Biologicals distributed 1.43 billion doses of vaccines to 179 countries in both the developed and the developing world. Through its accomplished and dedicated workforce, GSK Biologicals applies its expertise to the discovery of innovative vaccines that contribute to the health and well-being of people of all generations around the world. For further information, please visit www.gsk.com

The PATH Malaria Vaccine Initiative (MVI) is a global programme established at PATH through an initial grant from the Bill & Melinda Gates Foundation. MVI's mission is to accelerate the development of malaria vaccines and ensure their availability and accessibility in the developing world. MVI's vision is a world free from malaria. For more information, please visit www.malariavaccine.org.

PATH is an international, non-profit organisation that creates sustainable, culturally relevant solutions, enabling communities worldwide to break longstanding cycles of poor health. By collaborating with diverse public - and private - sector partners, PATH helps provide appropriate health technologies and vital strategies that change the way people think and act. PATH's work improves global health and well-being. For more information, please visit www.path.org.

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