Fact Sheet: Phase III safety and efficacy trial of the RTS,S malaria vaccine candidate

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]

The launch of the Phase III efficacy trial of the RTS,S malaria vaccine candidate marked an important milestone after more than 20 years of research and development. The trial started in May 2009 and is now underway at 11 sites in seven African countries (Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique and Tanzania). Together, the 11 sites completed enrolment in January 2011, with 15,460 infants and young children participating, making this the largest malaria vaccine trial to date.

Design of the trial

As one of the final stages of testing before regulatory file submission, the Phase III trial is designed to continue monitoring safety and potential side-effects, while evaluating the efficacy of the vaccine in infants and young children on a large scale. To this end, researchers enrolled two groups of participants: children aged 5 to 17 months and infants aged 6 to 12 weeks. The Phase III trial is a double-blind study, in which participants initially received three doses of either RTS,S or a 'control vaccine.' After a year and a half, some participants will receive a fourth RTS,S dose to evaluate the potential benefit of a booster.

Availability of results

The first results from the Phase III efficacy trial will be available by the end of 2011. These results will indicate the level of protection provided by RTS,S to children aged 5 to 17 months against clinical malaria over a one-year period after vaccination. They also will provide additional information about the safety of the vaccine and how well it is tolerated in this group of children. A similar analysis will be conducted in the infant group, which should be available by the end of 2012. An additional data set, which will include information about the vaccine's longer-term protective ability for both groups of children, should be available by the end of 2014 and will provide evidence for national and international public health organisations to evaluate the vaccine candidate's full potential for use. Data on severe malaria episodes are being gathered for all infants and children enrolled in the trial aged 6 weeks to 17 months. The efficacy

RTS,S Phase III sites and research partners

Burkina Faso – Nanoro
Institut de Recherche en Science de la Santé (IRSS) / Centre Muraz

Gabon – Lambaréné
Albert Schweitzer Hospital, Medical Research Unit
+ University of Tübingen

Ghana – Agogo (Kumasi)
School of Medical Sciences, Kwame Nkrumah University of Science and Technology
Kumasi Centre for Collaborative Research
Agogo Presbyterian Hospital

Ghana – Kintampo
Kintampo Health Research Centre, Ghana Health Service
+London School of Hygiene and Tropical Medicine

Kenya – Kilifi
Kenya Medical Research Institute
+ Wellcome Trust

Kenya – Kombewa (Kisumu)
Kenya Medical Research Institute
+ Walter Reed Army Institute of Research

Kenya – Siaya (Kisumu)
Kenya Medical Research Institute
+ Centers for Disease Control and Prevention

Malawi – Lilongwe
University of North Carolina Project

Mozambique – Manhica
Centro de Investigação em Saúde de Manhiça
+ Barcelona International Health Research Centre

Tanzania – Bagamoyo
Ifakara Health Institute
+ Swiss Tropical and Public Health Institute

Tanzania – Korogwe
National Institute for Medical Research, Tanzania
Kilimanjaro Christian Medical Centre

+ Indicates an affiliated partner

of RTS,S against severe malaria will be analysed when a predefined number of cases have accumulated and will be reported when they become available.

The RTS,S malaria vaccine candidate is currently under development and subject to the evaluation of its safety, quality and efficacy, as well as its benefits and risks, by regulatory and public health authorities. If the required regulatory and public health information, including safety and efficacy data from the Phase III programme, is deemed satisfactory, the World Health Organisation (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.

For more information, please see:
http://www.who.int/vaccine_research/diseases/malaria/vaccine_candidate_policy/en/index.html.

Availability of data from RTS,S Phase III efficacy trial

Group	12-month follow-up data	30-month follow-up data
5 to 17 month-olds	Expected release: Fourth quarter of 2011	Expected release: Fourth quarter of 2014
6 to 12 week-olds	Expected release: Fourth quarter of 2012	Expected release: Fourth quarter of 2014

The primary endpoint of this trial is the level of protection afforded by RTS,S to infants and young children against clinical malaria 12 months after primary immunisation. The trial will also provide further data on the safety of the vaccine. Secondary endpoints include the level of protection against severe malaria and death.

The health and safety of the study participants is the highest priority of the project partners. The Phase III trial is designed and conducted according to the highest international standards for safety, ethics and clinical practices. The trial has been designed in consultation with appropriate regulatory authorities and the WHO.

Affordable pricing

MVI, GSK and other partners are working to ensure that RTS,S—if approved for use—reaches the infants and children who need it most, as quickly as possible. 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.

NB: This vaccine candidate is in development and subject to evaluation of the benefits and risks by the regulatory authorities before being made available to the public.

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

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, visit www.malariavaccine.org.

PATH is an international non-profit organization 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, visit www.path.org.

***References**:*

1) Alonso P, et al. Lancet 2004; 364 1411-20
2) *Aponte JJ, et al. Lancet 2007; 370: 1543-51")*