RTS,S/AS01 for seasonal use FAQ

What is Seasonal Malaria Chemoprevention?

Seasonal Malaria Chemoprevention (SMC) is a highly effective intervention to prevent malaria in those most vulnerable to the disease—young children under 5 years of age. It involves administering monthly doses of a combination of antimalarial drugs to children aged 3–59 months during the peak malaria transmission season, which coincides with the rainy season and usually lasts 3 or 4 months. SMC has been shown to be 75% protective against uncomplicated and severe malaria in children under 5 years of age. However, despite widespread deployment of SMC and effective diagnosis and treatment programs, the burden of malaria in the Sahel and sub-Sahel region of Africa remains high. Six of the ten African 'High Burden to High Impact' malaria-endemic countries prioritized by the World Health Organization (WHO) are within this region.

What is seasonal malaria?

In certain regions, like the African Sahel, most malaria cases occur during the four-month rainy season. Some 25 million children under 5 years of age in the Sahel are given SMC to protect them from the disease during the months of highest malaria transmission.

A child in Burkina Faso awaits vaccination with his mother. Photo: PATH.

What is the RTS,S/AS01 malaria vaccine?

RTS,S/AS01 (RTS,S) is the first malaria vaccine to significantly reduce malaria and life-threatening severe malaria in young African children. It is the first malaria vaccine to reach children through routine immunization in areas of Ghana, Kenya, and Malawi—three countries with perennial malaria transmission—through a landmark pilot programme, the Malaria Vaccine Pilot Implementation Programme (MVIP). Pilot introductions are being led by the ministries of health, with WHO providing technical and scientific leadership and working in collaboration with GSK, PATH, and a range of other international and country partners. As of August 2021, more than 740,000 children have received at least one dose of the RTS,S vaccine and more than 2.1 million doses of the vaccine have been administered. The evaluation of the pilot introduction will inform a potential WHO recommendation for wider use of the vaccine in sub-Saharan Africa as early as October 2021.

The RTS,S vaccine acts against *Plasmodium falciparum*, the most deadly malaria parasite globally and the most prevalent in Africa. It is the only malaria vaccine to receive a positive scientific opinion from the European Medicines Agency, a stringent regulatory authority, and it is approved for use in the pilots by each national regulatory authority. The vaccine was developed by GSK over the last 30 years, and in partnership with PATH since 2001.

During the Phase 3 safety and efficacy trial of the RTS,S vaccine (conducted from 2009–2014 in 7 sub-Saharan countries with sites representing a range of malaria transmission settings) vaccine efficacy was highest during the first 6 months after vaccination. This led researchers to hypothesize that it may be a useful tool in preventing malaria in areas with highly seasonal transmission.

What do the Phase 3 results on RTS,S seasonal vaccination show?

The results of this Phase 3 trial show not only that RTS,S is as effective as SMC, the current standard of care, at preventing uncomplicated malaria in seasonal settings, but that combining the two interventions is markedly superior to either intervention alone at preventing uncomplicated malaria, severe malaria, and death from malaria, with nearly 70 percent increased protection over either intervention alone.

How was the study conducted?

The trial enrolled 5,920 children, randomized to receive SMC alone, the RTS,S malaria vaccine alone, or both interventions together.

All children participating in the study were given an insecticide treated bednet upon enrolment in 2017. Children in the RTS,S alone or combined group received three doses of RTS,S at monthly intervals from April to June 2017 followed by a fourth and fifth dose in in June 2018 and June 2019, respectively, prior to the malaria transmission seasons. The RTS,S alone group received four courses of SMC placebo at monthly intervals during the malaria transmission season each year.

Children in the SMC alone group received three doses of rabies vaccine (*Rabipur*^{R}) in 2017 and a dose of Hepatitis A vaccine (HAVRIX^{R}) in 2018 and 2019 as control vaccines. Children in the SMC alone group and the combined group each received four courses of SMC at monthly intervals each year. A course of SMC for a child over the age of 1 year is comprised of sulfadoxine/pyrimethamine 500/25 mg (SP) and amodiaquine (AQ) 150 mg on day 1 and AQ 150 mg on days 2 and 3.

What were the partners' roles in this study?

The London School of Hygiene and Tropical Medicine (LSHTM) led the study, serving as the regulatory sponsor and providing scientific oversight. The Institut de Recherche en Sciences de la Sante in Burkina Faso, and the Malaria Research and Training Center, University of Bamako, in Mali, recruited participants and conducted the trial.

In addition to providing technical expertise and advice, PATH provided partial funding for year 3 of the study and is helping to fund years 4 and 5 of the study, currently ongoing, along with other donors. GSK, the vaccine developer and manufacturer, donated the vaccine and provided strategic guidance.

What are the next steps?

A follow-on study is currently ongoing and will follow the children enrolled for an additional 2 years through the age of 5. Data from these additional 2 years should be available in 2022 or 2023.

These new data add to the RTS,S evidence that is being generated by the malaria vaccine pilot introduction underway in Ghana, Kenya, and Malawi. The evaluation of the pilots is providing information on the feasibility of reaching children with the 4-dose vaccine, and on the impact and safety of the vaccine in routine use.

The data from this trial on seasonal RTS,S vaccination will be considered along with the information from the pilot evaluation and other RTS,S evidence that have become available since 2015, when the pilots were recommended, to inform a potential WHO recommendation for wider use. Global advisory bodies for immunization and malaria will convene in October 2021 to review the full RTS,S evidence package and to consider a WHO recommendation.

References

For more information about the Malaria Vaccine Implementation Programme, please visit the WHO website.

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