

Difäm Health Community (DHC)

Podcast: Malaria vaccination

As of September 2022

Welcome to this podcast about vaccination against malaria. My name is xxx, I am a member of the health team of the German Institute for Medical Mission, also called Difäm. With me is my colleague, xxx. Malaria is still one of the most frequent diseases in African countries and a great risk especially for the lives of children. Can you tell us, please, what dimension malaria has worldwide?

Every year malaria parasites infect over 200 million people and kill over 600,000. Three quarters of deaths occur in sub-Saharan Africa particularly among young children. These numbers are still enormous although the WHO and UNICEF estimated that the death toll of malaria could be reduced by approximately 60 % between the years 2000 and 2015 largely due to the widespread use of insecticide-treated bed nets and artemisinin-based combination therapies.¹

Malaria has also a huge impact on economies. In countries where malaria is endemic, the per capita income levels are 70% lower than in countries where the disease does not play a major role. In some African countries, the treatment of malaria eats up to 40% of the national health budget. Malaria holds back prosperity in sub-Saharan Africa and the progress in the fight against malaria has stalled in recent years.¹

In October 2021, the WHO has approved a new vaccine against malaria. Is this vaccine the tool that the world waited for in order to eradicate malaria?

Well, at least it is a tool, which promises to reduce malaria cases and deaths. It is called RTS,S/AS01, the trade name is Mosquirix. However, the scientific world calls it RTS,S. The vaccine should be administered to children from the age of 5 to 6 months. Full immunization requires four doses; the first three doses are given in approximately monthly intervals and the fourth dose around the second birthday of the child.

The WHO recommended the vaccine in October 2021 for the use in areas with moderate to high malaria transmission due to plasmodium falciparum. It took more than 30 years until this recommendation could be issued.

This is not really a success story of international research and development. Let us talk about this vaccine in more detail. How does it work?

When the mosquito bites a human being, it releases sporozoites into the bloodstream. In this stage of evolution, these parasite sporozoites cannot enter the human erythrocytes – the red blood cells. The human body does not yet develop disease symptoms. In order to cause symptomatic malaria, the sporozoites have to enter the next stage of their evolution. They do this in the liver cells to which

the sporozoites migrate. In this pre-erythrocytic sporozoite stage, the malaria parasite can be attacked by the immune system, if it has been prepared by the vaccine. The vaccine prevents sporozoites from penetrating into the liver, where they can mature, multiply, re-enter the bloodstream, and infect red blood cells. However, it has to be clear: the vaccine does not prevent infection per se. It only has an influence on the development of symptoms.

RTS,S is a recombinant vaccine and consists of an antigen, the circumsporozoite protein (CSP) and a viral surface antigen of the hepatitis B virus. Together they assemble to virus-like particles. The CSP antigen causes the production of antibodies capable of preventing the invasion of liver cells and additionally elicits a cellular response enabling the destruction of already infected liver cells.³

[Thank you for the information on the immunology of the malaria vaccine. Where was the vaccine tested and when did we get the first results?](#)

In 2016, a 2-year pilot study on RTS,S vaccination as part of routine childhood immunization was terminated in Ghana, Kenya, and Malawi, settings with a high malaria burden throughout the year. After having administered more than 3 million vaccine doses, the study showed that the vaccine is safe, feasible and increases equity in access to malaria prevention. The study also provided evidence that parents do not stop using insecticide-treated bed nets or attending medical care with their child if it shows malaria-like symptoms. Indeed, communities were very interested in the immunization of their children against malaria. RTS,S can easily be integrated into routine immunization programmes. In the pilot study, 80% of the children in the targeted communities benefitted from the vaccine.²

GAVI, the Global Vaccine Alliance, has supported RTS,S since 2019. The WHO recommendation followed in October 2021. Findings from health economics and qualitative research led by PATH also supported the WHO recommendation. Modelling shows that the vaccine is a cost-effective addition to other recommended malaria interventions, even in regions where bed nets and seasonal chemoprevention is used. The RTS,S vaccine's cost-effectiveness is comparable to many other new vaccines.⁴

[This sounds all very promising. However, there is only one backdrop concerning the vaccine. It has only a limited efficacy of about 30%. This means that it prevents the malaria disease in only one third of vaccinated children. Other vaccines have to show at least 70% efficacy before they get an international recommendation. Why does the WHO recommend RTS,S nevertheless?](#)

You are right. The efficacy of RTS,S is very low. However, even with this very low efficacy, the vaccine will have a great impact because the malaria disease is so numerous in endemic settings. We have seen the same in the case of TB: the vaccine against TB is also not very efficient yet it helps many, because the disease affects millions of people.

After having received four doses of RTS,S, malaria episodes in children were reduced by about 40% and severe malaria cases by about 30% over a four-year period. Let me give you an example to illustrate it a bit more : At the trial site with the highest disease burden, more than 6,500 clinical malaria episodes were averted for every 1,000 children fully vaccinated with 4 vaccine doses: this means that in order to save one life we need to vaccinate 200 children.⁵

[Ghana, Kenya and Malawi are countries where we have a high disease burden all year round. What about countries where malaria is a seasonal disease?](#)

This is a very good question. The benefits of the vaccine in countries with seasonal malaria are currently being studied in phase 3 trials in Burkina Faso and Mali: vaccine doses are provided prior to the peak rainy season. Preliminary results show that the protective effect of RTS,S is comparable to seasonal chemoprevention. Actually, we achieve the best effect when we combine vaccination and chemoprevention. The result was an additional reduction of approximately 70 percent of malaria deaths and hospitalizations, and a 60 percent reduction of uncomplicated malaria.⁴

How long does the protective effect of the RTS,S vaccine last? Do children have to get booster shots of the vaccine?

It is not clear yet, how long the protective effect of an immunization with RTS,S will last. One study of a seven year follow-up has shown that the incidence of severe malaria decreased as children got older, regardless of whether the children were vaccinated or not. There was no evidence that episodes of severe malaria became more frequent again among vaccinated children after the seven years. However, research has to follow this up.⁴

What about side effects of the vaccine?

The side effects of the RTS,S vaccine were a major research question of the big pilot study in Ghana, Kenya and Malawi. The children who received the vaccine did not have an increased risk of meningitis and seizures as adverse effects. Many showed minor effects like swelling or pain at the injection site and fever. These are common side effects after immunization.

Thank you for this positive information. So, apart from the low efficacy RTS,S seems to be a good vaccine. However, are there other vaccine candidates in development against malaria?

Yes, there are a handful of other vaccine candidates but we are still waiting for phase III study results. The most promising alternative malaria vaccine is R21/Matrix-M (R21). It has shown an efficacy of 77% in a phase 2 trial and induced the development of significantly higher levels of antibodies than the RTS,S vaccine. It is the first vaccine that meets the WHO goal of an efficacy of at least 75%. The R21 vaccine also uses a CSP antigen in combination with the hepatitis B surface antigen but it uses a different adjuvant than RTS,S.⁵

One information is still lacking for our audience who are mainly practitioners. Is the vaccine already widely available?

It was only on 6th September 2022 when WHO prequalified the RTS,S vaccine. This is a prerequisite for the production of the vaccine. This means that there is currently not enough vaccine available for the 25 million children born each year in regions where malaria is endemic. In July 2022, WHO has therefore published a framework for the allocation of the limited malaria vaccine supply.⁷ The objective of this framework is to accelerate the production and to assure a fair distribution to the vaccine.

Thank you very much, xxx, for giving us this important information on malaria vaccination. Let me summarize the major findings: In regions where malaria is endemic throughout the year or occurs seasonally, we should immunize children at the age of 5 to 6 months with the vaccine RTS,S. The vaccine is well tolerated by children and leads only to common minor side effects like fever. It protects against the development of severe disease but it does not prevent the infection with the parasite per se. We hope that a more efficient vaccine will pass the phase III studies soon.

Thanks to all of you for listening to us. We invite you to join us on our next podcast about vaccines.

Be blessed and stay safe!

Internet sources as of 21/09/2022

- 1 https://cdn.who.int/media/docs/default-source/immunization/mvip/who-mvip-infographic-april-2022.pdf?sfvrsn=b9a755ae_1
- 2 <https://www.who.int/news/item/06-10-2021-who-recommends-groundbreaking-malaria-vaccine-for-children-at-risk>
- 3 <https://digitalcommons.unl.edu/cgi/viewcontent.cgi?referer=&httpsredir=1&article=1019&context=usarmyresearch>
- 4 https://www.malariavaccine.org/sites/mvi/files/content/page/files/RTSS%20fact%20sheet_FINAL_20220221.pdf
- 5 [www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00943-0/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00943-0/fulltext)
- 6 <https://www.smithsonianmag.com/science-nature/why-did-it-take-35-years-to-get-a-malaria-vaccine-180980151/>
- 7 https://cdn.who.int/media/docs/default-source/immunization/mvip/framework-for-allocation-of-limited-malaria-vaccine-supply.pdf?sfvrsn=35b12e4_2&download=true