



The RTS,S malaria vaccine: Journey from conception to recommendation

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ABSTRACT

The RTS,S malaria vaccine was recently recommended for use among children at risk in malaria endemic regions. Although significant efforts have been made to minimise malaria cases, the results of these innovations have not been totally satisfactory due to specific limitations. However, this revolutionary vaccine has a great tendency to put an end to malaria. Being the first vaccine against malaria, this commentary examines its journey from the idealisation and conception to the recommendation by the World Health Organization. The commentary also examines some of the challenges that might affect the execution of the vaccination programme in sub-Saharan Africa and other malaria endemic regions and suggest recommendations to overcome the possible them.

1. Commentary

In October 2021, the World Health Organization (WHO) recommended the widespread use of the RTS,S/AS01 (RTS,S) malaria vaccine with the trade name “Mosquirix” for children at risk in sub-Saharan Africa and other regions with moderate to high transmission of malaria caused by *Plasmodium falciparum* [1]. This ground-breaking vaccine was recommended based on results from a pilot programme that was conducted in Ghana, Kenya, and Malawi [1]. The RTS,S vaccine is the first vaccine recommended by the WHO for use against the malaria disease and its development dates back to the 20th century.

Malaria has been ravaging the health of people and causing a lot of fatalities for ages, and it is important to note that alternative prevention and treatment strategies have been developed over time, some of which have shown hopeful, but not entirely satisfying outcomes. Insecticide sprays, for example, have been used to eradicate malaria vectors. This approach, on the other hand, has its flaws and limitations, including the inability to cover a large area without increasing the concentration, which could be harmful to the health of the population. Aside from that, the usage of insecticide-treated bed nets (ITNs) is also recognised as a method used to reduce the number of malaria infections. These bed nets, however, are only useful when people are asleep, which is in contrast to malaria vectors, which can also attack outdoor and while people are awake. There have been several other advancements implemented to control malaria and to make malaria treatments more effective. However, innovations are needed to reduce the burden of malaria and save lives, and the RTS,S malaria vaccine appears to be the end of the reign of malaria among children in sub-Saharan Africa and other malaria-

endemic areas.

The RTS,S malaria vaccine is the most advanced candidate vaccine against human malaria. From conception and design in the early 1980s [2] to the approval and recommendation in 2021, the RTS,S vaccine has overcome huge challenges and disproved traditional vaccine standards. The RTS,S malaria vaccine is the result of about 30 years of research and was developed by PATH Malaria Vaccine Initiative (MVI) and GlaxoSmithKline (GSK) [3], with support from a network of African research centres [1] and also from the Bill and Melinda Gates Foundation [4]. The initial concept for RTS,S was based on what was known in the field at the time [3], and the first successful human trial demonstrating protection against *Plasmodium falciparum* sporozoite infection was conducted in 1996 at the Walter Reed Army Institute of Research (WRAIR) using the RTS,S vaccine developed by GSK [5].

The vaccine was given the name RTS,S because it was created by combining genes from the repeat (‘R’) and T-cell epitope (‘T’) of the pre-erythrocytic circumsporozoite protein (CSP) of the *Plasmodium falciparum* malaria parasite with a surface antigen (‘S’) of the hepatitis B virus and then mixed with additional hepatitis B surface antigen (HBsAg) to improve purification, hence the extra “S” [6]. The bite of an infected anopheles mosquito introduces sporozoites into the microvasculature, which are carried to the liver, where they move through hepatocytes and differentiate into hepatic merozoites capable of infecting erythrocytes [5]. However, vaccination with RTS,S induces antibodies against the circumsporozoite protein (CSP) and immobilizes the sporozoites -an infective form of *Plasmodium* that mosquitoes transmit- thereby preventing infection of hepatocytes [7].

Despite the proven effectiveness of the RTS,S malaria vaccine, it is

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important to highlight that there are challenges that could hinder its successful delivery, administration and operation. In recognition of the limited supply and high costs of vaccines in previous vaccination and immunization campaigns, there are concerns as to whether the RTS,S vaccine will be available and accessible to children in malaria-endemic areas. To ensure that vaccines reach every infant and child in need as soon as possible in sub-Saharan Africa and other malaria-endemic areas, vaccine demand must be forecasted in advance, and manufacturing capacity must be adjusted accordingly – good lessons can be learned from the COVID-19 vaccine rollout in specific areas. For example, it was evident that proper planning was a significant factor in getting the best results for the COVID-19 vaccine rollout among some African countries like Botswana, Ethiopia and Ghana [8]. In addition, low- and middle-income countries (LMICs) have substantial experience in conducting vaccination campaigns to respond to disease threats [9] and this valuable experience can be leveraged to ensure the success of the vaccination programs.

However, while the rollout of the RTS,S vaccine in sub-Saharan Africa is yet to begin, there are tendencies that most low- and middle-income countries may lack the capacity to obtain vaccines and facilities to meet their population demand. As a result, methods must be created to enable international organisations and agencies, such as the Global Alliance for Vaccines and Immunization (GAVI) and the United Nations Children's Fund (UNICEF), to finance vaccine acquisition.

In conclusion, as stated by the WHO Director-General, Dr Tedros Adhanom Ghebreyesus that “*the long-awaited malaria vaccine for children represents a breakthrough for science, child health, and malaria control*”, this ground-breaking vaccine offers hope to individuals, communities, and nations that have been afflicted by the disease, as well as the world at large. The journey of the RTS,S vaccine from conception to recommendation resembles a story about a determined fight to the finish line which highlights the importance of resilience in science and global

health. The WHO recommendation ushers in a new era in malaria therapy, one that is both pleasant and effective in reducing and eventually eliminating malaria infection cases.

Conflict of interest

The author declares no conflict of interest.

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