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The development of malaria vaccine: a beacon of hope?

To the Editor

Malaria has been a major disease of public health importance affecting millions of people worldwide, with sub-Saharan Africa having the highest burden. In 2021, malaria was responsible for 619,000 deaths of which the World Health Organization (WHO) Africa Region accounted for 96% of the death cases [1]. Over the years, significant measures such as the use of drugs, insecticide-treated nets, vector control and other intervention approaches have been employed to decrease and control the burden of malaria yet, it remains a threat to the lives of millions of children. Despite all these intervention approaches, the development of an effective vaccine remains a crucial goal in eradicating this disease. It is however a concern that just few countries still have access to the vaccine following the approval of the first malaria vaccine by WHO.

Malaria vaccine development is an active area with numerous challenges and complexity such as the life cycle of the parasite, *Plasmodium falciparum* and the significant antigenic diversity [2]. In the quest for vaccine development, an understanding of the immune response of the malaria parasite is also crucial [3]. The prospect of malaria vaccination amidst the difficulties encountered in vaccine development stems from the immunization of human volunteers, rodents and primates with irradiated sporozoites since the 1960s [3]. Several vaccine candidates under clinical trials are known to target specific stages of the parasite, namely: transmission-blocking vaccines (TBVs), pre-erythrocytic vaccines (PEVs), and blood-stage vaccines (BSVs) [2,

3]. WHO in October 2021 approved RTS, S/AS01, a four-dose vaccine for use in children between 5–17 months of age at first vaccination, following phase III efficacy trials in seven sub-Saharan African countries including Ghana, Kenya and Malawi [4]. The development of RTS,S/AS01 seems to be a breakthrough for the elimination of malaria in Africa.

The first-generation vaccine, RTS/S is a recombinant protein-based vaccine which targets the sporozoite stage of the *Plasmodium falciparum* life cycle, preventing liver infection, where the parasite would otherwise mature, multiply, and infect the host erythrocyte [5, 6]. Although the efficacy of RTS,S/AS01 is modest, it offers a significant public health benefit. The results of the pilot study carried out between 2009 and 2014 in Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique, and Tanzania, showed that the vaccine prevented 39% of clinical malaria cases and 29% of severe malaria cases over four years of follow-up in children between the ages of 5 and 17 months of age who received three doses of the RTS,S vaccine together with a booster dose [7].

Following the approval of RTS,S/AS01 by the WHO, it has been recommended for broader use, especially in countries where malaria is endemic. Aside from countries where this vaccine was used for pilot study, no other country has been reported to have this malaria vaccine deployed to. The delay in the deployment of the vaccine to where it is needed is due to shortfalls in production, thus, ramping up production will take some time [8]. Even with the increase in production, GlaxoSmithKline (GSK) will not be able to meet the expected annual supply of about 50–100 million doses,

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thus, the high risk of demand exceeding supply [8]. In response to the limited supply, the WHO has developed a framework which ensures that children at the highest risk in endemic counties are prioritized to receive the vaccine, to guide vaccine allocation at the global and country levels [9]. The WHO is working actively with partners to increase manufacturing capacities and facilitating the first and next generations of vaccines. GSK has decided to decentralize the manufacturing to Bharat Biotech, a biotechnology company in Hyderabad, India [8]. This should help to bolster supplies in the long run. The recent discovery and distribution of the malaria vaccine present a chance to improve the fragile health systems in many sub-Saharan African nations.

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