

Vaccine for malaria: new hope

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In news— WHO has recently approved RTS,S/AS01 (Mosquirix) developed by GlaxoSmithKline for immunising children was a major milestone.

RTS,S/AS01 (Mosquirix) vaccine-

- **RTS, S/AS01 is a recombinant protein-based malaria vaccine.**
- In October 2021, the vaccine was endorsed by the World Health Organization for “broad use” in children, making it the first malaria vaccine candidate, and first vaccine to address parasitic infection, to receive this recommendation.
- **The vaccine acts against P. falciparum, the most deadly malaria parasite globally,** and the most prevalent in Africa.
- Among children who received 4 doses in large scale clinical trials, the vaccine was able to prevent approximately 4 in 10 cases of malaria over a 4-year period.
- Although RTS,S/AS01 has modest efficacy and **reduces severe malaria cases by only about 30 per cent after four doses given to children under age 5,** it still provides significant public health benefits, and could save thousands of lives every year.
- **It took more than 30 years and approximately \$700 million for this breakthrough,** which underscores the scientific and logistic challenges in developing a vaccine against a parasitic disease like malaria.
- **GSK has granted Bharat Biotech licence to manufacture Mosquirix,** and by 2029, the Hyderabad-based company is expected to be the sole global manufacturer of this vaccine.
- However, **RTS,S/AS01 fails to meet the WHO’s own**

benchmark for malaria vaccine efficacy of 75 per cent set in 2015. In September 2021, another malaria vaccine, **R21/Matrix M, developed by the University of Oxford in the UK, demonstrated an efficacy of 77 per cent** in phase 1 and 2 trials among 450 children in Burkina Faso.

- In early September 2022, this vaccine once again made headlines after it showed a high efficacy of 80 per cent & it was maintained after two years.

RTS,S and R21(R21 is a novel pre-erythrocytic candidate malaria vaccine)-

- **Both are similar in that they both contain the same part of a major protein that is found on the surface of the liver stage parasite, called sporozoite.**
- Both also **contain hepatitis B virus surface antigen (HBsAg)**, a protein that has an ability to self-assemble and that helps as the formation of virus-like particles of the CSP antigen fused with it.
- The important difference between the two vaccines is in the amount of the HBsAg.
- RTS,S has about 20 percent of the fusion protein, with the remaining 80 percent made up of HBsAg antigen, produced separately.
- R21, on the other hand, is made up entirely of the CSP fusion protein moieties, resulting in a much higher proportion of CSP antigen displayed on the virus-like particle surface, which significantly raises its exposure to the immune system of the host.
- To boost immune responses, all protein based recombinant vaccines rely heavily on a strong adjuvant.
- RTS,S is formulated with an adjuvant called AS01 developed at GSK; R21 employs an adjuvant called Matrix-M developed by Novavax (Sweden).
- Matrix M contains saponin-plant based material and stimulates both antibody and cellular immune responses to vaccines. Both adjuvants have shown high levels of

efficacy and safety.

- Matrix-M has been used in a variety of vaccine formulations against influenza, and more recently in the Novovax Covid-19 vaccine.
- All malaria vaccines under development need to be tested in the safe and scientific robust Controlled Human Malaria Infection (CHMI) model after completing phase 1 safety studies.
- This has been established in many countries of Europe, the UK, Colombia, and Thailand. Both RTS, S and R21 were tested in CHMI before further safety and efficacy field trials.

What is Malaria?

- Malaria is a tropical disease caused by Plasmodium parasites that are transmitted to humans by insect bites from infected female Anopheles mosquitoes, which mainly bite at dusk and at night.
- Symptoms include a high temperature of 38C or above, feeling hot and shivery, headaches, vomiting, muscle pains, diarrhoea.
- Malaria can also be spread through blood transfusions and the sharing of needles.
- The 5 different types of plasmodium parasite that cause malaria in humans are:
 - Plasmodium falciparum – mainly found in Africa, it's the most common type of malaria parasite and is responsible for most malaria deaths worldwide.
 - Plasmodium vivax – mainly found in Asia and South America, this parasite causes milder symptoms than Plasmodium falciparum, but it can stay in the liver for up to 3 year.
 - Plasmodium ovale – fairly uncommon and usually found in West Africa, can remain in the liver for several years without producing symptoms.

- Plasmodium malariae – this is quite rare and usually only found in Africa.
- Plasmodium knowlesi – this is very rare and found in parts of Southeast Asia.
- Malaria can be treated and its symptoms can be sublimed through correct medication. A few of the most common medications for malaria are:
 - Quinine.
 - Doxycycline.
 - Chloroquine.
 - Artemisinin.
 - Mefloquine.
 - Atovaquone.