The results of an early-stage clinical trial have brought closer the prospect of a vaccine to help protect infants and children from becoming infected with a parasite that causes the most deadly form of malaria, a disease that, according to the WHO, kills more than one million people every year (1).

Although the primary goal of the phase 1/IIb clinical trial was to assess the safety of the vaccine (RTS,S/AS02D) in infants in Mozambique, where malaria is endemic, it was also able to provide statistically significant data regarding the clinical efficacy of the vaccine. The results, published recently in The Lancet (2), indicate that the vaccine was safe and — like the standard vaccines that protect against diphtheria, tetanus, pertussis (whooping cough), and Haemophilus influenzae type b (DTP/Hib) and polio (OPV) — only provoked local swelling and pain. In terms of clinical efficacy, the vaccine was shown to reduce by 65% the number of infections with Plasmodium falciparum, the parasite that causes the most deadly form of malaria.

Most people at risk of developing malaria live in developing countries, and although individuals of all ages can contract malaria, children under the age of two are particularly vulnerable (1). Current approaches to curbing this disease rely on early diagnosis and rapid treatment, as well as programs that aim to control transmission of the disease-causing parasite either by eliminating the mosquitoes that inoculate individuals with the parasite (indoor residual insecticide spraying) or by preventing individuals from being bitten by the mosquitoes (insecticide-treated bed nets). However, there is currently only one group of drugs that are effective treatments for malaria — artemisinin-based combination therapies (ACTs) — as many cases of the disease are now caused by P. falciparum that is resistant to former antimalarial drugs such as chloroquine and sulfadoxine-pyrimethamine. Further, there are no effective alternatives to artemisinins on the market or nearing the end of development, meaning that additional approaches, such as vaccines, to reducing the burden of disease and death caused by malaria are needed.

The new vaccine, RTS,S/AS02D, was developed by GlaxoSmithKline (GSK) and comprises RTS,S, a hybrid recombinant protein consisting of two portions of the P. falciparum circumsporozoite protein fused to a portion of the hepatitis B virus S antigen, and AS02D, an adjuvant that boosts the immune response to RTS,S. In the trial it was shown that three doses of RTS,S/AS02D, given at 10, 14, and 18 weeks of age, primed the immune system of infants to produce large amounts of antibodies specific for the circumsporozoite protein (2). These antibodies stop P. falciparum from entering the cells of the liver, which is where the parasite multiplies, and are thought to provide the protection against malaria engendered by the vaccine.

Although the vaccine was developed by GSK, the trial was carried out in collaboration with a number of other organizations. In particular, financial support was provided by the PATH Malaria Vaccine Initiative (3), and the vaccine’s Safe and Effective for Anemia in Infants (SAFE) program was funded by a consortium of donors, including the Bill & Melinda Gates Foundation. "This is a huge step forward,” said Pedro Alonso of the University of Barcelona, who led the trial (3).

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