

SCIENCE

Malaria vaccine 'beginning to fade'

New study in Kenyan children shows protection wanes to near zero in just four years

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There is more cautionary news for the world's most advanced malaria vaccine. A new study in Kenyan children shows that its protection wanes over time, dropping to near zero after four years.

The results, published in the March 21 issue of *The New England Journal of Medicine*, are another strike against the chances that the vaccine will be widely used in its current form.

The vaccine, called RTS,S, is the only one ever to be tested in a phase III clinical trial. That trial reported promising initial results in 2011, cutting rates of malaria by half in toddlers. But findings published in November clouded its prospects, as the vaccine failed to protect young babies as much as hoped.

RTS,S (the name is an abbreviation of the protein components in the vaccine) was developed in the late 1980s by researchers at GlaxoSmithKline Biologicals in Rixensart, Belgium, and later in partnership with the PATH Malaria Vaccine Initiative. It contains an engineered protein that combines a protein fragment from the *Plasmodium falciparum* parasite and a protein from the hepatitis B virus, which helps provoke a strong immune response.

Phase II trials in Kenya and elsewhere suggested that the vaccine cut rates of malaria



Dr Ally Olotu (right) of KEMRI-Wellcome Trust Research Programme examines a young patient at his Kilifi research station.

by roughly half. Based on those findings, researchers launched the ambitious phase III trial involving more than 15,000 children at 11 sites in seven countries across sub-Saharan Africa. Although the interim outcomes published last fall were disappointing, the study is still ongoing, with full results expected in 2014.

In the meantime, Ally Olotu, Philip Bejon, and their colleagues at the Kenya Medical Research Institute-Wellcome Trust Research Programme in Kilifi, Kenya, continued to follow the nearly 450 children in the phase II trial. Now, they report that in the 223 children who received the vaccine, protection fades over time and is almost completely gone after four years. They also found that the pattern differs in areas of higher and lower malaria transmission: In the former, protection faded even faster, disappearing after about two years.

Olotu and Bejon say that may be because the control group – which was carefully observed and treated for any malaria

KEY QUESTIONS

What is RTS,S?

The name is an abbreviation of the protein components in the vaccine.

What does it contain?

It contains an engineered protein that combines a protein fragment from the *Plasmodium falciparum* parasite and a

protein from the hepatitis B virus, which helps provoke a strong immune response.

What was the outcome of the phase II trials?

Phase II trials in Kenya and elsewhere suggested that the vaccine cut rates of malaria by roughly half.

cases that appeared – developed natural immunity more quickly in the areas of higher transmission.

The news is not all dim. Because so many children get malaria in the region and many get it multiple times, the researchers calculated that for every 100 children vaccinated, 65 cases of malaria were prevented. That suggests that decisions about whether and how to use the potentially expensive vaccine will be complex, Bejon says.

"This shows again that the vaccine has its limitations," says Robert Sauerwein, a malaria vaccine researcher at Radboud University Nijmegen Medical Centre in the Netherlands.

Although researchers will gain valuable insights from the ongoing trials, "it shows we have to do better." Ultimately, RTS,S will likely be used in combination with other vaccine components in a second-generation vaccine, says malaria vaccine researcher Adrian Hill of the Jenner Institute at the University of Oxford in the United Kingdom. Sauerwein agrees. RTS,S "is definitely not a big tool, but it's a small tool," he says. "We can't afford to throw any tool away."

Adapted from ScienceNOW, the online daily news service of the journal Science. <http://news.sciencemag.org>



The vaccine has its limitations ... it shows we have to do better"

Robert Sauerwein, malaria researcher