New studies show malaria vaccine candidate advancing in Africa

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Results published online today in the *New England Journal of Medicine* revealed that the world's most clinically advanced malaria vaccine candidate provides both infants and young children with significant protection against malaria. Two separate phase II trials reaffirmed earlier study results and support the ongoing efforts, pending regulatory approvals, to launch the phase III study of GlaxoSmithKline (GSK) Biologicals' RTS,S/AS vaccine candidate across Africa.

In infants, data show for the first time that the vaccine candidate can be administered as part of existing African national immunization programs. In children aged 5 to 17 months, the candidate RTS,S/AS01 reduced the risk of clinical episodes of malaria by 53 percent over an eight-month follow-up period and was shown to have a promising safety profile. The studies were conducted in Kenya and Tanzania and were presented today at the American Society for Tropical Medicine and Hygiene (ASTMH) annual meeting.

RTS,S/AS is the leading candidate in a global effort coordinated by the PATH Malaria Vaccine Initiative (MVI) to develop a malaria vaccine. Malaria kills almost one million people each year—most of them infants and young children in Africa, the intended recipients for this vaccine candidate.

"Today's study results strongly show that our investments in developing malaria vaccines are beginning to pay dividends," said Christian Loucq, MVI director. "We are closer than ever before to developing a malaria vaccine for children in Africa. History has shown that vaccines are the most powerful tool to control and eliminate infectious diseases. Clearly, the world urgently needs a safe and effective vaccine to win the war against this terrible disease."

The studies published today build on previous findings indicating the efficacy of RTS,S/AS, including a phase 2 trial, published in The Lancet in 2007, that demonstrated "proof of concept" that RTS,S/AS could prevent malaria infection in infants.

"The vaccine works alongside standard infant vaccines of WHO's Expanded Program of Immunization (EPI), has a favorable safety profile, and has consistently shown a significant efficacy level. We can begin to foresee the difference this scientific breakthrough could make in the lives of millions of African children who suffer and die from this disease year after year," said Joe Cohen, a co-inventor of the vaccine and vice-president of Research & Development, Emerging Diseases & HIV at GSK Biologicals. "The energy and motivation levels are at an all-time high, as the partnership finalizes preparations to launch the historic phase III trial early next year."

Infant Study: Effective co-administration with EPI Vaccines

The infant study enrolled 340 infants under 12 months of age in Tanzania and found that RTS,S/AS02, when administered at 8, 12, and 16 weeks of age with a commonly used childhood vaccine, did not interfere with the protective immune responses to each of the vaccine components. The childhood vaccine contained antigens for Diphtheria (D), Tetanus (T), whole-cell pertussis (Pw) and haemophilus influenzae B (Hib). In countries where a malaria vaccine is needed most, the current immunization schedule for infants, called the WHO Expanded Program on Immunization (EPI), would provide an optimal delivery platform.

Researchers evaluated the safety and immune responses when administering the RTS,S/AS02 vaccine in conjunction with an EPI schedule. It was a randomized double-blind trial with participants simultaneously receiving either RTS,S/AS02 and

DTP w/Hib as well as oral polio vaccine; or a hepatitis B vaccine and DTP w/Hib as well as oral polio vaccine.

Additionally, the study reported 65 percent reduction against first infection from malaria in those infants who received three doses of the RTS,S/AS02 vaccine and were followed over a six-month period. This study builds upon results published in October 2007 in The Lancet, which found a similar level of efficacy for RTS,S/AS02 when it was given in a staggered fashion with the administration of DTPw/Hib vaccine.

"This finding has a very strong implication for protecting infants: RTS,S/AS efficacy data are very encouraging when administered alongside the childhood vaccines now widely in use and those vaccines maintain their desired efficacy alongside RTS,S," said Salim Abdulla of the Ifakara Health Institute of the Tanzanian Ministry of Health. Abdulla led a team that included researchers from the Swiss Tropical Institute and the London School of Hygiene and Tropical Medicine, GSK Biologicals, and MVI.

Child study: 53% efficacy against clinical malaria in children

The other trial enrolled 894 children 5-17 months old in both Kenya and Tanzania. It was designed to evaluate the safety and efficacy of the RTS,S/AS, combined with another GSK's proprietary Adjuvant System, coded AS01. The study was a double-blind randomized clinical trial in which children received either three doses of the RTS,S/AS01 vaccine candidate or a rabies vaccine.

It found that the RTS,S/AS01 formulation reduces clinical malaria episodes by 53 percent for up to an average of eight months. Earlier studies in Mozambique using RTS,S formulated with a different GSK Adjuvant System (AS02) demonstrated 35 percent efficacy against clinical disease for 18 months among children 1? years old. Researchers concluded that these study results support the use of RTS,S/AS01 for upcoming Phase 3 trials.

"These findings build a solid case for phase III testing, which the partners in this endeavor are looking forward to starting in the near future,"said Philip Bejon of Kenya Medical Research Institute (KEMRI)-Wellcome Collaborative Research Programme and the Centre for Tropical Medicine, University of Oxford, the study's lead author.

The team for the efficacy trial of RTS,S/AS01 in young children comprised researchers from the KEMRI-Wellcome Collaborative Research Programme (Kilifi, Kenya), the National Institute for Medical Research (Tanzania), the Joint Malaria Programme (Korogwe, Tanzania), and other institutions in collaboration with GSK and the MVI.

References:

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2. Bejon P, Lusingu J, Olotu A, et al. Efficacy of RTS,S/AS01E: clinical malaria in 5 to 17 month old children. N Engl J Med 2008;359:

Source: PATH Malaria Vaccine Initiative