Investigational malaria vaccine found safe and protective

August 8 2013

An investigational malaria vaccine has been found to be safe, to generate an immune system response, and to offer protection against malaria infection in healthy adults, according to the results of an early-stage clinical trial published Aug. 8 in the journal *Science*.

The vaccine, known as PfSPZ Vaccine, was developed by scientists at Sanaria Inc., of Rockville, Md. The clinical evaluation was conducted by researchers at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, and their collaborators at the Walter Reed Army Institute of Research and the Naval Medical Research Center, both in Silver Spring, Md.

Malaria is transmitted to humans by the bite of an infected mosquito. After the bite occurs, infectious malaria parasites in the immature, sporozoite stage of their life cycle first travel to the liver, where they multiply, and then spread through the bloodstream, at which time symptoms develop.

The PfSPZ Vaccine is composed of live but weakened sporozoites of the species *Plasmodium falciparum*, the most deadly of the malaria-causing parasites.

"The global burden of malaria is extraordinary and unacceptable," said NIAID Director Anthony S. Fauci, M.D. "Scientists and health care providers have made significant gains in characterizing, treating and preventing malaria; however, a vaccine has remained an elusive goal. We

are encouraged by this important step forward."

The Phase I trial, which took place at the NIH Clinical Center in Bethesda, received informed consent from and enrolled 57 healthy adult volunteers ages 18 to 45 years who never had malaria. Of these, 40 participants received the vaccine and 17 did not. To evaluate the vaccine's safety, vaccinees were split into groups receiving two to six intravenous doses of PfSPZ Vaccine at increasing dosages. After vaccination, participants were monitored closely for seven days. No severe adverse effects associated with the vaccine occurred, and no malaria infections related to vaccination were observed.

Based on blood measurements, researchers found that participants who received a higher total dosage of PfSPZ Vaccine generated more antibodies against malaria and more T cells—a type of immune system cell—specific to the vaccine.

To evaluate whether and how well the PfSPZ Vaccine prevented malaria infection, each participant—the vaccinees as well as the control group that did not receive vaccine—was exposed to bites by five mosquitoes carrying the *P. falciparum* strain from which the PfSPZ Vaccine was derived. This controlled human malaria infection procedure—a standard process in malaria vaccine trials—took place three weeks after participants received their final vaccination. Participants were monitored as outpatients for seven days and then admitted to the NIH Clinical Center, where they stayed until they were diagnosed with malaria, treated with anti-malarial drugs and cured of infection, or shown to be free of infection.

The researchers found that the higher dosages of PfSPZ Vaccine were associated with protection against malaria infection. Only three of the 15 participants who received higher dosages of the vaccine became infected, compared to 16 of 17 participants in the lower dosage group

who became infected. Among the 12 participants who received no vaccine, 11 participants became infected after mosquito challenge.

"In this trial, we showed in principle that sporozoites can be developed into a malaria vaccine that confers high levels of protection and is made using the good manufacturing practices that are required for vaccine licensure ," said Robert A. Seder, M.D., chief of the Cellular Immunology Section of the NIAID Vaccine Research Center and principal investigator of the trial.

An important challenge in the continued development of PfSPZ Vaccine is that the vaccine currently is administered intravenously—a rare delivery route for vaccines. Previous studies at lower doses have shown that the more common intradermal (into the skin) and subcutaneous (under the skin) routes did not yield as strong an immune response as the intravenous route.

"Despite this challenge, these trial results are a promising first step in generating high-level protection against malaria, and they allow for future studies to optimize the dose, schedule and delivery route of the candidate vaccine," said Dr. Seder.

A number of follow-up studies are planned, including research to evaluate the vaccine's different dose schedules, possible protection against other *Plasmodium* strains and the durability of protection. The researchers may also evaluate whether higher doses administered subcutaneously or intradermally provide the same level of protection as that found in this study.

More information: Seder et al. Protection against malaria by intravenous immunization with a non-replicating sporozoite vaccine. *Science Express*. DOI: 10.1126/science.1241800 (2013).