Malaria vaccine candidate, RTS,S reduces the risk of malaria by half in African children

October 18 2011

First results from a large-scale Phase III trial of RTS,S*, published online today in the *New England Journal of Medicine* (NEJM), show the malaria vaccine candidate to provide young African children with significant protection against clinical and severe malaria with an acceptable safety and tolerability profile. The results were announced today at the Malaria Forum hosted by the Bill & Melinda Gates Foundation in Seattle, Washington.

Half the world's population is at risk of malaria. The disease is responsible for close to 800,000 deaths each year, most of whom are children under five in sub-Saharan Africa

5 to 17 month-old children

The trial, conducted at 11 trial sites in seven countries across sub-Saharan Africa, including a UNC-led site in Lilongwe, Malawi, showed that three doses of RTS,S reduced the risk of children experiencing clinical malaria and severe malaria by 56 percent and 47 percent, respectively. This analysis was performed on data from the first 6,000 children aged 5 to 17 months, over a 12-month period following vaccination. Clinical malaria results in high fevers and chills. It can rapidly develop into severe malaria, typified by serious effects on the blood, brain, or kidneys that can prove fatal. These first Phase III results are in line with those from previous Phase II studies.

The widespread coverage of insecticide-treated bed nets (75 percent) in this study indicated that RTS,S can provide protection in addition to that already offered by existing malaria control interventions.

6 to 12 week-old infants

The trial is ongoing and efficacy and safety results in 6 to 12 week-old infants are expected by the end of 2012. These data will provide an understanding of the efficacy profile of the RTS,S malaria vaccine candidate in this age group, for both clinical and severe malaria.

Combined data in 6 to 12 week-old infants and 5 to 17 month-old children

An analysis of severe malaria episodes so far reported in all 15,460 infants and children enrolled in the trial at 6 weeks to 17 months of age has been performed. This analysis showed 35 percent efficacy over a follow-up period ranging between 0 and 22 months (average 11.5 months).

"The publication of the first results in children aged 5 to 17 months marks an important milestone in the development of RTS,S," said Irving Hoffman, PA, MPH, co-principal investigator at the Lilongwe site. "These results confirm findings from previous Phase II studies and support ongoing efforts to advance the development of this malaria vaccine candidate," said Hoffman, who is also associate professor of medicine in the UNC School of Medicine.

Long-term efficacy

The RTS,S malaria vaccine candidate is still under development. Further information about the longer-term protective effects of the vaccine, 30

months after the third dose, should be available by the end of 2014. This will provide evidence for national public health and regulatory authorities, as well as international public health organizations, to evaluate the benefits and risks of RTS,S.

Safety

The overall incidence of serious adverse events (SAEs)** in this trial was comparable between the RTS,S candidate vaccine (18 percent) recipients and those receiving a control vaccine (22 percent)

Differences in rates of SAEs were observed between the vaccines groups for specific events, such as seizures and meningitis, and were higher in the malaria vaccine group. Seizures were considered to be related to fever and meningitis was considered unlikely to be vaccine-related. These events will continue to be monitored and additional information about the safety profile of the RTS,S malaria vaccine candidate will become available over the next three years.

"Making progress against this disease has been extremely difficult, and sadly, many have resigned themselves to malaria being a fact of life in Africa. This need not be the case," said Francis Martinson, MPH, PhD, co-principal investigator in Lilongwe and country director of UNC Project-Malawi. "Renewed interest in malaria by the international community, and scientific evidence such as that we are reporting today, should bring new hope that malaria can be controlled."

More information: The article appears online now at www.nejm.org/doi/full/10.1056/NEJMoa1102287

*RTS,S contains QS-21 Stimulon® adjuvant licensed from Antigenics Inc, a wholly owned subsidiary of Agenus Inc. (NASDAQ: AGEN), MPL and liposomes.

**A serious adverse event refers to any medical event that occurs during the course of a clinical trial and that results in death, is life threatening, requires inpatient hospitalization, or results in a persistent or significant disability or incapacity needs, regardless of whether the SAE is considered to be caused by the study vaccination. All SAEs are reported to regulatory authorities.

Provided by University of North Carolina School of Medicine