Malaria vaccine a letdown for infants (Update)

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Two children stricken down with malaria rest at the local hospital in the small village of Walikale, Congo, in this Sunday, Sept. 19, 2010 file photo. Malaria is spread by mosquitoes and kills more than 650,000 people every year, mostly young children and pregnant women in Africa. An experimental malaria vaccine developed by GlaxoSmithKline and the PATH Malaria Vaccine Initiative, helped develop a new experimental malaria vaccine which was thought promising but is now turning out to be a disappointment, with a new study showing it is only about 30 percent effective at protecting infants from the killer disease according to results released in South Africa Friday Nov. 9, 2012. (AP Photo/Schalk van Zuydam, file)

An experimental malaria vaccine once thought promising is turning out to be a disappointment, with a new study showing it is only about 30 percent effective at protecting infants from the killer disease.

That is a significant drop from a study last year done in slightly older children, which suggested the vaccine cut the malaria risk by about half—though that is still far below the protection provided from most vaccines. According to details released on Friday, the three-shot regimen reduced malaria cases by about 30 percent in infants aged 6 to 12 weeks, the target age for immunization.

Dr. Jennifer Cohn, a medical coordinator at Doctors Without Borders, described the vaccine's protection levels as "unacceptably low." She was not linked to the study.

Scientists have been working for decades to develop a malaria vaccine, a complicated endeavor since the disease is caused by five different species of parasites. There has never been an effective vaccine against a parasite. Worldwide, there are several dozen malaria vaccine candidates being researched.

In 2006, a group of experts led by the World Health Organization said a malaria vaccine should cut the risk of severe disease and death by at least half and should last longer than one year. Malaria is spread by mosquitoes and kills more than 650,000 people every year, mostly young children and pregnant women in Africa. Without a vaccine, officials have focused on distributing insecticide-treated bed nets, spraying homes with pesticides and ensuring access to good medicines.

In the new study, scientists found babies who got three doses of the vaccine had about 30 percent fewer cases of malaria than those who didn't get immunized. The research included more than 6,500 infants in Africa. Experts also found the vaccine reduced the amount of severe

malaria by about 26 percent, up to 14 months after the babies were immunized.

Scientists said they needed to analyze the data further to understand why the vaccine may be working differently in different regions. For example, babies born in areas with high levels of malaria might inherit some antibodies from their mothers which could interfere with any vaccination.

"Maybe we should be thinking of a first-generation vaccine that is targeted only for certain children," said Dr. Salim Abdulla of the Ifakara Health Institute in Tanzania, one of the study investigators.

Results were presented at a conference in South Africa on Friday and released online by the New England Journal of Medicine. The study is scheduled to continue until 2014 and is being paid for by GlaxoSmithKline and the PATH Malaria Vaccine Initiative.

"The results look bad now, but they will probably be worse later," said Adrian Hill of Oxford University, who is developing a competing malaria vaccine. He noted the study showed the Glaxo vaccine lost its potency after several months. Hill said the vaccine might be a hard sell, compared to other vaccines like those for meningitis and pneumococcal disease—which are both effective and cheap.

"If it turns out to have a clear 30 percent efficacy, it is probably not worth it to implement this in Africa on a large scale," said Genton Blaise, a malaria expert at the Swiss Tropical and Public Health Institute in Basel, who also sits on a WHO advisory board.

Eleanor Riley of the London School of Hygiene and Tropical Medicine, said the vaccine might be useful if used together with other strategies, like bed nets. She was involved in an earlier study of the vaccine and had

hoped for better results. "We're all a bit frustrated that it has proven so hard to make a malaria vaccine," she said. "The question is how much money are the funders willing to keep throwing at it."

Glaxo first developed the vaccine in 1987 and has invested $300 million in it so far.

WHO said it couldn't comment on the incomplete results and would wait until the trial was finished before drawing any conclusions.

More information: RTS,S malaria candidate vaccine reduces malaria by approximately one-third in African infants

Results from a pivotal, large-scale Phase III trial, published online today in the *New England Journal of Medicine*, show that the RTS,S malaria vaccine candidate can help protect African infants against malaria. When compared to immunization with a control vaccine, infants (aged 6-12 weeks at first vaccination) vaccinated with RTS,S had one-third fewer episodes of both clinical and severe malaria and had similar reactions to the injection. In this trial, RTS,S demonstrated an acceptable safety and tolerability profile.

Eleven African research centres in seven African countries [1] are conducting this trial, together with GlaxoSmithKline (GSK) and the PATH Malaria Vaccine Initiative (MVI), with grant funding from the Bill & Melinda Gates Foundation to MVI.

Dr. Salim Abdulla, a principal investigator for the trial from the Ifakara Health Institute, Tanzania, said: "We've made significant progress in recent years in our battle against malaria, but the disease still kills 655,000 people a year—mainly children under five in sub-Saharan Africa. An effective malaria vaccine would be a welcome addition to our tool kit, and we've been working toward this goal with this RTS,S trial.

This study indicates that RTS,S can help to protect young babies against malaria. Importantly, we observed that it provided this protection in addition to the widespread use of bed nets by the trial participants."

Efficacy

When administered along with standard childhood vaccines,[2] the efficacy of RTS,S in infants aged 6 to 12 weeks (at first vaccination) against clinical and severe malaria was 31% and 37%,[3] respectively, over 12 months of follow-up after the third vaccine dose.[4] Insecticide-treated bed nets were used by 86% of the trial participants, which demonstrated that RTS,S provided protection beyond existing malaria control interventions. The efficacy observed with RTS,S last year in children aged 5-17 months of age against clinical and severe malaria was 56% and 47%, respectively. Follow-up in this Phase III trial will continue and is expected to provide more data for analyses to better understand the different findings between the age categories.

Dr. Abdulla added: "The efficacy is lower than what we saw last year with the older 5-17 month age category, which surprised some of us scientists at the African trial sites. It makes us even more eager to gather and analyze more data from the trial to determine what factors might influence efficacy against malaria and to better understand the potential of RTS,S in our battle against this devastating disease. We were also glad to see that the study indicated that RTS,S could be administered to young infants along with standard childhood vaccines and that side effects were similar to what we would see with those vaccines."

Safety

There was no increase in overall reporting of serious adverse events [5](SAEs) between the infants vaccinated with the RTS,S malaria

vaccine candidate and infants in the control group, which received a comparator vaccine. Side effects primarily included local injection site reactions, which were less frequent following RTS,S vaccinations compared to the DTP-HepB/Hib vaccine. Fever was reported more frequently following RTS,S vaccinations than the control vaccine group (30.6% versus 21.1% of vaccine doses, respectively).

Two new cases of meningitis were reported in the 6-12 week-old infant age category in addition to the 9 reported last year; one in the RTS,S group and one in the control vaccine group. Further analysis revealed a bacterial cause of the meningitis in 7 of the 11 cases.

Sir Andrew Witty, CEO, GSK said: "While the efficacy seen is lower than last year, we believe these results confirm that RTS,S can help provide African babies and young children with meaningful protection against malaria. They take us another important step forward on the journey towards having a new intervention available against this disease, which is a huge burden on the health and economic growth of Africa. We remain convinced that RTS,S has a role to play in tackling malaria and we will continue to work with our partners and other stakeholders to better understand the data and to define how the vaccine could best be used to provide public health benefit to children in malaria endemic areas in Africa."

David Kaslow, Director of the PATH Malaria Vaccine Initiative, said: "Determining the role of RTS,S in Africa will depend on analyses of additional data. We are now an important step closer to that day. Success in developing malaria vaccines depends on many factors: at the top of the list are partnerships and robust evidence, coupled with an understanding that different combinations of tools to fight malaria will be appropriate in different settings in malaria-endemic countries. My congratulations go out to the team at GSK and to the African research centres for their exemplary conduct of this trial."

"This is an important scientific milestone and needs more study," said Bill Gates, co-founder of the Bill & Melinda Gates Foundation. "The efficacy came back lower than we had hoped, but developing a vaccine against a parasite is a very hard thing to do. The trial is continuing and we look forward to getting more data to help determine whether and how to deploy this vaccine."

The vaccine is being developed in partnership by GSK and MVI, together with prominent African research centres[1]*. The collaborators are represented on the Clinical Trials Partnership Committee, which oversees the conduct of the trial. An extended team of organisations work on RTS,S, including scientists from across Africa, Europe, and North America. Major funding for clinical development of RTS,S comes from a grant by the Bill & Melinda Gates Foundation to MVI.

Looking ahead

Follow-up in this Phase III trial will continue to provide more data for analyses to better understand the different findings between the age categories. These data and analyses should also provide insights into the vaccine candidate's efficacy in different malaria parasite transmission settings. More data on the longer-term efficacy of the vaccine during 30 months of follow-up after the third dose, and the impact of a booster dose are expected to be publicly available at the end of 2014.

The data and analyses will inform the regulatory submission strategy and, if the required regulatory approvals are obtained and public health information, including safety and efficacy data from the Phase III programme, is deemed satisfactory, the World Health Organization (WHO) has indicated that a policy recommendation for the RTS,S malaria vaccine candidate is possible as early as 2015, paving the way for decisions by African nations regarding large-scale implementation of the vaccine through their national immunisation programmes. An

effective vaccine for use alongside other measures such as bed nets and anti-malarial medicines would represent a decisive advance in malaria control.

GSK and MVI are committed to making this vaccine available to those who need it most, should it be approved and recommended for use. In January 2010, GSK announced that the eventual price of RTS,S (also known as MosquirixTM) will cover the cost of manufacturing the vaccine together with a small return of around 5% that will be reinvested in research and development for second-generation malaria vaccines or vaccines against other neglected tropical diseases.

Source: Burness Communications