Malaria vaccine shows continued protection during 18 months of follow-up

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A vaccine previously shown to reduce malaria in young infants and children reduces larger numbers of malaria cases in areas of higher malaria transmission, according to results from an ongoing clinical trial published in *PLOS Medicine*. The effect of vaccination diminished over time, but protection against clinical malaria remained evident 18 months after vaccination.

In the new report, the RTS,S Clinical Trials Partnership* update estimates of vaccine efficacy (the reduction in the risk of malaria in participants who received the vaccine compared to those who received a comparator vaccine) and calculate the number of cases of malaria that the vaccine prevented in a phase 3, randomized, controlled clinical trial of the malaria vaccine RTS,S/AS01 given to young infants and children in Africa.

The study included 6,537 infants aged 6–12 weeks and 8,923 children aged 5–17 months who were randomly assigned to receive three doses of RTS,S/AS01 or comparator vaccine. During 18 months following vaccination, the researchers report vaccine efficacy of 45% [95% confidence interval (CI): 41%–49%, intention-to-treat analysis] in children age 5-17 months, and 27% vaccine efficiency [95% CI: 21%–33%, intention-to-treat analysis] in infants age 6-12 weeks. In both age groups, vaccine efficacy was highest in the first 6 months after vaccination. Across all 11 study sites, RTS,S/AS01 averted an average of 829 (range 37 to 2365) cases of clinical malaria per 1,000 children vaccinated, and 449 (Range -10 to 1402) cases in infants vaccinated,

over 18 months following vaccination.

Safety analyses found overall serious adverse events (SAE) to occur less often in children age 5-17 months who received the vaccine [18.6% (95% confidence interval 17.6%–19.6%), compared with 22.7% (95% CI 21.2%–24.3%) in children who received a comparator vaccine]. In infants age 6-12 weeks overall SAE were not found to differ significantly with immunization. As noted in earlier reports, more meningitis cases were reported as SAE in participants who received the malaria vaccine than in those who received a comparator immunization (16 cases among the 5,949 children in the RTS,S/AS01 vaccine group and one case among the 2,974 children in the control group; and nine cases among 4,358 young infants in the RTS,S/AS01 group and three among 2,179 young infants in the control group) and no causal relationship to the vaccine has been established.

Going forward the study will analyze further efficacy and safety results following administration of a booster immunization given to study participants just after the time period analyzed in the current report. The authors note that "Translated to the population at risk of malaria, reductions in clinical cases on this scale as a result of vaccination with RTS,S/AS01 would have a major public health impact."

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