High efficacy and good safety profile for the R21/Matrix-M malaria vaccine in African children

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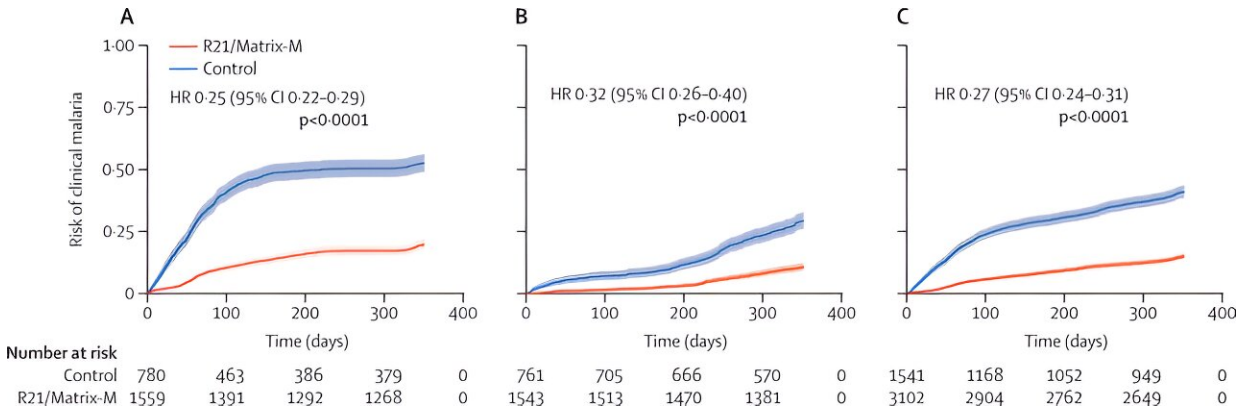

Kaplan-Meier estimates of the time to first episode of clinical malaria in the modified per-protocol population at seasonal sites (A), standard sites (B), and all sites (C). Credit: *The Lancet* (2024). DOI: 10.1016/S0140-6736(23)02511-4

Phase III trial results of the R21/Matrix-M vaccine developed by Oxford University and Serum Institute of India Pvt Ltd, leveraging Novavax's Matrix-M adjuvant, has confirmed high efficacy and supported regulatory approvals and licensure in several African countries.

The R21/Matrix-M vaccine was designed in 2011 as a potential improvement on the RTS, S/AS01 malaria vaccine designed in the 1980s. A Phase II trial in Burkina Faso, reporting in 2021, was the first

to show that R21/Matrix-M could reach the WHO-specified target of 75% efficacy in African children.

Recent WHO endorsement will lead to the initial rollout of R21/Matrix-M in the coming months. The new results are published in *The Lancet*.

The trial investigators immunized over 4,800 young children in a trial in Burkina Faso, Kenya, Mali and Tanzania and found on average 78% vaccine efficacy over the first year of follow-up across all sites in the 5–17 month age group, the age range group which is studied for most malaria vaccines.

Efficacy over this period was broadly similar across sites and in different transmission settings. Safety data from the trial have been reassuring with no serious adverse events linked to immunization. No other vaccine has reported over 55% efficacy in the same age group.

A booster dose at a year maintained good efficacy over the following 6–12 months. The vaccine also reduced infection rates in children measured at 12 and 18 months after vaccination suggesting a potentially beneficial effect in reducing malaria transmission.

R21/Matrix-M vaccine was well tolerated, with injection site pain and fever as the most frequent adverse events. Number of adverse events of special interest and serious adverse events did not significantly differ between the vaccine groups. There were no treatment-related deaths.

Malaria is the largest cause of death in young African children with over 600,000 deaths globally each year. Two vaccines have recently achieved and completed World Health Organization (WHO) prequalification and initial deployments are starting early this year.

Professor Adrian Hill, chief investigator of the R21/Matrix-M Phase III

trial said "The continued high efficacy of this new vaccine in field trials is very encouraging, and consistent with the high efficacy and excellent durability observed in a smaller four-year Phase IIb trial. These data support an important role for the unique high-density nanoparticle display of the conserved repeat region of the malaria parasite circumsporozoite protein, a feature in the design of the R21 vaccine, in providing such high vaccine efficacy and, thereby, an important new tool for malaria control."

Significantly increased immune responses to the R21/Matrix-M vaccine and slightly higher vaccine efficacy were observed in 5- to 17-month-olds compared to 18- to 36-month-olds malaria vaccines, supporting planned vaccine deployment initially from 5 months of age in young African children.

The vaccine is licensed to the Serum Institute of India (SII), the world's largest vaccine manufacturer and a long-term partner of the University of Oxford. This is critical because vaccinating those at high risk of malaria will be important in stemming the spread of the disease, as well as protecting the vaccinated. Matrix-M adjuvant is manufactured by Novavax AB and provided to Serum Institute of India for formulation into the final vaccine drug product.

Adar Poonawalla, CEO, Serum Institute of India, said, "*The Lancet* study on R21/Matrix-M Phase III trials mark a significant advancement in our battle against this global threat. Our collaboration with the University of Oxford has been instrumental in developing the R21/Matrix-M malaria vaccine. We are dedicated to making this vaccine available, especially in Africa, where malaria poses a substantial threat to millions of lives, bringing us closer to a malaria-free world."

Professor Alassane Dicko, Principal Investigator in Mali of the R21/Matrix-M vaccine said "It has been very exciting to generate high

efficacy data with the new R21/Matrix-M vaccine so quickly. I predict that this vaccine should be very impactful in preventing malaria deaths in African children."

John C Jacobs, CEO of Novavax commented "Approximately 1,300 children die from malaria every day, a staggering statistic for a preventable disease. The R21/Matrix-M Phase III efficacy data published in *The Lancet* reinforce the potential of R21/Matrix-M vaccine to protect children against this disease."

"We are proud of the role of Novavax's patented saponin-based Matrix-M adjuvant, which has been demonstrated to enhance the immune response, in the outcome of this clinical trial and are eager to see the realized impact of the vaccine when it is rolled out globally."

More information: Mehreen S Datoo et al, Safety and efficacy of malaria vaccine candidate R21/Matrix-M in African children: a multicentre, double-blind, randomised, phase 3 trial, *The Lancet* (2024). DOI: 10.1016/S0140-6736(23)02511-4

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