Malaria vaccine candidate has demonstrated efficacy over 3-4 years of follow-up

Final results from Phase III trial suggest substantial public health benefits could be provided by the RTS,S malaria vaccine candidate in endemic regions in sub-Saharan Africa

Barcelona, 24 April 2015-. Final results from a large-scale Phase III trial of the RTS,S malaria vaccine candidate, including the impact of a booster dose, published today in The Lancet, show that the vaccine candidate helped protect children and infants from clinical malaria for at least three years after first vaccination.

The latest results demonstrated that vaccination with RTS,S, followed by a booster dose of RTS,S administered 18 months after the primary schedule, reduced the number of cases of clinical malaria in children (aged 5-17 months at first vaccination) by 36% to the end of the study[1] (over an average follow-up of 48 months across trial sites) and in infants (aged 6-12 weeks at first vaccination) by 26% to the end of the study (over an average follow-up of 38 months across trial sites). Efficacy decreased over time in both age groups. Without the booster dose, the 3-dose primary schedule reduced clinical malaria cases by 28% in children and 18% in infants to the study end. The efficacy of RTS,S was evaluated in the context of existing malaria control measures, such as insecticide treated bed nets, which were used by approximately 80% of the children and infants in the trial.

For children in the 5-17 month age category who received a booster dose 18 months after the primary schedule, an average of 1,774 cases of clinical malaria were prevented for every 1,000 children vaccinated across the trial sites, over an average of 48 months of follow-up. For infants aged 6-12 weeks at first vaccination with RTS,S, who received a booster dose, 983 cases of clinical malaria, on average, were prevented for every 1,000 infants vaccinated across trial sites over an average of 38 months of follow-up. More cases were averted in areas of higher malaria transmission. In the absence of a booster dose, 1,363 cases of clinical malaria were prevented, on average, for every 1,000 children aged 5-17 months at first vaccination and 558 cases for every 1,000 infants aged 6-12 weeks at first vaccination to the end of the study.

Statistically significant efficacy against severe malaria to the end of the study period was observed only in children who received the booster dose. There was indication of increased risk for severe malaria in children who did not receive the booster dose, compared to those in the control group.

Eleven research centres in seven African countries[2] conducted the efficacy and safety trial, in partnership with GSK and the PATH Malaria Vaccine Initiative (MVI), with grant funding from the Bill & Melinda Gates Foundation to MVI. The trial, started in March 2009 and concluded in January 2014, enrolled 15,459 participants, in two age categories: children (aged 5-17 months at first vaccination) and infants (aged 6-12 weeks at first vaccination).

Safety

RTS,S continued to display an acceptable safety and tolerability profile during the entire study period. The incidence of fever in the week after vaccination was higher in children who received RTS,S than in those receiving control vaccine. In some children who experienced

fever, the febrile reaction was accompanied by generalized convulsions, but all those affected fully recovered within seven days.

The meningitis signal previously reported remains in the older age category, including two cases reported after the booster dose of RTS,S. This could be a chance finding, as comparisons were made across groups for many different diseases, and because some of these cases happened years after vaccination without any obvious relationship to vaccination. The occurrence of meningitis will be followed closely during Phase IV studies, if RTS,S is licensed.

Dr Kwaku Poku Asante, a principal investigator in the trial and chairperson of the RTS,S Clinical Trials Partnership Committee said "We finally have in our sights a candidate vaccine that could have a real impact on this terrible disease that affects many children during their first years of life. The large number of children affected by malaria, sometimes several times per year, means that this vaccine candidate, if deployed correctly, has the potential to prevent millions of cases of malaria. On behalf of the African scientists and research centers that worked on the RTS,S trial, we give thanks to our national health authorities, and to the trial participants, for enabling us to reach this important milestone."

Dr Moncef Slaoui, Chairman Global Vaccines at GSK, said: "We are extremely encouraged that the results point to continued and significant public health benefit for those children whose lives are so disrupted by this awful disease. We might reasonably now expect that the impact of this vaccine candidate when used with existing interventions will allow more children to survive the early years which we know is the most dangerous time to be infected with malaria. We are working hard to submit the necessary evidence to regulatory authorities and the World Health Organisation so that they can take an informed decision on whether the RTS,S vaccine candidate should be made available as an additional tool for malaria prevention."

Dr David C. Kaslow, Vice President of Product Development at PATH, said: "Credit for reaching this scientific milestone goes to the thousands of African families and hundreds of scientists, clinicians, and health professionals who have made a commitment for many years to this vaccine trial. The public-private partnership behind RTS,S has successfully collected pivotal human efficacy and safety data that regulators and policymakers can now use to decide on its use. While eradication is the ultimate goal, malaria has yet to be eliminated or even fully controlled in many parts of the world; these data suggest that malaria vaccines can help us take some critical steps along that path."

Next steps

The European Medicines Agency (EMA) is currently reviewing the regulatory application for RTS,S through the Art. 58 procedure initiated in July 2014.

A positive opinion from the EMA's Committee for Medicinal Products for Human Use, together with a potential policy recommendation from the World Health Organisation (anticipated by the end of 2015), would be the basis for licensure applications to National Regulatory Authorities in sub-Saharan African countries. If positive, these regulatory decisions would help pave the way for the introduction of RTS,S through African national immunisation programmes. If RTS,S is approved, GSK has committed to making the vaccine available at a not-for-profit price.

ISGlobal is the result of an innovative partnership between academic, government and philanthropic institutions that was set up to further the work undertaken by the international community to meet the challenges posed by health in a globalised world. It forms the nexus of a hub of excellence dedicated to research, training and medical care that originated through an initiative of the Hospital Clínic and the University of Barcelona and is

now building on those beginnings to expand its capabilities. The goal of ISGlobal's current portfolio of projects is to reduce the health inequities that affect may different populations all over the world.

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The PATH Malaria Vaccine Initiative (MVI) is a global program established at PATH through an initial grant from the Bill & Melinda Gates Foundation. MVI's mission is to accelerate the development of malaria vaccines and catalyze timely access in endemic countries. MVI's vision is a world free from malaria. For more information, please visit www.malariavaccine.org.

[1]Intention to Treat (ITT) analysis, for this statistical reference and those that follow
[2] Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique, and Tanzania

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References

1Intention to Treat (ITT) analysis, for this statistical reference and those that follow
2 Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique, and Tanzania