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SHORT COMMUNICATION

Advancing Vaccine Strategies for Combatting Placental Malaria: A Path to Effective Implementation

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Pregnant women are particularly vulnerable to malaria infection, especially during their first and second pregnancy, despite pre-existing immunity to malaria acquired during childhood. When the parasite-infected red blood cells sequester in the intervillous spaces of the placenta, it leads to various adverse pregnancy outcomes such as maternal anaemia, hypertensive disorders in pregnancy, premature delivery, and infant low birth weight (LBW), which are associated with a higher risk of maternal and foetal/neonate mortality. Anaemia, undernutrition, and HIV infection increase the risk of malaria-associated adverse pregnancy outcomes. The World Health Organisation (WHO) estimates that in 2022, there were approximately 35.4 million pregnancies in the WHO African region of which 36% were exposed to malaria infection, with an estimated 393,000 neonates with low birthweight as a result [1].

The current three-pronged strategy recommended by WHO to protect pregnant women from malaria includes: intermittent preventive treatment (IPTp) with sulphadoxine-pyrimethamine (SP), insecticide treated nets (ITNs) and case management of febrile illness and anaemia. However, the current approaches are becoming less effective due to the emergence of widespread resistance of both mosquitoes to insecticides and of parasites to anti-malarial drugs. This highlights the critical need for new therapies and prevention strategies to protect both the health of the mother and her unborn child during pregnancy, particularly in the first trimester where the effects of malaria initiate a pathological trajectory with high likelihood of adverse outcomes for both the mother and her unborn baby. A safe, effective, and affordable placental malaria vaccine would successfully complement the current strategies, especially with the gaps for prevention in the first trimester and support global efforts to eradicate malaria.

Two placental malaria vaccine candidates, PRIMVAC and PAMVAC [2,3], are currently under development. These two vaccine candidates are derived from the VAR2CSA protein which is expressed on the surface of *P. falciparum*-infected erythrocytes (PEs) during pregnancy and mediates PEs' adhesion to the placental receptor chondroitin sulfate

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A (CSA) [4]. PRIMVAC and PAMVAC aim at generating inhibitory antibodies able to recognise VAR2CSA on the surface of infected erythrocytes and to block their interactions with the placental CSA ligand. Indeed, the capacity of anti-VAR2CSA antibodies to block the adhesion of PEs to CSA is thought to play a major role in protection [5], although other antibody-dependent effector mechanisms, such as opsonic phagocytosis, could also actively participate in parasite clearance.

Both vaccine candidates were previously tested in phase 1 clinical trials in Europe and Africa demonstrating that they are safe, well-tolerated and induce good immune response [4,5]. Building on these promising results, further activities are ongoing to further advance their clinical development and demonstrate efficacy in the target population.

In addition to evidence of the intervention's efficacy under trial conditions, evidence of the intervention's sustainability through cost analysis of expected averted adverse events and the general perceptions of benefit and risk by end users and health care providers are necessary for the successful uptake and policy implementation of effective new interventions. For this, EVI and the Malawi University of Science and Technology (MUST) are conducting a pilot study in Malawi on

Modelling Cost-Effectiveness, Acceptability and Feasibility of Vaccines against Placental Malaria

This study will combine the development of a cost-effective model for placental malaria vaccines together with ethnographic research to assess the acceptability and feasibility of implementing PM vaccines to prevent negative outcomes related to malaria during pregnancy.

The economic evaluation will assess,

1. The cost per unit of providing placental malaria vaccines at the health facility level.
2. The incremental cost-effectiveness ratio of placental malaria vaccines per disability-adjusted life year (DALY) averted.
3. The projected costs of scaling up the implementation of placental malaria vaccines as an intervention at the regional or national level.

The ethnographic research aims to investigate the perceptions, perspectives and beliefs of those at the receiving end, women of reproductive age, and of health care providers to better understand how placental malaria vaccination may align or conflict with traditional and cultural notions, and practices related to pregnancy and vaccination in rural and urban Malawi. A secondary focus of the study is to examine the collaboration between modern healthcare providers and traditional leaders and to seek community engagement that can help implement PM vaccines into existing healthcare practices, especially in rural areas where biomedical healthcare facilities are more difficult to access.

The recommendations of this study should guide policy makers in the further development of cost-effective strategies, policies and patient centred advocacy campaigns for vaccine acceptance and feasibility of placental malaria vaccines.

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