European Vaccine Initiative (EVI)

Advancing the clinical development of placental malaria vaccines

Placental malaria - a serious threat to the health of pregnant women and their babies

Since recent years, malaria cases have been on the rise after a period of decline. In 2022 alone, 249 million cases were reported worldwide. This number resulted in an estimated 608,000 deaths attributed to malaria. Pregnant women are particularly vulnerable to malaria, as infection during pregnancy can lead to placental malaria, posing risks to both maternal and foetal health. This condition contributes to adverse outcomes such as anaemia and hypertension in expectant mothers, premature delivery, and infant low birth weight (LBW). These outcomes are associated with a higher risk of maternal and foetal/neonate mortality. The World Health Organisation (WHO) estimates that in 2022, there were approximately 35.4 million pregnancies in the WHO African region. Thirty-six percent of those pregnancies were exposed to malaria infection, with an estimated 393,000 neonates with low birthweight as a result (WHO malaria report 2022)[1].

Existing malaria control strategies during pregnancy primarily involve the use of long-lasting insecticidal bed nets and intermittent preventive treatment with sulphadoxine-pyrimethamine (IPT-SP). However, the efficacy of these methods is compromised by the emergence of insecticide-resistant Anopheles mosquitoes and drug-resistant malaria parasites. Therefore, additional prophylactic measures, such as placental malaria vaccines, are urgently needed to mitigate the morbidity and mortality associated with placental malaria for both mothers and newborns.

Two different approaches to combat placental malaria

European Vaccine Initiative (EVI) has established a portfolio of promising placental malaria vaccine candidates. Under PDP IV, EVI will further advance and accelerate the development and clinical testing of the two most advanced vaccine candidates, R21 adjuvanted with Matrix-M1 (R21/MM) and PRIMVAC. Leveraging the success of a malaria vaccine that has demonstrated efficacy in African children, the R21/MM vaccine will undergo extensive safety and efficacy testing in the Republic of Mali. This trial aims to generate sufficient data to support the extended use of R21/MM in healthy women of childbearing potential.

Another approach to combat placental malaria involves a targeted, disease-specific vaccination strategy. In this case, the aim is to induce antibody responses that prevent massive sequestration of parasites in the placenta of pregnant women. This way, the health of both the mother and her foetus or newborn is protected. Based on Phase I clinical trial data, PRIMVAC has been identified as the most promising vaccine candidate for targeting placental malaria. To advance its development, a comprehensive multi-site clinical efficacy trial will be conducted in endemic populations in Burkina Faso and Benin.

In addition to the development and testing of these two vaccine candidates, novel vaccine candidates from emerging vaccine technologies will be evaluated. This line of research aims to test novel approaches for improving the vaccine-induced immune responses and their protective efficacy.

[1] *WHO World Malaria Report 2023, ISBN: 978 92 4 006489 8*

These 2nd generation candidates will be tested and compared for safety and immunogenicity and prioritised for early clinical testing (phase Ia/b trial). EVI's long-term overarching objective is to contribute to developing a safe, effective and affordable vaccine for placental malaria available withing the next decade.

Integrated into these research activities, EVI will carry out capacity strengthening, and advocacy activities aimed at enhancing clinical research capacities in sub-Saharan Africa, fostering North-South collaborations and supporting further implementation strategies for a PM vaccine in the endemic countries.

Partners

EVI works with partners across the world to achieve its mission. Primary partners in the activities are:

Phase IIb efficacy trials for R21/MM:
- Malaria Research & Training Center (MRTC), Mali;
- University of Oxford (UOXF), United Kingdom;
- Serum Institute of India Private Limited (SIIPL), India.

Phase II efficacy trial for PRIMVAC and activities for other (2nd generation) placental malaria vaccines:
- Fondation pour la Recherche Scientifique (FORS), Benin;
- Groupe de Recherche Action en Santé (GRAS), Burkina Faso;
- Radboud University Medical Center (RUMC), The Netherlands;
- Institut National de la santé et de la recherche médicale (Inserm), France; and
- University of Copenhagen (UCPH), Denmark.

Focus on health needs of women and girls

By developing specific vaccines for placental malaria and extending the use of malaria vaccines recommended for children to women of childbearing age, EVI seeks to address specific health needs of women and girls. These efforts thus prioritise gender considerations, for instance by ensuring representation of women in community engagement activities for clinical trials. Moreover, during implementation and roll-out of the vaccines, equitable access to public health services is also a priority. By advancing the development of malaria vaccines specifically designed to protect women and their babies from placental malaria and ensuring their accessibility, EVI is directly advancing gender equality and reducing health disparities.

Equitable access

To ensure affordability and accessibility of the vaccines to the target group, adequate and relevant product characteristics for use in Low- and Middle-Income Countries (LMICs) are taken into account at EVI from the outset of product development. For in-country distribution of any vaccine supported by EVI, EVI strives to collaborate with established entities, including international vaccine procurers such as GAVI and UNICEF, local distributors like national ministries of health, as well as vaccine manufacturers based in LMICs. Furthermore, EVI operates under the guiding principle of equitable access, meaning that products are first made available to populations most in need and ensuring prices are affordable to the populations in LMICs.

Budget

Cost of activities:	€27,547,700
Contribution by the Netherlands Ministry of Foreign Affairs (PDP IV Fund):	€17,247,700

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Product Development Partnerships IV Fund - PDP IV

The Product Development Partnerships IV Fund (PDP IV) promotes the development and accessibility of healthcare products. Specifically, PDP IV targets diseases and conditions related to poverty and sexual and reproductive health and rights (SRHR). The fund focuses on the development and availability of more effective, safe, affordable, and demand-driven medicines, vaccines, diagnostics, and other products. Women and girls between the reproductive ages of 15 to 49 in Low-Income Countries (LICs) and Middle-Income Countries (MICs) are the main target group.

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We encourage Dutch companies and organisations to cooperate and share knowledge with companies, organisations and governments in developing countries. We focus on themes like food security, water security, renewable energy, private sector development and responsible and sustainable international value chains. In doing so, we always pay attention to gender equality, climate and responsible business conduct (RBC). To help solve social issues in developing countries, we identify the local context and needs.
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