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## **PRESS RELEASE**

# **Africa-Europe partnership to launch historic Phase 3 clinical trial in early pregnancy**

*The trial will leverage clinical and social research to better serve women of reproductive age at risk of malaria*

- In a world first, a global consortium plans to undertake a Phase 3 clinical trial assessing antimalarial medicines in women in their first trimester of pregnancy
- The trial will evaluate the efficacy, safety, tolerability and cost-effectiveness of antimalarial drugs to treat uncomplicated malaria
- This pioneering approach challenges the *status quo* in which pregnant women are typically excluded from clinical trials and addresses a critical gap by focusing on an often-neglected group: women in their first trimester

**Kisumu, Kenya and Geneva, Switzerland 10 July 2024.** The **Safety of Antimalarials in the FIRst TRimEster (SAFIRE)** consortium, made up of scientific and social research experts in malaria in pregnancy, has today kicked off the preparation of a historic project: the first-ever Phase 3 clinical trial testing the efficacy and safety of antimalarials in women in their first trimester of pregnancy.

With financial support from the [Global Health EDCTP3 Joint Undertaking \(EDCTP3\)](#), a partnership funded by African and European countries as well as the European Union, and the Swiss [State Secretariat for Education, Research, and Innovation \(SERI\)](#), SAFIRE will generate robust evidence on the efficacy, safety and tolerability of antimalarials in the first trimester of pregnancy by conducting an [adaptive platform trial](#) and social research. Its results will feed into policy and guidelines to ensure that women have optimal treatment options in early pregnancy. The enrolment of women in the trial will start in 2025 pending data from the MiMba pregnancy registry and [PYRAPREG studies](#).

Dr Hellen Barsosio, one of the project’s scientific co-leads and a Research Scientist of maternal and newborn health at Kenya Medical Research Institute (KEMRI), said “We are thrilled to begin this first-of-its-kind trial. Pregnant women are typically excluded from clinical trials for fear of causing harm to the mother and the baby she is carrying. Determining which antimalarial medicines are efficacious and well tolerated in the first trimester will benefit all women of childbearing age, including those who may be unaware that they are pregnant, by enabling them to take these medicines without risk of causing harm to themselves or their unborn babies”.

Despite the [significant health risks associated with malaria in pregnancy](#) — such as miscarriage, stillbirth, preterm delivery and low birthweight, severe maternal anaemia, severe malaria and maternal mortality — women in their first trimester are left with few medicines for treatment (and

none for prevention). Artemisinin-based combination therapies (ACTs) [are the first-line malaria treatment recommended by WHO](#). However, there is only one ACT, artemether-lumefantrine (AL), [recommended for use as of 2022](#) to treat uncomplicated malaria in the first trimester. Although this is a major step forward towards achieving equity in malaria treatment choice — regardless of gender or pregnancy status — [emerging drug resistance](#) in several African countries is now a major concern.

One method of resistance mitigation is to [diversify the ACTs used](#) to treat malaria. However, this may result in inadvertently exposing women in their first trimester to drugs other than AL. To proactively address potential risks, the trial will initially evaluate two treatment arms: pyronaridine-artesunate (PA) with the widely used AL serving as the comparator.

PA is an ACT recommended by WHO to treat malaria in the general population. To date, preclinical data and clinical data generated for the medicine through ongoing [pregnancy registries](#) are reassuring for both mothers and their newborns.

## Protecting pregnant women through, not from, research

The SAFIRE consortium, formed to address the evidence gap in the use of antimalarial drugs in early pregnancy, is coordinated by the [Amsterdam University Medical Center](#), with scientific co-leadership by the [University of Sciences, Techniques and Technologies of Bamako \(USTTB\)](#) and [KEMRI](#). The Phase 3b clinical trial is co-sponsored by [Medicines for Malaria Venture \(MMV\)](#) and the [Liverpool School of Tropical Medicine \(LSTM\)](#), who will provide scientific technical input. It will be the first [Bayesian adaptive platform trial](#) that assesses the efficacy, safety and tolerability of antimalarial treatments in the first trimester of pregnancy, a significant step for global health research.

The data generated by SAFIRE; which will begin in Burkina Faso, Kenya and Mali; will support the design of future trials targeting other infectious diseases, especially those that affect pregnant women in low- and middle-income countries.

## Social sciences for disease elimination

In addition to scientific leadership, social and implementation research will play a key role in the trial: representatives from participating institutions will lead formative research as a first step to inform the final trial design and identify culturally appropriate identification, recruitment and retention of participants throughout the trial.

According to Maud Majeres Lugand, Associate Director of Social Research at MMV, “Engaging with the community to build trust, and understand possible recruitment barriers like cultural sensitivities as well as women’s concerns about taking medicines in early pregnancy, will be crucial for an ethical and successful enrolment of women in the clinical study”.

## Racing against the clock

In addition to achieving global goals for health and gender equity, there are financial incentives for eliminating malaria: it is [a substantial economic and social burden](#), incurring financial costs for

households, both directly in terms of seeking healthcare and indirectly by causing loss in productive economic activity, which in turn reduces economic growth. Identifying more effective means of preventing illness and death from maternal malaria can reduce the economic burden on households and enhance the effectiveness of public investments in malaria control.

Yet the global health community is behind on its commitment to end malaria by 2030, outlined in health agendas including the [UN Sustainable Development Goals](#) and [WHO's Global technical strategy for malaria](#). Prof. Kassoum Kayentao of USTTB, and scientific co-lead of SAFIRE, says “It took 20 years for WHO to recommend AL to treat malaria in the first trimester. There is an urgent need to provide alternative therapeutic options in this very sensitive phase of pregnancy”.

SAFIRE's ultimate goal is to accelerate progress toward malaria elimination. Data from the study will be communicated to inform policy design and on-the-ground implementation by healthcare practitioners. “The trial will provide an evidence base to make an additional ACT available for malaria treatment in the first trimester, and also contribute to addressing the lack of equity in enrolling pregnant women in clinical trials”, Prof. Kayentao adds.

Dr Michael Makanga, Executive Director of Global Health EDCTP3, says “Malaria during pregnancy can cause serious maternal and newborn health issues. That is why we are supporting this crucial project, SAFIRE, with over €5 million. With an innovative and inclusive adaptive platform trial approach, we hope it will provide sound evidence for the further development of safe and efficient treatment options for pregnant women

## Notes for editors

### Background on malaria

According to the latest WHO World Malaria Report released in 2023, there were an estimated 608,000 malaria deaths globally in 2022. In 2019, before the COVID-19 pandemic struck, the number of deaths stood at 552,000. The global tally of malaria cases reached 249 million in 2022, compared to 244 million in 2021.

Despite successes; including an expansion of preventive methods such as intermittent preventive treatment of malaria in pregnancy and the approval of an ACT for use in the first trimester of pregnancy; eradication efforts face many challenges, particularly in WHO's African Region which shouldered over 94% of cases and 95% of deaths globally in 2022. Children under the age of 5 accounted for nearly 80% of all malaria deaths in the region.

Malaria in pregnancy [poses grave risks for pregnant women and the babies they are carrying](#): it can lead to tragic outcomes like miscarriage, stillbirth, preterm delivery and low birthweight, severe maternal anaemia, severe malaria and maternal mortality. Women of childbearing age are among the most susceptible to malaria due to changes that take place in the immune system during pregnancy.

According to [the World Health Organization \(WHO\)'s 2023 World malaria report](#), 12.7 million pregnancies – 36% of the pregnancies in Africa – were exposed to malaria in 2022. More than half of malaria infections during pregnancy are estimated to occur before the second trimester. Experts have warned that failing to prioritize the prevention and treatment of malaria in early pregnancy could harm broader malaria elimination efforts.

[Read more about malaria in pregnancy.](#)

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Infectious Diseases Research Collaboration	<a href="https://www.idrc-uganda.org/">https://www.idrc-uganda.org/</a>
Centre National de Recherche Scientifique et Technologique, IRSS	<a href="http://www.crun.bf">www.crun.bf</a>
University of Kinshasa	<a href="https://www.unikin.ac.cd/">https://www.unikin.ac.cd/</a>
Kenya Medical Research Institute	<a href="https://www.kemri.go.ke/">https://www.kemri.go.ke/</a>
University of Sciences, Techniques and Technologies/International Center for Excellence in Research	<a href="http://www.usttb.edu.ml/">http://www.usttb.edu.ml/</a>
Amsterdam University Medical Centre	<a href="https://www.amsterdamumc.org/en/about.htm">https://www.amsterdamumc.org/en/about.htm</a>
Medicines for Malaria Venture	<a href="https://mmv.org">https://mmv.org</a>

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Institution	Website
Centers for Disease Control and Prevention	<a href="https://www.cdc.gov">https://www.cdc.gov</a>

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