A prospective study to evaluate the safety, effectiveness and impact of the RTS, S/AS01E vaccine in young children in sub-Saharan Africa (EPI-MALARIA-003 VS AME) (115056)

First published: 20/03/2019

Last updated: 03/06/2026

Study Finalised

Administrative details

EU PAS number

EUPAS28541

Study ID

50529

DARWIN EU® study

No

Study countries

Ghana

Kenya

Malawi

Study description

The RTS, S/AS01E vaccine has been developed for routine immunization of children living in malaria-endemic countries of sub-Saharan Africa. This study is a post-implementation safety study (after vaccine implementation), with the primary objective to evaluate the safety of vaccine after its administration. In addition to the primary objective, the study will also evaluate the impact and effectiveness of the vaccine. Active surveillance refers to prospective cohort monitoring of the AESI and other diseases during study follow-up visits at the community level as well outpatient and inpatient visits. Enhanced hospitalisation surveillance (EHS) is defined as case detection during hospitalisation through monitoring of medical records and registries for the study participants not enrolled in active surveillance. The study targets enrolling at least 45,000 children in active surveillance (AS), including 22,500 in the exposed clusters and 22,500 in the unexposed clusters for evaluation of the vaccine safety, effectiveness and impact. In the exposed clusters are included a minimum of 20,250 children vaccinated with RTS,S/AS01E for evaluation of the vaccine safety, and a minimum of 2,250 unvaccinated children for evaluation of effectiveness and impact assuming that 80% of the 22,500 study participants will receive three doses of RTS,S/AS01E,10% will receive one or two doses and 10% will not have any dose. Malaria Vaccine Implementation Programme is considering implementing the malaria vaccine in unexposed clusters as from 2023. This decision will directly impact the temporal (before/after) and concurrent (exposed vs. unexposed clusters) comparisons. Based on this, the EHS recruitment will be stopped as from 1 Jan 2023 in sites that were not involved in the NCT02374450 study and study conclusion will be conducted in a timely manner for already enrolled subjects in those sites (EHS will stop in all sites in Malawi, Siaya and Nyando sites in Kenya and unexposed sites in Ghana).

Study status

Finalised

Research institutions and networks

Institutions

GlaxoSmithKline (GSK)

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Institution

Kintampo Health Research Centre Ghana, Navrongo Health Research Centre Ghana, Malawi College of Medicine Malawi, Malawi Liverpool Welcome Trust Malawi, KEMRI (WRP) Kenya, KEMRI (Ahero Clinical Trials Unit) Kenya, KEMRI (CGHR) Kenya

Contact details

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Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 18/10/2017

Study start date
Actual: 21/03/2019

Data analysis start date
Planned: 21/03/2019

Actual: 21/03/2019

Date of final study report
Planned: 14/05/2026

Actual: 14/05/2026

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

GlaxoSmithKline

Study protocol

gsk-115056-protocol-redact-02.pdf (1.92 MB)

Protocol Amendment 3 Anonymised 14 Apr 2025.pdf (2.68 MB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Disease epidemiology

Effectiveness study (incl. comparative)

Safety study (incl. comparative)

Data collection methods:

Combined primary data collection and secondary use of data

Study design:

Disease surveillance study with prospective cohort event monitoring including both temporal (before-after comparison with EPI-MAL-002; Interim Analysis only) and concurrent (cluster design comparison of exposed and unexposed clusters; Interim and Final Analysis) comparisons

Main study objective:

• To estimate the incidence of adverse events of special interest (AESI) in children vaccinated with RTS,S/AS01E.

• To estimate the incidence of aetiology-confirmed meningitis in children vaccinated with RTS,S/AS01E.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Cluster Design

Study drug and medical condition

Medicinal product name, other

Mosquirix™ (RTS,S/AS01E vaccine)

Anatomical Therapeutic Chemical (ATC) code

(J07XA01) malaria vaccines

malaria vaccines

Medical condition to be studied

Meningitis

Population studied

Short description of the study population

The study population is defined as study participants < 5 years of age living in a geographically limited area with a demographic surveillance system in place, and a well-developed infrastructure to monitor population health and vaccination programmes.

Age groups

- Infants and toddlers (28 days – 23 months)
- Children (2 to < 12 years)

Estimated number of subjects

45000

Study design details

Setting

Specific locations in sub-Saharan Africa with moderate to high malaria transmission.

A geographically confined region equipped with a demographic surveillance system and robust infrastructure for tracking population health and vaccination programs.

Outcomes

- Incidence rates of adverse events of special interest (AESI);
- Incidence rates of aetiology-confirmed meningitis cases;
- Incidence rates of probable meningitis (final classification);
- Incidence rates of clinically suspected meningitis (final classification);
- Number of meningitis cases identified at site level (first line laboratory);
- Incidence rates of cerebral malaria cases (diagnosed by Rapid Diagnostic Test [RDT] and/or microscopy);
- Incidence rates of malaria episodes diagnosed by RDT and/or microscopy;
- Incidence rates of anaemia cases at hospital entry among hospitalised children;
- Incidence rates of hospitalisation cases;
- Number of deaths.

Data analysis plan

All data analyses will be computed in a descriptive manner. Data regarding the hospitalisation will be uniformly collected whether the child is enrolled in active surveillance or in enhanced hospitalisation surveillance.

Summary results

Safety signals observed in Phase 3 were not confirmed by the EPI-MAL-003 Final Analysis, and no new signals were identified. Meningitis events were rare and evenly distributed over RTS,S/AS01E vaccinated and unvaccinated groups.

Cerebral malaria events were rare and occurred both in RTS,S/AS01E vaccinated and unvaccinated groups. Deaths occurred at similar rates in males and females. There was no evidence of an association between vaccine exposure and any prespecified AESI. Over 1 year after the full (4-dose) vaccination schedule, a positive impact against hospitalizations due to malaria, any and severe malaria, and hospitalizations due to anemia was observed.

Documents

Study report

Clinical Study Report EPI-MAL-003 Final-Anonymised 26 May 2026.pdf (6.07 MB)

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s)

Other data source

Data source(s), other

Health and Demographic Surveillance System (HDSS) or equivalent surveillance system.

Data sources (types)

Electronic healthcare records (EHR)

Other

Data sources (types), other

Prospective patient-based data collection, Health and Demographic Surveillance System (HDSS) or equivalent surveillance system

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No