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A study of three malaria vaccines to prevent the transmission of malaria in adults in Mali: TBVax2

Submission date
19/06/2022

Recruitment status
No longer recruiting

Registration date
28/06/2022

Overall study status
Completed

Last Edited
01/10/2025

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Malaria is a disease that affects many people in Africa, including Mali. Malaria is caused by small germs that are carried between people by certain mosquitoes. When a person is bitten by an infected mosquito, they may develop malaria. While some people who are infected do not show any symptoms, others may become very sick or even die.

The goal of this study is to develop a vaccine that will safely reduce the spread of malaria in the community by preventing mosquitos from carrying the malaria germs from person to person. The kind of vaccine being developed could decrease the number of malaria germs in the entire community, and could later be combined with a vaccine that prevents people from getting infected.

The combination vaccine being tested in this study contains a protein (Pfs230) that is found on the surface of the malaria germ, a recombinant Pfs48/45 6C domain fused with glutamate-rich protein (R0.6C) and the individual vaccine ProC6C is a recombinant Pfs48/45 6C domain fused with Pfs230-Pro domain using a Circumsporozoite protein linked. The other vaccine parts, EPA, Alhydrogel, and Matrix-M are products that are added to the vaccine to improve the body's immune response to that protein. The immune response is what the body uses to fight germs. The Pfs230 protein has been previously tested combined with other agents in Mali. The R0.6C and ProC6C have also been previously tested, and have been shown to be safe and induced good immune responses. This is the first time these two vaccine parts (R0.6C and Pfs230) have been combined together into one vaccine and the first tests in humans. The study will start with a low dose of the experimental malaria vaccine. If there are no safety concerns after testing this dose, we study will continue with higher doses.

This study aims to learn if the experimental malaria vaccine is safe and what side effects it may cause in Malian adults. The study also aims to see if people who get the vaccine develop similar immune responses that have been seen with other vaccines that reduce the spread of malaria in the community. Volunteers with be given 3 injections of a study vaccine and be followed during the malaria transmission season. The volunteers will receive physical exams and blood samples

will be collected to study how the immune system reacts to the vaccine. The results of research tests from volunteers who received the experimental malaria vaccine will be compared to the results from volunteers who received the approved rabies vaccine to look for differences.

Who can participate?
Healthy adult volunteers resident in Doneguebougou, Mali, or surrounding villages

What does the study involve?
The study will comprise about 23 study visits over about 14 to 16 months. At 3 of these visits, the volunteers will receive an injection of either the experimental malaria vaccine or a comparator vaccine. The comparator vaccine is a rabies vaccine (Verorab Rabies Vaccine or a similar rabies vaccine). The Verorab Rabies Vaccine is approved in Mali. Volunteers will receive only one of these vaccines in this study, not both, and will not know which vaccine they receive. Both the experimental malaria vaccine and the comparator rabies vaccine will be called the "study vaccines."

Blood will be collected from a vein in the volunteer's arm using a needle or by fingerstick at most visits. The blood samples will be used for clinical and research tests. Females who can get pregnant will have pregnancy testing during this study. Because the experimental malaria vaccine can have risks during pregnancy, you cannot be in this study if you are pregnant or planning to become pregnant.

What are the possible benefits and risks of participating?
Participants will not receive direct benefits from this study. We hope that what we learn in this study will help us make an effective new malaria vaccine that will help prevent the spread of malaria.

Participants are at risk of experiencing:
1. Study vaccines: You may experience side effects or symptoms from the study vaccines. The most common side effects seen in people who received these vaccines or parts of the vaccines are the following:
1.1. Side effects near the injection site: pain, swelling, redness, or small lumps under the skin near the injection site
1.2. General side effects throughout the body:
1.2.1. Fever
1.2.2. Headache
1.2.3. Muscle or joint pain
1.2.4. Feeling tired or ill
1.2.5. Nausea
1.2.6. Vomiting
1.2.7. Diarrhea
1.2.8. Swelling of lymph nodes

Side effects from a study on vaccines are generally mild and usually get better without treatment. While most symptoms are mild, it is possible that you could develop serious side effects from the vaccine or other side effects that we do not know about. We will monitor you closely for all side effects and give you treatment if needed.

2. Blood draws: Side effects from blood draws may include pain, bruising, bleeding, infection or feeling lightheaded.

Where is the study run from?
University of Sciences, Techniques and Technologies of Bamako (Mali)

When is the study starting and how long is it expected to run for?
February 2022 to February 2024

Who is funding the study?
European and Developing Countries Clinical Trials Partnership (Netherlands)

Who is the main contact?
Prof Issaka Sagara
isagara@icermali.org

Contact information

Type(s)
Public

Contact name
Prof Issaka Sagara

ORCID ID
https://orcid.org/0000-0002-8555-9983

Contact details
Faculty of Medicine and Odonto-Stomatology & Faculty of Pharmacy
University of Sciences, Techniques and Technologies of Bamako (USTTB)
PO Box 1805 Point G
Bamako
Mali
BP 1805
+22 376459079
isagara@icermali.org

Type(s)
Principal investigator

Contact name
Dr Abdoulaye Katile

Contact details
Faculty of Medicine and Odonto-Stomatology & Faculty of Pharmacy
University of Sciences, Techniques and Technologies of Bamako (USTTB)
PO Box 1805 Point G
Bamako
Mali
BP 1805
+22 376253304
katile@icermali.org

Type(s)

Scientific

Contact name
Dr Patrick Duffy

Contact details
LMIV/NIAID/NIH
29 Lincoln Drive
Building 29B, Room 4NN06
Bethesda
United States of America
MD 20892
+1 301 761-5089
patrick.duffy@nih.gov

Type(s)
Scientific

Contact name
Prof Michael Theisen

Contact details
Serum Statens Institute (SSI)
Copenhagen
Denmark
2300
+45 32 68 32 68
mth@ssi.dk

Additional identifiers

Study information

Scientific Title
Phase I, dose-escalating, randomized, comparator-controlled trial of the safety, tolerability, and immunogenicity of the co-administration of transmission-blocking vaccines (R0.6C-AlOH/ Matrix-M™ with Pfs230D1 EPA/Matrix-M™) and individual comparators (R0.6C-AlOH/ Matrix-M™; ProC6C-AlOH/ Matrix-M™ and Pfs230D1 EPA/Matrix-M™) against Plasmodium falciparum in adults in Mali: TBVax2

Acronym
TBVax2

Study objectives
Malaria is transmitted by Anopheles mosquitoes. During a blood meal from an infected person, the female mosquito ingests parasites, including gametocytes, the sexual forms of the parasite. Inside the mosquito midgut, male and female gametes fertilize to form a zygote, which further develops into an elongated ookinete form. The ookinete migrates to the outer surface of the midgut and develops into an oocyst, which undergoes multiple rounds of nuclear division to produce thousands of sporozoites that then migrate to the salivary glands. When the mosquito

takes another blood meal, it injects sporozoites with its saliva, transmitting the malaria parasite to another person. This is a Phase 1, dose-escalating, randomized, comparator-controlled study to assess the safety, tolerability, immunogenicity, and transmission-blocking activity (TBA) of a 3 dose regimen of Study Agents (four total) versus rabies vaccine in healthy adults. This will be a first-in-human assessment of the co-administration of R0.6C-AlOH/Matrix-M with Pfs230D1-EPA /Matrix-M.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/04/2022, University of Sciences, Techniques and Technologies of Bamako (USTTB) Ethics Committee (FMOS-FAPH/USTTB, BP 1805 Point G, Bamako, Mali; +223-2022-5277; mdiakite@icermali.org), ref: 2022/84/CE/USTTB

Primary study design
Interventional

Study design
Phase I dose-escalating randomized comparator-controlled study

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of Plasmodium falciparum transmission in humans

Interventions
This is a study to assess the safety, tolerability, immunogenicity, and transmission-blocking activity (TBA) of a three-dose regimen of Study Agents (four total) versus rabies vaccine in healthy adults. This will be a first-in-human assessment of the co-administration of R0.6C-AlOH /Matrix-M with Pfs230D1-EPA/Matrix-M. Participants will be randomized to one of the study arms. Participants will be followed for 12 months from the last dose of the study vaccine for safety and tolerability, as well as immunogenicity and functional antibody responses.

1. Group 1: Pilot Group
1.1. Arm 1a (n=5): 30 µg ProC6C-AlOH/15 µg Matrix-M (this arm is to be enrolled only if safety has not already been demonstrated in the ongoing first-in-human trial PACTR202201848463189)
1.2. Arm 1b (n=5): 30 µg R0.6C-AlOH/15 µg Matrix-M co-administered with 12.5 µg Pfs230D1-EPA /25 µg Matrix-M
1.3. Arm 1c (n=5): rabies vaccine (standard dose)

2. Group 2: Main Group
2.1. Arm 2a (n=20): 100 µg R0.6C-AlOH/50 µg Matrix-M and normal saline
2.2. Arm 2b (n=20): 100 µg ProC6C-AlOH/50 µg Matrix-M and normal saline
2.3. Arm 2c (n=20): 40 µg Pfs230D1-EPA/50 µg Matrix-M and normal saline (Pfs230D1-EPA regimen may be adjusted based on results of ongoing clinical trial NCT05135273)
2.4. Arm 2d (n=20): 100 µg R0.6C-AlOH/25 µg Matrix-M co-administered with 40 µg Pfs230D1-EPA/25 µg Matrix-M (Pfs230D1-EPA regimen may be adjusted based on ongoing clinical trial PACTR202201848463189)
2.5. Arm 2e (n=20): rabies vaccine (standard dose)

Added 13/02/2024:
Arm 3 (n=5): 40 µg Pfs230D1-EPA/50 µg Matrix-M given at 0, 1, and 6 months.

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
R0.6C-AlOH/Matrix-M™, ProC6C/Matrix-M™, Pfs230D1-EPA/Matrix-M™, R0.6C-AlOH/Matrix-M™ Co-administered with Pfs230D1-EPA/Matrix-M™, Verorab Rabies Vaccine

Primary outcome(s)
1. Incidence of serious adverse events (SAEs) possibly, probably or definitely related to co-administered vaccinations, measured clinically and by laboratory assessments, measured 7 days after each vaccination in the period from first vaccinations up to 1 month after the last immunization:
1.1. That results in death
1.2. That is life-threatening (places the participant at immediate risk of death from the event as it occurred)
1.3. That requires inpatient hospitalization or prolongs an existing hospitalization
2. Incidence of solicited grade 3 local and systemic adverse events (AEs) possibly, probably or definitely related to co-administered vaccinations, measured clinically and by laboratory assessments, measured 7 days after each vaccination in the period from first vaccinations up to 1 month after the last immunization:
2.1. Systemic adverse events:
2.1.1. Fever (temperature ≥ 38.0°c)
2.1.3. Headache
2.1.4. Nausea/vomiting
2.1.5. Diarrhea
2.1.6. Abdominal pain
2.1.7. Fatigue
2.1.8. Malaise
2.1.9. Myalgia
2.1.10. Arthralgia
2.1.11. Urticarial
2.2. Local reactogenicity following the injection:
2.2.1 Pain/tenderness
2.2.2. Erythema/redness
2.2.3. Swelling
2.2.3. Induration
2.2.4. Pruritus
2.2.5. Limitation of arm movement

Key secondary outcome(s)
1. The functional transmission reducing activity (TRA) measured using the standard membrane feeding assay of volunteer sera at two weeks after the third immunizations, compared to baseline within each of the Study Agent Groups
2. The TRA measured using the standard membrane feeding assay of volunteer sera at other time points (2 weeks after first and second immunizations and 4 months post third vaccination)

compared to baseline (D0) in each of the Study Agent Groups
3. The Study Agent antibody quantity in volunteer sera measured by ELISA two weeks after each dose and at 4 months post dose compared to baseline (D0) in each of the three dose-adjuvant combinations
4. Incidence of adverse events possibly, probably or definitely related to any investigational vaccines measured clinically and by laboratory assessments at study duration period

Completion date
19/02/2024

Eligibility

Key inclusion criteria
1. Aged between 18 years old and <50 years old
2. Available for the duration of the trial
3. Known resident or long-term resident (more than 1 year) of Doneguebougou or surrounding villages
4. Able to provide proof of identity to the satisfaction of the study clinician completing the enrollment process
5. In good general health and without clinically significant medical history in the opinion of the investigator
6. Females of childbearing potential must be willing to use reliable contraception from 21 days prior to Study Day 0 and until 1 month after the last vaccination
7. Willing to have blood samples stored for future research

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
All

Total final enrolment
115

Key exclusion criteria
1. Pregnant, as determined by a positive urine or serum beta human choriogonadotropin (β hCG) test (if female). Note: Pregnancy is also a criterion for discontinuation of any further vaccine dosing.

2. Behavioral, cognitive, or psychiatric disease that in the opinion of the investigator affects the ability of the subject to understand and comply with the study protocol at a level appropriate for the subject's age.
3. Hemoglobin, white blood cell (WBC), absolute neutrophil count, or platelet levels outside the local laboratory-defined limits of normal. Subjects may be included at the investigator's discretion for "not clinically significant" values outside of normal range and ≤ Grade 2.
4. Alanine transaminase (ALT) or creatinine (Cr) level above the local laboratory-defined upper limit of normal. Subjects may be included at the investigator's discretion for "not clinically significant" values outside of the normal range and ≤ Grade 2.
5. Infected with HIV
6. Evidence of clinically significant neurologic, cardiac, pulmonary, hepatic, endocrine, rheumatologic, autoimmune, hematological, oncologic, or renal disease by history, physical examination, and/or laboratory studies
7. History of receiving any investigational product within the past 30 days
8. Current or planned participation in an investigational vaccine study until the time period of the last required study visit under this protocol
9. Medical, occupational, or family problems as a result of alcohol or illicit drug use during the past 12 months
10. History of a severe allergic reaction or anaphylaxis
11. Known:
11.1. Severe asthma, defined as asthma that is unstable or required emergent care, urgent care, hospitalization, or intubation during the past 2 years, or that has required the use of oral or parenteral corticosteroids at any time during the past 2 years
11.2. Autoimmune or antibody-mediated disease including but not limited to:
11.2.1. Systemic lupus erythematosus
11.2.2. Rheumatoid arthritis
11.2.3. Multiple sclerosis
11.2.4. Sjögren's syndrome or autoimmune thrombocytopenia
11.3. Immunodeficiency syndrome
11.4. Seizure disorder (exception: history of simple febrile seizures)
11.5. Asplenia or functional asplenia
11.6. Use of chronic (≥14 days) oral or intravenous (IV) corticosteroids (excluding topical or nasal) at immunosuppressive doses (i.e., prednisone >10 mg/day) or immunosuppressive drugs within 30 days of Study Day 0
11.7. Allergy to latex or neomycin
12. Receipt of:
12.1. Live vaccine within 4 weeks prior to enrollment or a killed vaccine within 2 weeks prior to enrollment
12.2. Immunoglobulins and/or blood products within the past 6 months
12.3. Investigational malaria vaccine in the last 2 years
13. Any other condition that in the opinion of the investigator would jeopardize the safety or rights of a subject participating in the trial, interfere with the evaluation of the study objectives or would render the subject unable to comply with the protocol

Date of first enrolment
30/06/2022

Date of final enrolment
31/08/2022

Locations

Countries of recruitment
Mali

Study participating centre
Doneguebougou Research Unit
Faculty of Medicine and Odonto-Stomatology & Faculty of Pharmacy
University of Sciences, Techniques and Technologies of Bamako (USTTB)
PO Box 1805 Point G
Bamako
Mali
BP 1805

Sponsor information

Organisation
Université des Sciences, des Techniques et des Technologies de Bamako

ROR
https://ror.org/023rbaw78

Funder(s)

Funder type
Research organisation

Funder Name
European and Developing Countries Clinical Trials Partnership

Alternative Name(s)
The European & Developing Countries Clinical Trials Partnership, The European & Developing Countries Clinical Trials Partnership (EDCTP), European and Developing Countries Clinical Trials, Le partenariat Europe-Pays en développement pour les essais cliniques, A Parceria entre a Europa e os Países em Desenvolvimento para a Realização de Ensaios Clínicos, EDCTP

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from (Issaka Sagara, isagara@icermali.org). The type of data which will be made available include the demographic data (age, gender) adverse events data (clinical and laboratory parameters), the immunology (antibody to the different transmission-blocking vaccine candidates), the vaccine arm and the Study ID. Those data will be available at the latest one year after the last vaccination and can be kept at the different repositories as lasting as required by the specific regulatory requirement. Data will be protected from unauthorized person usage. The data will be shared with different stakeholders, including EDCTP, the ethics committee, the DSMB (Data Safety and Monitoring Board) and the regulatory health authorities. The data will be analysed according to predefined data analysis plan. The consent form already states that data will be published or shared with the above-indicated stakeholders but the personal identification code (PIC) will not be revealed.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other files	Interim safety report version 3	15/06/2023	11/01/2024	No	No
Other unpublished results	Interim safety report version 5	09/05/2025	26/09/2025	No	No
Participant information sheet	Participant information sheet		24/06/2022	No	Yes
Protocol file	version 3.0	15/06/2022	08/08/2022	No	No
Protocol file	version 4.0	07/09/2022	26/09/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes