Phase I and IIa trial for assessment of safety, immunogenicity and efficacy against sporozoite challenge of the candidate malaria vaccine PfLSA-3-rec.

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To screen two different formulations of the recombinant malaria vaccine PfLSA-3-rec, one adjuvated with aluminium hydroxide and one with Montanide Isa 720, by assessing the safety and immunogenicity (phase I) profile of each formulation in humans,...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON30669

Source
ToetsingOnline

Brief title
LSA-3-rec

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
malaria; Plasmodium flaciparum infection

Research involving
Human

Sponsors and support

Primary sponsor: Institut Pasteur

Source(s) of monetary or material Support: EU Frame Work Programme 5

Intervention

Keyword: Liver stage antigen-3, LSA-3, malaria vaccine, pre-erythrocytic

Outcome measures

Primary outcome

Phase I: The proportion and severity of adverse events in both intervention groups.

Phase IIa: The proportion of volunteers reaching day 21 post-infection without or with a delayed onset of parasitemiae compared to control group (parasitemiae defined as >=2 parasites per 200 fields in a thick blood film).

Secondary outcome

Phase I and IIa: Immunogenicity evaluation: antibody and cellular responses to vaccination with PfLSA-3-rec vaccine formulations.

Phase IIa: The length of time (in hours) between parasite inoculation and detection of parasitemia, if any, up to 21 days.

Study description

Background summary

Malaria is responsible for over 2 million deaths each year. The development of an efficient vaccine would present by far the best solution for solving this disastrous situation. Liver-Stage-Antigen-3 (LSA-3) is an antigen that is mainly exhibited by Plasmodium falciparum sporozoites and liver-stage parasites. It is characterized by its remarkable antigenicity in humans with a wide range and a variety of B and T-lymphocyte epitopes, by its extremely high immunogenicity and by an excellent protective efficacy against sporozoite challenge in animal models. Therefore, PfLSA-3-rec is a promising candidate vaccine against P. falciparum in humans.

Study objective

To screen two different formulations of the recombinant malaria vaccine PfLSA-3-rec, one adjuvated with aluminium hydroxide and one with Montanide Isa 720, by assessing the safety and immunogenicity (phase I) profile of each formulation in humans, as well as its protective efficacy following a sporozoite challenge (phase IIa).

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Study design

The phase I of the study is designed as a randomized, double-blind, uncontrolled, unicentre, parallel intervention trial with two intervention arms (aluminium hydroxide vs. Montanide Isa720 as adjuvants).
The phase IIa is a controlled, open-label, unicentre trial assessing the efficacy of the candidate vaccine in a sporozoite challenge (experimental human malaria infection) by comparison of immunised with non-immunised volunteers

Intervention

Subcutaneous administration of the recombinant malaria vaccine PfLSA-3-rec, three times to all volunteers.
Intervention arm 1: PfLSA-3-rec with aluminium hydroxide as adjuvant
Intervention arm 2: PfLSA-3-rec with Montanide Isa 720 as adjuvant

Study burden and risks

Benefits: As for any phase I and phase IIa vaccine trial, the benefits for the immunized subjects are minimal in absence of any data on efficacy of the PfLSA-3-rec vaccine in the prevention of malaria: the only advantage for these subjects might be a possible protection from malaria infection after vaccination. However, as for the phase IIa control group volunteers, no direct benefit can be claimed.
Risks: In animal experiments (chimpanzees, Aotus monkeys and mice) no severe adverse events were observed after vaccination with the LSA-3 vaccine. In addition, as LSA-3 is an unregistered immunological medicinal product, assessment and approval will be obtained from the National Institute for Public Health and the Environment (RIVM.) The adjuvants aluminium hydroxide and Montanide Isa 720 are both registered for use in humans and are considered safe.
Burden: The phase I is associated with 19 visits to the examination site, with periodical physical examination and completion of a diary after each vaccination. In addition, blood will be drawn 13 times with a total amount in the phase I of around 422mL. The phase IIa is associated with a short period (around one to two weeks) of intense clinical monitoring with frequent site visits (up to three times a day) and blood examinations. As it is unpredictable

if and/or when subjects will develop a positive thick blood smear for malaria, it is impossible to state the exact number of site visits and blood examinations. However, the maximum number (in case a subject does not develop a positive blood smear) of site visits and blood examinations will be 49 with a maximum amount of collected blood of 541mL.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Male and female age >=18 and <= 45 years
-Good general health based on history, physical en laboratory examination
-Available for and willingness to undergo a P. falciparum sporozoite challenge following the immunization course
-Resident near the Radboud University Medical Center Nijmegen, having 24h access to a

telephone
-Living with a third party that could contact the clinicians in case of alteration of conscience
-Agreement to refrain from blood donation during the course of the study and afterwards
-Negative pregnancy test and the use of effective contraception during the whole study period

Exclusion criteria

-Any history of malaria
-Known exposure to malaria in the previous 6 months, defined as a visit to a malaria-endemic region. For practical purposes, all regions for which malaria chemoprophylaxis is advised by The Dutch National Coordination Centre for Travellers Health (LCR) are considered malaria-endemic
-Planned to travel to endemic malaria areas during the study period
-Prior administration of an investigational malaria vaccine
-Administration of a vaccine or gammaglobulin not foreseen by the clinical trial protocol within 30 days prior to the first immunisation and up to six months after the last immunisation.
-Participation in any other clinical trial within 90 days prior to the onset of the trial or more than four clinical trials in the past year
-The use of chronic immunosuppressive drugs or other immune modifying drugs within three months of vaccination (inhaled and topical corticosteroids are allowed)
-Positive serological tests for P falciparum (LSA-3) ELISA and/or a positive P. falciparum PCR
-Known hypersensitivity to vaccine components
-Contra-indications to Riamet® including treatment taken by the volunteers that interfere with Riamet® (e.g. concurrent use of medicines that prolong QT-interval)
- Symptoms, physical signs and laboratory values suggestive of systemic disorders, including renal, hepatic, cardiovascular, pulmonary, skin, immunodeficiency, psychiatric and other conditions, which could interfere with the interpretation of the study results or compromise the health of the volunteers
-An estimated, ten year risk of fatal cardiovascular disease of >=5%, as estimated by the Systematic Coronary Risk Evaluation (SCORE) system.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-09-2007
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO Date:	29-03-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-09-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-09-2007
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-01-2008
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2006-001743-66-NL
CCMO	NL14715.000.06