Phase I and IIa Trial for Assessment of Safety, Immunogenicity (Phase Ia) and Efficacy (Phase IIa) Against Sporozoite Challenge of P. Falciparum Pre-Erythrocytic and Blood Stage (PfPEBS-LSP) Malaria Vaccine Candidate

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Using a single formulation of PfPEBS LSP administered at two different doses, one of 5*g and the other one of 30*g, both adjuvanted with aluminium hydroxide, in two immunizations at 28 days interval, to evaluate a) the safety and immunogenicity (...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Protozoal infectious disorders
Study type	Interventional

Summary

ID

NL-OMON37083

Source
ToetsingOnline

Brief title
PEBS-POC1

Condition

- Protozoal infectious disorders

Synonym
Malaria, Plasmodium falciparum

Research involving

Human

Sponsors and support

Primary sponsor: Vac4All
Source(s) of monetary or material Support: Vac4All

Intervention

Keyword: malaria, PEBS, phase I & IIa, vaccine

Outcome measures

Primary outcome

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

Phase IIa: Efficacy against Liver stages: The proportion of volunteers reaching day 21 post infection without or with a delayed onset of parasitemia compared to control group

Secondary outcome

Phase I and lla: Immunogenicity evaluation: Functional activity of antibody and cellular responses elicited by PfPEBS-LSP vaccine formulation.

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 1 million deaths each year. The development of an efficient vaccine would present an essential complementary tool for controlling, if not eliminating this Plasmodium infection.

PfPEBS is an antigen 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 both, Pre-erythrocytic and erythrocytic stages of the parasite. The PEBS candidate presents the unique feature to associate the characteristics of LSA3 and MSP3, two major vaccine candidates against the pre-erythrocytic and the asexual blood stages of the parasite, respectively. Therefore, PfPEBS peptide is a promising candidate vaccine against P.falciparum in humans.

Study objective

Using a single formulation of PfPEBS LSP administered at two different doses, one of 5*g and the other one of 30*g, both adjuvanted with aluminium hydroxide, in two immunizations at 28 days interval, to evaluate a) the safety and immunogenicity (phase I) profile of each dose in humans, b) the induction of an ADCI parasite-killing-effect against erythrocytic stages, and c) to evaluate protective efficacy following a sporozoite challenge (phase IIa).

Study design

The phase I of the study is designed as a randomized, double-blind, controlled, against aluminium hydroxide alone, unicentre, parallel intervention trial of PfPEBS with aluminium hydroxide as adjuvant. The phase IIa is a controlled, double-blind, bi-centre trial assessing the efficacy of the candidate vaccine against a sporozoite challenge (experimental human malaria infection) by comparison of immunised with control volunteers.

Intervention

Intramuscular administration of the malaria vaccine PfPEBS-LSP, two times at 28 days interval to all volunteers.

Study burden and risks

1. side effects: fever, nausea, flu-symptoms, headache
2. strict medical control visits during 10 days starting on day 5 after inoculation

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 infected mosquito challenge following the immunization course
•Resident in or near Lausanne for the duration of the study having 24h access to a mobile telephone
•Willingness to stay in special accommodation (hotel or equivalent) from day 5 up to one day after parasite positivity , or up to day 15 post EHMI
•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 if deemed appropriate
•Willingness to undergo an HIV test and other serologies
•Willingness to allow investigators to notify their general practitioner, if any, of participation in this trial
•Willingness to allow investigators to request medical information, relevant for participation in this trial, from their general practitioner, if any
•Written informed consent following proper understanding of the meaning and procedures of the Phase I and IIa parts of the trial
•Agreement to inform study doctor and to release medical information concerning contra-

indications for participation in the study
•Willingness to undergo screening for drugs such as amphetamines, opiates and cocaine

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 travel clinic 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 immunization and up to six months after the last immunization.
•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 medication (defined as more than 14 days), especially immunosuppressive agents or antibiotics during the study period
•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 (PEBS) ELISA and/or a positive P. falciparum whole parasite ELISA
•Known hypersensitivity to vaccine components
•History of severe reactions or allergy to mosquito bites
•Contra indications to Malarone® including treatment taken by the volunteers that interfere with Malarone® (e.g. concurrent use of medicines that prolong QT interval)
•History of allergic disease to or reactions likely to be exacerbated by any component of the vaccine
•Any confirmed or suspected immunosuppressive or immunodeficiency condition, including asplenia.
•History of diabetes mellitus or cancer (except basal cell carcinoma of the skin)
•History of >2 hospitalisations for invasive bacterial infections
•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.
•History of arrhythmia or prolonged QT interval or other cardiac disease
•Positive history for cardiac disease in the 1st and 2nd degree relative < 50 years old
•Clinically significant abnormalities in electrocardiogram (ECG) at screening
•Body Mass Index < 18 kg/m2 or > 32 kg/m2
•Blood pressure > 150/90 in two measurements
•Seropositive for HIV, HBV or HCV
•Any clinically significant deviation from the normal range in biochemistry or haematology

blood tests or in urine analysis.
•Volunteers unable to be closely followed for social, geographic or psychological reasons
•Previous history of drug or addiction to alcohol abuse interfering with normal social function during a period of one year prior to enrolment in the study
•Having not reached 10 correct responses to the knowledge questionnaire

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	36
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Lyophilised PEBS synthetic protein (PfPEBS)
Product type:	Medicine
Brand name:	Malarone
Generic name:	Atovaquon/proguanil
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	08-06-2012

Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	31-08-2012
Application type:	First submission
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	EUCTR2012-002294-54-NL
ClinicalTrials.gov	NCT01605786
CCMO	NL41025.000.12