Chemoprophylaxis and Plasmodium falciparum NF54 sporozoite immunization challenged by heterologous infection

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Primary objective: To determine whether CPS-immunization with NF54 Plasmodium falciparum parasites provides protection against challenge with the genetically distinct P. falciparum clones, NF135.C10 or NF166.C8.Secondary objectives:• To investigate...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Protozoal infectious disorders
Study type	Interventional

Summary

ID

NL-OMON41057

Source
ToetsingOnline

Brief title
BMGF2b

Condition

- Protozoal infectious disorders

Synonym
malaria, Plasmodium falciparum

Research involving
Human

Sponsors and support

Primary sponsor: Medische Microbiologie
Source(s) of monetary or material Support: Bill and Melinda Gates Foundation

Intervention

Keyword: heterologous, malaria, sporozoites, vaccine

Outcome measures

Primary outcome

Time to parasitemia in volunteers after malaria challenge infection.

Secondary outcome

• Antigen specificity of CPS-immunization induced antibodies for protection

against pre-erythrocytic stages of Plasmodium falciparum.

• The specificity of CPS-immunization induced T cell responses against

pre-erythrocytic stages of Plasmodium falciparum.

Study description

Background summary

Malaria, a disease caused by the parasite Plasmodium, is one of the world*s major infectious diseases. With approximately 627.000 deaths a year, it is both a chief cause of morbidity and mortality as well as a significant contribution to ongoing poverty in endemic countries. Ultimately, the key to malaria control, and hopefully eradication, would be an effective vaccine. Though a number of vaccine-candidates have entered the pipeline of pre-clinical and clinical development, they have yet to achieve the level of efficacy necessary for effective malaria prevention. Controlled human malaria infections (CHMIs) have been demonstrated to be a powerful tool in malaria vaccine research. It has been shown previously that if healthy human volunteers taking chloroquine chemoprophylaxis are repeatedly exposed to Plasmodium sporozoites through the bites of infected mosquitoes, they are fully protected against a later challenge infection with a homologous Plasmodium parasite. This process is known as ChemoProphylaxis and Sporozoites, or CPS-immunization. One of the obstacles to developing an effective vaccine is the genetic heterogeneity of malaria parasite clones. To further consider the development of whole sporozoite based vaccines and in order to better understand the protective immunity induced by CPS-immunization, it is essential to investigate whether heterologous protection against genetically diverse P. falciparum clones can be

induced.

Study objective

Primary objective:
To determine whether CPS-immunization with NF54 Plasmodium falciparum parasites provides protection against challenge with the genetically distinct P. falciparum clones, NF135.C10 or NF166.C8.
Secondary objectives:
• To investigate Plasmodium falciparum specific T cell responses in CPS-immunized volunteers.
• To delineate the antibody repertoire directed against Plasmodium falciparum in CPS-immunized volunteers.

Study design

This is a single center, randomized, double-blind study. A total of 40 volunteers will be included and divided into six groups. The first group (n=10) will receive CPS-immunization with NF54 and a challenge infection with NF135.C10 parasites. The second group (n=10) will receive CPS-immunization with NF54 and a challenge infection with NF166.C8 parasites. The third group (n=5) will receive CPS-immunization with NF54 and challenge infection with NF54 parasites. Groups 4, 5 and 6 (n=5 for each group) will receive chloroquine prophylaxis and bites from uninfected mosquitoes during the immunization phase and challenge infection with NF135.C10, NF166.C8 or NF54, respectively.

Intervention

A total of three CPS-immunizations will be performed with bites from 15 Plasmodium falciparum infected mosquitoes or uninfected controls per immunization over a period of three months, during which all volunteers will take chloroquine prophylaxis. All volunteers will undergo malaria challenge infection by exposure to bites from up to 5 Plasmodium falciparum sporozoite infected mosquitoes, infected with either NF135.C10, NF166.C8 or NF54 parasites.

Study burden and risks

The study is associated with several short periods of intense clinical monitoring with frequent site visits (up to two times a day) and blood examinations. As it is unpredictable when subjects will develop a positive qPCR or thick blood smear, it is impossible to state the exact number of site visits and blood examinations. However, the maximum number of site visits and blood examinations will be 61. The maximum amount of collected blood over the period of 8 months will be 1000 mL. Additionally, periodical physical examinations

will be performed and the subject is asked to complete a diary.

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

- Subject is aged >= 18 and <= 35 years and in good health.
- Subject has adequate understanding of the procedures of the study and agrees to abide strictly thereby.
- Subject is able to communicate well with the investigator, is available to attend all study visits, lives in proximity to the trial centre (<10 km) or (if >10km) is willing to stay in a hotel close to the trial centre during part of the study (day 5 post-infection until three days post-treatment). Furthermore the subject will remain within the Netherlands during the challenge period, not travel to a malaria-endemic area during the study period, and is reachable (24/7) by mobile telephone throughout the entire study period.

- Subject agrees to inform his/her general practitioner about participation in the study and to sign a request to release by the GP any relevant medical information concerning possible contra-indications for participation in the study.
- Subject agrees to refrain from blood donation to Sanquin or for other purposes throughout the study period and for a defined period thereafter according to current Sanquin guidelines.
- For female subjects: subject agrees to use adequate contraception and not to breastfeed for the duration of study.
- Subject has signed informed consent.
- Subject agrees to refrain from intensive physical exercise (disproportionate to the subjects usual daily activity or exercise routine) for ten days following each immunization and during the malaria challenge period.

Exclusion criteria

- Any history, or evidence at screening, of clinically significant symptoms, physical signs or abnormal laboratory values suggestive of systemic conditions, or psychiatric disorders, which could compromise the health of the volunteer during the study or interfere with the interpretation of the study results.
- Body weight <50 kg or Body Mass Index (BMI) <18.0 or >30.0 kg/m2 at screening.
- A heightened risk of cardiovascular disease, as determined by: an estimated ten year risk of fatal cardiovascular disease of >=5% at screening, as determined by the Systematic Coronary Risk Evaluation (SCORE); history, or evidence at screening, of clinically significant arrhythmia*s, prolonged QT-interval or other clinically relevant ECG abnormalities; or a positive family history of cardiac events in 1st or 2nd degree relatives <50 years old.
- A history of functional asplenia, sickle cell trait/disease, thalassaemia trait/disease or G6PD deficiency.
- History of epilepsy in the period of five years prior to study onset, even if no longer on medication.
- Positive HIV, HBV or HCV screening tests.
- Chronic use of i) immunosuppressive drugs, ii) antibiotics, iii) or other immune modifying drugs within three months prior to study onset (inhaled and topical corticosteroids and oral anti-histamines exempted) or expected use of such during the study period.
- History of malignancy of any organ system (other than localized basal cell carcinoma of the skin), treated or untreated, within the past 5 years.
- Any history of treatment for severe psychiatric disease by a psychiatrist in the past year.
- History of drug or alcohol abuse interfering with normal social function in the period of one year prior to study onset, or positive urine toxicology test for cocaine or amphetamines at screening or prior to infection or positive urine toxicology test for cannabis at inclusion or prior to infection.
- For female subjects: positive urine pregnancy test at screening or prior to infection.
- Any history of malaria, positive serology for P. falciparum, or previous participation in any malaria (vaccine) study.
- Known hypersensitivity to or contra-indications (including co-medication) for use of chloroquine, Malarone or artemether-lumefantrine, or history of severe (allergic) reactions to mosquito bites.

- Receipt of any vaccinations in the 3 months prior to the start of the study or plans to receive any other vaccinations during the study period or up to 8 weeks thereafter.
- Participation in any other clinical study in the 30 days prior to the start of the study or during the study period.
- Being an employee or student of the department of Medical Microbiology of the Radboudumc or the department of Internal Medicine.
- Any other condition or situation that would, in the opinion of the investigator, place the subject at an unacceptable risk of injury or render the subject unable to meet the requirements of the protocol.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-02-2015
Enrollment:	40
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	26-06-2014
Application type:	First submission

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-10-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-12-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-02-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-07-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-06-2016
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
ClinicalTrials.gov	NCT02098590
CCMO	NL48732.091.14