Phase 1 study to evaluate the safety, tolerability, and pharmacokinetics and pharmacodynamics of monoclonal antibody TB31F in healthy malaria-naïve adults in the Netherlands

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(protocol section 2) This phase 1 study aims to assess the safety and tolerability of monoclonal antibody TB31F administered intravenously or at escalating dose levels or subcutaneously in healthy, malaria naïve, adults. This study will also...

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON50099

Source
ToetsingOnline

Brief title
Safety, tolerability, and pharmacokinetics and pharmacodynamics of TB31F

Condition

- Other condition
- Protozoal infectious disorders

Synonym
Plasmodium falciparum; malaria

Health condition

malaria

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: PATH-Malaria Vaccine Initiative

Intervention

Keyword: Malaria, Plasmodium falciparum, TB31F, Transmission blocking

Outcome measures

Primary outcome

(protocol section 8.1.1)

- Number and severity of solicited local adverse events of all severities from

first product administration through day 7;

- Number and severity of solicited general AEs from first product

administration through day 28;

- Number and severity of unsolicited adverse events from first product

administration through end of study;

- Number and severity of serious adverse events from first product

administration through end of study.

Secondary outcome

(protocol section 8.1.1)

- TB31F serum concentration at each dose level through end of study;

- Percentage of transmission reducing activity at different time points by

SMFA.

Study description

Background summary

(protocol section 1.1) A major challenge for malaria elimination is the highly efficient spreading of malaria parasites. Circulating gametocytes do not cause clinical pathology or symptoms but play an essential role in the onward transmission of malaria infections. Gametocytes of P. falciparum synthesize Pfs48/45. Male gametocytes lacking Pfs48/45 are unable to bind to female gametocytes in the mosquito gut. A transmission blocking medicine aims to prevent the sexual development of parasites in the mosquito*s midgut. Antibodies (Abs) in the blood are ingested during the blood meal of the mosquito, preventing sporozoite development. TB31F interrupts transmission of P. falciparum in the Standard Membrane Feeding Assay.

Study objective

(protocol section 2) This phase 1 study aims to assess the safety and tolerability of monoclonal antibody TB31F administered intravenously or at escalating dose levels or subcutaneously in healthy, malaria naïve, adults. This study will also evaluate the pharmacokinetics of TB31F and the functional activity of mAb TB31F in the standard membrane feeding assay.

Study design

(see protocol section 3) The trial will be carried out by the Radboud University Medical Center (Radboudumc). Five groups will receive a single dose of mAb TB31F administered by intravenous infusion or subcutaneously. Group 1 (n=5) will receive 0.1 mg/kg TB31F, Group 2 (n=5) will receive 1 mg/kg TB31F, group 3 (n=5) will receive 3 mg/kg TB31F, group 4 (n=5) will receive 10 mg/kg mAb TB31F and group 5 (n=5) will receive 100mg.

Twentyfive (n=25) subjects will be enrolled, as well as 1 reserve subject per group. Safety follow-up will be done at following times: 0 hours, end of infusion (EOI), 1, 3, 6 and 24 hours after product administration, and on days 2, 7, 14, 21, 28, 56 and 84 after product administration. Group 5 subjects will have an additional follow-up visit on day 4 and day 10 after administration. All subjects will be followed for approximately 84 days after mAb TB31F administration.

Intervention

Single intravenous or subcutaneous administration of TB31F

Study burden and risks

There are no benefits to participating in this study. Subjects are not protected against malaria after participating. TB31F has not been administered in humans before, therefore we do not know what side effects TB31F can give. Participating in this trial includes the burden mAb TB31F administration, placement of intravenous infusion catheter(s), multiple blood sampling tests, possible side effects from premedication, frequent follow-up visits, physical examinations, screening for HIV, Hepatitis B and Hepatitis C, a pregnancy test (for females), filling out a study journal, possible COVID-19 diagnostics and abiding to all study rules. However, the information that we get from this study will help us further in the development of transmission-blocking interventions against malaria.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 28
Nijmegen 6525 GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 28
Nijmegen 6525 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Subject must sign written informed consent to participate in the trial.
* Subject is able to understand planned study procedures and demonstrate comprehension of the protocol procedures and knowledge of study by passing a quiz.
* In the opinion of the investigator, the subject can and will comply with the requirements of the protocol.
* Subjects are available to attend all study visits and are reachable by phone throughout the entire study period from day -1 until day 84 (end of study).
* The subject will remain within reasonable travelling distance from the study center from day -1 till day +7 after mAb TB31F administration.
* Subject is a male or non-pregnant female age * 18 and * 35 years and in good health at time of mAb administration.
* Subject agrees to their general practitioner (GP) being informed about participation in the study and agrees to sign a form to request the release by their GP, and medical specialist when necessary, of any relevant medical information concerning possible contra-indications for participation in the study to the investigator(s).
* The subject agrees to refrain from blood donation to Sanquin or for other purposes throughout the study period according to current Sanquin guidelines.
* Female subjects of non-childbearing potential may be enrolled in the study. All subjects must agree to use continuous adequate contraception until 2 months after completion of the study.

Exclusion criteria

(Protocol section 4.3.)
* Acute or chronic disease at time of TB31F administration, clinically significant pulmonary, cardiovascular, hepatic or renal functional abnormality, as determined by physical examination or laboratory screening tests:
o Acute disease is defined as the presence of a moderate or severe illness with or without fever. Subjects with a minor illness on the day of TB31F administration will be temporarily excluded from participation, but may be re-evaluated for inclusion at a later date. Subjects with a positive SARS-CoV2 test at inclusion will be (temporarily) excluded from participation but may be re-evaluated for inclusion at a later date (following current Radboudumc guidelines).
o Fever * 38.0°C (100.4°F).
o Any abnormal and clinically significant baseline laboratory screening tests (appendix 1).
* History of malignancy of any organ system (other than localized basal cell carcinoma of the skin), treated or untreated, within the past 5 years.
* 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.
* Positive urine toxicology test for cannabis, cocaine or amphetamines at screening or at inclusion.
* Screening tests positive for Human Immunodeficiency Virus (HIV), active Hepatitis B Virus (HBV), Hepatitis C Virus (HCV).
* Use of any investigational or non-registered product (drug or vaccine) during the study period other than the study product.
* Participation in any other clinical study in the 30 days prior to the start of the study or during the study period.
* History of adverse reactions to monoclonal antibodies
* Prior receipt of an investigational antimalarial monoclonal antibody.
* Administration of immunoglobulins and/or any blood products within the three months preceding the first dose of study mAb or planned administration during the study period.
* Any history of malaria, positive serology for P. falciparum, or previous participation in any malaria (vaccine) study or CHMI.
* Body weight > 115 kg
* Being an employee or student of the department of Medical Microbiology or Medium Care of the Radboudumc.
* History of drug or alcohol abuse interfering with normal function in the period of one year prior to study onset.
* 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

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	14-02-2020
Enrollment:	25

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	TB31F
Generic name:	TB31F

Ethics review

Approved WMO Date:	03-06-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-11-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-02-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-06-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-07-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-11-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-11-2020

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
Other	clinicaltrials.gov (NCT04238689)
EudraCT	EUCTR2019-001904-39-NL
CCMO	NL69779.091.19

Study results

Date completed:	04-03-2021
Results posted:	04-03-2022

First publication
04-03-2022