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A study to evaluate the use of a cholera vaccine as an immune challenge for the mucosal immune system

Submission date
03/05/2023

Recruitment status
No longer recruiting

Registration date
04/05/2023

Overall study status
Completed

Last Edited
04/05/2023

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The immune system protects the body against infections by bacteria and viruses. Many diseases are caused by an overactive immune system that attacks the own body instead of bacteria and viruses. These diseases are called autoimmune diseases. Many drugs are developed to treat autoimmune diseases, these drugs must inhibit the immune system. However, it is difficult to measure the effect of these new drugs in healthy people, as the immune system is not active in healthy people. This study aims to activate the immune system through a cholera vaccination, to find out whether this vaccination can be used when studying new drugs treating auto-immune diseases. This study specifically focuses on the part of the immune system that is present in the barriers of the body, such as the gut and the nose.

Who can participate?
Healthy volunteers aged 18 to 45 years

What does the study involve?
The participants of the study will receive a cholera vaccination. This consists of a drink that must be taken two times. To activate the immune system in the nose, the cholera vaccination will also be administered as a nose spray. To find out whether these vaccinations can be used to measure the effects of new drugs, the effects of an existing drug will be investigated. To this aim, CellCept, a drug normally used by patients that have received a transplantation, will be administered to half of the participants. The other half of the participants will receive placebo (dummy drugs). In this way, the effects of CellCept on the vaccination can be compared to the effects of placebo.

What are the possible benefits and risks of participating?
There are no benefits in participating, except for contributing to the easier development of new drugs. All medication that is used during the study is already registered and used in practice. Therefore, risks are low. It is already known that the cholera vaccination has little or no adverse events. The most common adverse events of CellCept are gastrointestinal complaints.

Where is the study run from?
The Centre for Human Drug Research (Netherlands)

When is the study starting and how long is it expected to run for?
December 2022 to June 2023

Who is funding the study?
The Centre for Human Drug Research (Netherlands)

Who is the main contact?
B. Eveleens Maarse, beveleensmaarse@chdr.nl

Contact information

Type(s)
Scientific

Contact name
Miss Boukje Eveleens Maarse

Contact details
Zernikedreef 8
Leiden
Netherlands
2333 CL
+31 (0)71 5246 400
clintrials@chdr.nl

Additional identifiers

Clinical Trials Information System (CTIS)
2023-000084-31

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CHDR2249

Study information

Scientific Title
A randomized, single-blind, placebo-controlled study to evaluate an oral cholera vaccination with intranasal rechallenge as an adaptive immune challenge model

Study objectives
The aims of the current study are:
1. To characterize the oral cholera vaccination as a challenge model for gut mucosal immunity
2. To explore a nasal cholera rechallenge as an additional readout for this challenge model
3. To benchmark the model by evaluating the effects of a registered immunosuppressant, versus

placebo. Mycophenolate mofetil (MMF) will be used to this end, as this drug inhibits lymphocyte proliferation and thereby targets both B- and T-cell-mediated immunity.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/03/2023, Stichting BEBO (Doctor Nassaulaan 10, 9401 HK Assen, The Netherlands; +31 (0)592 405871; info@stbebo.nl), ref: NL83700.056.23

Study design
Single-center randomized single-blind placebo-controlled study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Oral cholera vaccination with intranasal rechallenge as an adaptive immune challenge model

Interventions
Oral dose CellCept used as an immunosuppressive agent
Dukoral oral vaccine/intranasal used as cholera vaccine
As comparative drugs, placebo tablets will be used.

This study will have two treatment arms, randomized in a 1:1 manner. The participants on active treatment will receive 2dd 1000 mg mycophenolate mofetil for a duration of 6 days (administration in the morning and evening, oral tablets), the participants in the other groups will receive placebo at the same timepoints. Follow-up will take place by means of a telephonic call by the physician, and during all following visits of the study (until Day 28). The randomization list is generated by an independent statistician and is sent to the pharmacy without interference from other members of the study team.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Cellcept (mycophenolate mofetil), Dukoral

Primary outcome(s)
1. Systemic immune response is measured as serum cholera antigen specific IgA levels at Days 1, 14, 18, 20 and 28
2. Systemic immune response is measured as serum cholera antigen specific IgG levels at Days 1, 14, 18, 20 and 28

Key secondary outcome(s))

1. Local immune response is measured as saliva cholera antigen specific IgA levels at Days 1, 14, 18, 20 and 28
2. Local immune response is measured as nasal cholera antigen specific IgA levels at Days w, 7 and 10

Completion date
30/06/2023

Eligibility

Key inclusion criteria
1. Signed informed consent prior to any mandated procedure
2. Healthy male and female volunteers, 18 to 45 years of age, inclusive at screening
3. Body mass index (BMI) between 18 and 30 kg/m², inclusive, and with a minimum weight of 50 kg
4. All subjects must practice effective contraception during the study and be willing and able to continue contraception for at least 90 days after their last dose of study treatment
5. The participant has clinical laboratory evaluations (including clinical chemistry, hematology and complete urine analysis) within the reference range for the testing laboratory, unless the results are deemed not clinically significant by the investigator
6. Participants who are overtly healthy as determined by medical evaluation including medical history, vital signs, physical examination, laboratory tests and ECGs at Screening and on Day -2
7. The participant should be able to take MMF/placebo two times per day for 6 days and to refrain from eating 2 hours before intake
8. Has the ability to communicate well with the Investigator in the Dutch language and is willing to comply with the study restrictions

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
45 years

Sex
All

Key exclusion criteria
1. The participant has signs and/or symptoms of an infection 2 weeks prior to dosing, or recurrent infection, or has had an infection requiring antibiotic treatment (e.g. sepsis, pneumonia, abscess) within 42 days prior to the start of MMF/placebo administration
2. The participant has (a history of) autoimmune disease such as multiple sclerosis, inflammatory

bowel disease, rheumatoid arthritis or other immune-inflammatory disease
3. The participant has a history of trauma with likely damage to the spleen, or has had surgery to the spleen or splenectomy
4. The participant has a known immunodeficiency
5. Positive Hepatitis B surface antigen (HBsAg), anti-hepatitis B core, hepatitis C, or human immunodeficiency virus antibody (HIV-Ab) at screening
6. Serious psychiatric or medical conditions that, in the opinion of the investigator, could interfere with treatment, compliance, or the ability to give consent.
7. The participant has taken any over-the-counter (OTC) or any prescription medication (with the exception of paracetamol) less than 14 days or 5 half-lives (whichever is longer) prior to the first IMP dosing, and considered as relevant by the investigator
8. Participant has received live attenuated vaccination within 42 days prior to Screening or intends to have vaccinations during the course of the study. SARS-CoV-2 vaccinations are not allowed 1 week prior to Screening and from 2 weeks before dosing until EOS
9. Participant has received any investigational drug of experimental procedure within 90 days or 5 half-lives, whichever is longer, prior to study intervention administration, or the participant was enrolled in an investigational drug or device study within 90 days prior to the first IMP dosing
10. The participant has a history of hypersensitivity or allergies to any drug or to any of the components of the study interventions (i.e. Dukoral oral cholera vaccination, MMF or placebo)
11. The participant has lost or donated more than 400 ml of blood or blood products within 90 days prior to the start of MMF or placebo treatment (Day -2) or plans to donate blood during the study
12. The participant has had an acute, clinically significant illness or intervention by a surgeon or dentist within 14 days prior to screening
13. Current (or within the past 6 months) nicotine use in excess of 5 cigarettes per day, or unable not to smoke during visits
14. History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 14 units of alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquillisers, or any other addictive agent
15. Previous vaccination against cholera or enterotoxigenic Escherichia coli
16. Travel in the last 3 years to a country where cholera or enterotoxigenic E. coli is prevalent

Date of first enrolment
18/04/2023

Date of final enrolment
30/06/2023

Locations

Countries of recruitment
Netherlands

Study participating centre
Centre for Human Drug Research
Zernikedreef 8

Leiden
Netherlands
2333 CL

Sponsor information

Organisation
Centre for Human Drug Research

ROR
https://ror.org/044hshx49

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository.

IPD sharing plan summary
Stored in non-publicly available repository