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Study to investigate the effects of different doses of lipopolysaccharide on immune cells in the blood and bone marrow of healthy young men

Submission date
12/01/2023

Recruitment status
No longer recruiting

Registration date
21/02/2023

Overall study status
Completed

Last Edited
21/01/2025

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
To study the effect of new drugs, sometimes the so-called lipopolysaccharide (LPS) challenge is used, which is injected intravenously. LPS is part of a bacterium and has been used safely in several studies at the Centre for Human Drug Research to induce an immune response. During this study, the effects of LPS on different types of immune cells in blood and bone marrow will be measured. Measuring these effects will provide valuable information that can be used to design future studies with new drugs. In this study, the effects of different doses of LPS on immune cells in the blood and bone marrow of healthy young men will be investigated.

Who can participate?
Healthy male volunteers (aged 18 to 35)

What does the study involve?
Screening: Up to 42 days before the start of the treatment period
Treatment and study assessments: Days 1 to 8 (in Part A, only Day 1 is applicable)
Clinic period: Days 1 and 7 to 8
Follow-up visit: 7 to 11 days after the last bone marrow sampling

What are the possible benefits and risks of participating?
There is no benefit expected for the healthy volunteers. Specific post-procedural risks associated with the bone marrow sampling procedure are rare and include excessive bleeding, infection and long-lasting discomfort at the bone marrow puncture site. Symptoms such as pain, fatigue, puncture site reaction, nausea, transient low blood pressure, stiffening of the hip joint, and difficulty in walking can be expected. Additionally, risks associated with the intravenous LPS challenge include the on-target pharmacological and adverse effects resulting in mild systemic inflammatory response, which can cause flu-like symptoms (e.g., chills, headache, sensitivity to light, nausea, myalgia and arthralgia), increase in core temperature and increase in pulse rate, with reduction of mean arterial pressure. Most symptoms are dose-related and are expected to

resolve within 12hours, although headache and nausea can still be present day afterwards. Subjects will be monitored up to 24hours or up to the resolution of possible symptoms in the clinical research unit.

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

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

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

Who is the main contact?
Dr Igor Radanovic (Project leader), iradanovic@chdr.nl (The Netherlands)

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CHDR2225

Study information

Scientific Title
Study to evaluate the effects of intravenously administered lipopolysaccharide on the bone marrow immune cell compartment in healthy male volunteers

Acronym
Bone marrow

Study objectives
The study will evaluate the feasibility, safety and tolerability of bone marrow sampling in healthy volunteers and assess the early effects of the intravenous lipopolysaccharide challenge model in the bone marrow compartment, specifically in the hematopoietic stem cell niche by using immunophenotyping, cytomorphology, and immunohistology.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/07/2022, Foundation for the Assessment of Ethics in Biomedical Research Medical Ethical Review Committee (Stichting Beoordeling Ethiek Biomedisch Onderzoek Medisch Ethische ToetsingsCommissie; Doctor Nassaulaan 10, 9401 HK Assen, The Netherlands; +31 592-405871; info@stbebo.nl), ref: NL81720.056.22

Study design
Open-label study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Healthy volunteers

Interventions
An open-label study to evaluate the effects of the single dose (either 1 or 2 ng/kg) of iv lipopolysaccharide (LPS) challenge on the bone marrow immune compartment.

LPS, purified lipopolysaccharide prepared from Escherichia Coli: 113: H10:K negative (U.S. Standard Reference Endotoxin) will be used. Subjects will receive 1 ng/kg or 2 ng/kg LPS intravenously. This proof-of-concept study will evaluate the early effects of systemic inflammatory challenge (LPS) in the bone marrow compartment and the data will be used for the evaluation of future compounds that will be tested in a similar setting.

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Safety and tolerability (vital signs, weight and height, physical examination, ECG, safety laboratory assessments) measured using standard techniques. For vital signs, weight and height performed at Screening, Day 1 (-1h, 1h, 6h), Day 7/8 (-2h, 1h, 2h, 6h, 24h), Follow-up; Physical examination performed at Screening, Day 1 (6h), Day 7/8 (-2h, 24h) and Follow-up; Safety laboratory assessments performed at Screening, Day 1 (-1h), Day 7/8 (4h), Follow-up
2. Pain measured using the Visual Analogue Scale at Day 1 (-1h, 0h, 1h, 6h), Day 7/8 (03h, 1h, 2h, 4h, 6h, 24h) and at Follow-up
3. Effects of the intravenous lipopolysaccharide (LPS) challenge model in bone-marrow aspiration and biopsies measured using immunophenotyping, cytomorphology and immunohistology at baseline and 4h post-LPS
4. Effects of the LPS challenge model measured using whole-blood immunophenotyping and cytokine measurement at baseline and 4h post-LPS
5. Immune cell expression profile in whole blood and blood marrow samples measured RNA-sequencing at baseline and 4h post-LPS
6. Feasibility measured using a Subject Experience Questionnaire at Follow-up

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
30/12/2022

Eligibility

Key inclusion criteria
1. Male participants between 18 and 35 years of age (inclusive), at the time of signing the informed consent
2. Participants who are overtly healthy as determined by medical evaluation including medical history, physical examination, laboratory tests, and ECG
3. A body mass index (BMI) between 18.0 and 30.0 kg/m2 (inclusive), and a minimum body weight of 50 kg
4. Able to give written informed consent and willing to comply with all study-related procedures

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
35 years

Sex
Male

Total final enrolment
13

Key exclusion criteria
1. Clinically significant abnormalities, as judged by the investigator, in test results (including physical examination, laboratory tests, ECG and vital signs)
2. History of medical conditions, which in the opinion of the investigator may compromise the participant’s safety or the scientific value of the study, posing an unacceptable risk to the participant or interfering with the participant's ability to comply with study procedures or abide by study restrictions
3. History of trauma with likely damage to the spleen or surgery to the spleen, or history of hip fracture or surgery in the pelvic area
4. Previous participation in a systemic (i.v./inhaled) LPS challenge trial within a year before the first study day
5. Any active inflammatory or infectious disease (e.g., periodontitis), with the exception of common viral or fungal skin infections such as plantar warts or athlete’s foot
6. Febrile illness within 30 days before the start of the first study day
7. Antibiotic use, operation or intervention by surgeon/dentist within one month before the first study day
8. Hemorrhagic diathesis (easy bruising, epistaxis, gastrointestinal bleeding, history of serious bleeding)
9. Clinically significant hypertension (defined as systolic blood pressure > 145 mmHg or diastolic blood pressure >90 mmHg, repeatedly measured after 5 minutes in resting supine position), or clinically significant hypotension(defined as systolic blood pressure < 90 mmHg or diastolic

blood pressure < 50 mmHg, repeatedly measured after 5 minutes in resting supine position)
10. Clinically significant abnormalities in the 12-lead ECG (QRS complex > 120ms, PR interval > 210ms, QTcFinterval > 470ms)
11. Positive test results for hepatitis B, hepatitis C, HIV antibody or any other obvious disease associated with immune deficiency
12. Subjects with a positive urine drug screen/alcohol test result at screening or first admission or a history of substance abuse in the last 12 months prior to the start of the study
13. Subjects who smoke more than 6 cigarettes or the equivalent of tobacco per day and are unwilling to abstain from smoking during the study period (from screening until EOS)
14. Loss or donation of blood over 500 mL within 3 months prior to screening or donation of plasma within 14 days prior to screening
15. Participation in an investigational drug or device study within 3 months between the last dosing in the previous study and admission to the CRU in the present study or more than 4 times in the past year
16. Any vaccination within the last 3 months; COVID-19 vaccination (or infection as confirmed by a PCR test) is allowed up until 4 weeks prior to admission to the CRU; COVID-19 booster vaccination is allowed up until 2 weeks prior to admission to the CRU

Date of first enrolment
26/09/2022

Date of final enrolment
06/12/2022

Locations

Countries of recruitment
Netherlands

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Sponsor information

Organisation
Centre for Human Drug Research

ROR
https://ror.org/044hshx49

Funder(s)

Funder type
Research organisation

Funder Name
Centre for Human Drug Research

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be published as a supplement to the results publication.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes