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A study in healthy volunteers to evaluate the effect of lipopolysaccharide in the skin in a single individual

Submission date
26/09/2023

Recruitment status
No longer recruiting

Registration date
24/11/2023

Overall study status
Completed

Last Edited
20/02/2025

Condition category
Skin and Connective Tissue Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Lipopolysaccharide (LPS) is part of a bacterium that causes an inflammatory reaction in a controlled manner. LPS has been used for about 30 years and can also be administered into the blood. LPS injections in the blood make people feel temporarily 'unwell'. The Centre for Human Drug Research (CHDR) has set up a model to be able to study local inflammation of the skin in healthy people. The sensation of 'unwell' was not seen in previous studies at CHDR where LPS was administered into the skin. This inflammatory model can be used to investigate the effect of (new) anti-inflammatory drugs. In previous studies at CHDR, LPS has always been administered at one timepoint. By examining whether the reaction of the skin remains the same after repeated administration of LPS, the model can be further developed. It could then be used in the future to investigate, for example, the effect of different doses of an anti-inflammatory agent on the skin reaction by injecting LPS at different timepoints. The aim of the study is to examine the reaction of the skin after repeated administration of the substance (LPS). In addition, the researchers will examine whether the skin's immune system responds more mildly over time and whether the reaction on the back is the same as on the arm.

Who can participate?
Healthy volunteers, males and females, between 18 and 45 years old

What does the study involve?
Participants receive a total of seven LPS injections each (one on the volar forearm [same side as the palm of the hand] and six on the upper back) for non-invasive imaging and to measure white blood cell (monocyte) infiltration via suction blistering on the back.

What are the possible benefits and risks of participating?
The invasive measurement in this study consists of blister formation. This will be limited to six blisters per participant. To minimize the risk of post-inflammatory hyperpigmentation (discoloration of the skin), Fitzpatrick skin types 4-6 are excluded. In conclusion, the risks associated with LPS injections in the skin are low and acceptable for the subjects to participate in the study. No medical benefit can be expected from this study.

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?
August 2023 to March 2024

Who is funding the study?
F. Hoffmann-La Roche (Switzerland)

Who is the main contact?
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Contact information

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Additional identifiers

Protocol serial number
CHDR2336

Study information

Scientific Title
A study in healthy volunteers to evaluate the effect of repeated lipopolysaccharide skin challenges in a single individual

Study objectives
The aim of this study is to assess the safety of repeated local lipopolysaccharide (LPS) challenges and to investigate if immune tolerance to LPS occurs in the skin. The latter will be assessed by the recruitment of monocytes and neutrophils to sites of an intradermal LPS challenge performed at D1, D15 and D29.

Additionally, the response will be assessed at six different administration sites. Therefore, in this study, participants will receive multiple intradermal LPS injections on the upper back over time. Subjects will receive one additional injection in the lower arm, to assess the difference in clinical response between the lower arm and the upper back. This design permits studying the response to repeated intradermal LPS within one participant, as well as a comparison of the response between intradermal LPS applied on the lower arm and the upper back. If a similar immune response is seen at the D1, D15 and D29 timepoints, future IMP studies would then be able to implement this design such that each subject would act as its own control and could also be used to ascertain dose-response relationship.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 02/11/2023, Foundation Biomedical Research (Stichting Beoordeling Ethiek Biomedisch Onderzoek) (Dr. Nassaulaan 10, Assen, 9401 HK, Netherlands; +31 (0)592 405871; info@stbebo.nl), ref: NL84863.056.23

Primary study design
Interventional

Study design
Single-centre non-randomized study

Study type(s)
Safety

Health condition(s) or problem(s) studied
Repeated lipopolysaccharide skin challenges

Interventions
This is a single-centre, repeated LPS challenge study to explore the effects of local intradermal LPS challenges over time in healthy volunteers. Each subject receives one LPS injection on the volar forearm for non-invasive imaging, and six LPS injections over time to measure monocyte infiltration via suction blistering on the back.

Intervention Type
Other

Primary outcome(s)

1. Safety
1.1. Treatment-emergent (serious) adverse events ((S)AEs)
1.2. Safety labs tests (acute phase proteins (CRP), leukocyte differentiation at Study day 1: baseline + 24 hours post dose; Study day 15: baseline + 24 hours post dose; Study day 29: baseline + 24 hours post dose; Study day 37 follow-up visit, once
1.3. Vital signs (Heart rate, Blood pressure) at Study day 1: baseline + 2 hours, 4 hours, 10 hours and 24 hours post dose; Study day 15: baseline + 10 hours and 24 hours; Study day 29: baseline + 10 hours and 24 hours; Study day 37 follow up visit, once
1.4. Numeric Rating Scale (NRS) pain score at Study day 1: baseline + 2 hours, 4 hours, 10 hours and 24 hours post dose
2. Dermal imaging/scoring
2.1. Perfusion by Laser Speckle Contrast Imaging (LSCI) at Study day 1: baseline + 2 hours, 4 hours, 10 hours and 24 hours post dose; Study day 15: baseline + 2 hours, 4 hours, 10 hours and 24 hours post dose; Study day 29: baseline + 2 hours, 4 hours, 10 hours and 24 hours post dose
2.2. Erythema by Antera 3D camera at Study day 1: baseline + 2 hours, 4 hours, 10 hours and 24 hours post dose; Study day 15: baseline + 2 hours, 4 hours, 10 hours and 24 hours post dose; Study day 29: baseline + 2 hours, 4 hours, 10 hours and 24 hours post dose
2.3. Erythema grading score: Clinical Erythema Assessment (CEA) at Study day 1: baseline + 10 hours and 24 hours post dose; Study day 15: baseline + 10 hours and 24 hours post dose; Study day 29: baseline + 10 hours and 24 hours post dose
3. Blister exudate analysis
3.1. Neutrophils and monocyte subsets at Study day 1: 10 hours and 24 hours post dose; Study day 15: 10 hours and 24 hours post dose; Study day 29: 10 hours and 24 hours post dose

Key secondary outcome(s)
1. Blister exudate analysis
1.1. Other immune cell subsets (lymphocytes etc)
1.2. Cytokines and/or chemokines, such as CCL2 at Study day 1: 10 hours and 24 hours post dose; Study day 15: 10 hours and 24 hours post dose; Study day 29: 10 hours and 24 hours post dose
2. Blood analysis
2.1. Serum and plasma biomarkers (e.g. cytokines and/or chemokines) at Study day 1: baseline + 2 hours, 4 hours, 10 hours and 24 hours post dose; Study day 15: baseline + 10 hours and 24 hours; Study day 29: baseline + 10 hours and 24 hours; Study day 37 follow up visit, once

Completion date
15/03/2024

Eligibility

Key inclusion criteria
1. Healthy male and female subjects, 18 to 45 years of age, inclusive. Healthy status is defined by the absence of evidence of any active or chronic disease following a detailed medical and surgical history, a complete physical examination including vital signs, 12-lead ECG, haematology, blood chemistry, blood serology and urinalysis. In the case of uncertain or questionable results, tests performed during screening may be repeated before enrollment to confirm eligibility or judged to be clinically irrelevant for healthy subjects.
2. Body mass index (BMI) between 18 and 30 kg/m² and a minimum weight of 50 kg, inclusive
3. Fitzpatrick skin type I-III (Caucasian)

4. Subjects and their partners of childbearing potential must use effective contraception for the duration of the study
5. Able and willing to give written informed consent and 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

Total final enrolment
9

Key exclusion criteria
1. History of pathological scar formation (keloid, hypertrophic scar) or keloids or surgical scars in the target treatment area that in the opinion of the investigator, would limit or interfere with dosing and/or measurement in the trial.
2. Any current and/or recurrent pathologically, clinically significant skin condition at the treatment area (lower arm and upper back, i.e., atopic dermatitis); including tattoos.
3. Requirement of immunosuppressive or immunomodulatory medication within 30 days prior to enrolment or planned to use during the course of the study.
4. Known immunodeficiency
5. Use of topical medication (prescription or over-the-counter [OTC]) in the local treatment area or any medication that may interfere with the study objectives as judged by the investigator within 30 days of study drug administration, or less than 5 half-lives (whichever is longer)
6. Participation in an investigational drug or device study within 3 months, or 5 half-lives whichever is longer, prior to screening or more than four times in the past year.
7. Loss or donation of blood over 500 ml within 3 months prior to screening or donation of plasma within 14 days of screening.
8. Any (medical) condition that would, in the opinion of the investigator, potentially compromise the safety or compliance of the patient or may preclude the patient’s successful completion of the clinical trial.
9. Pregnant, a positive pregnancy test, intending to become pregnant during the study conduct, or breastfeeding.
10. Positive hepatitis B surface antigen (HbsAg), hepatitis C antibody (HCV ab), or human immunodeficiency virus antibody (HIV ab) at screening.
11. A history of ongoing, chronic or recurrent infectious disease
12. Hypersensitivity for dermatological marker at screening
13. Current smoker and/or regular user of other nicotine-containing products (e.g., patches)

14. History of or current drug or substance abuse considered significant by the PI (or medically qualified designee), including a positive urine drug screen.
15. Presence of current, clinically relevant infections
16. Any vaccination within the last 4 weeks before day 1. Intention to receive any vaccination(s) before the last day of follow-up.

Date of first enrolment
23/10/2023

Date of final enrolment
08/02/2024

Locations

Countries of recruitment
Netherlands

Study participating centre
Centre for Human Drug Research
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Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		17/02/2025	20/02/2025	No	No