ISRCTN29254828 https://doi.org/10.1186/ISRCTN29254828

A study to test the effect of experimental drugs EDP1815 and EDP2939 on skin inflammation in healthy volunteers after KLH and imiquimod challenge

Submission date
20/06/2022

Recruitment status
No longer recruiting

Registration date
01/07/2022

Overall study status
Completed

Last Edited
24/05/2024

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
EDP1815 and EDP2939 possibly have a regulating effect on the immune reaction. Therefore, they may be used in the treatment of diseases involving an overactive immune reaction, such as the skin diseases eczema and psoriasis. In this study, the effect of EDP1815 and EDP2939 on the immune reaction will be measured. Two different immune reactions will be induced, one by injections (KLH reaction) and one with a cream on the skin (imiquimod reaction).

Who can participate?
Healthy volunteers aged 18 to 45 years (inclusive)

What does the study involve?
Participants will take EDP1815 or EDP2939 every day for 2 months. They will receive KLH injections on 3 different days. After 2 months, the KLH reaction will be induced on the skin with an injection in the skin. The reaction will be measured by different cameras. For 3 consecutive days, the imiquimod cream will be applied to the skin. This reaction will also be measured by different cameras. Inflammation of the skin after imiquimod application will also be measured in blister fluid. To this purpose, four blisters will be made on the skin where imiquimod was applied.

What are the possible benefits and risks of participating?
There are no benefits of participating. Participants possibly contribute to a new treatment of auto-immune diseases. EDP1815 and EDP2939 have already been administered to people and there have been no side effects of concern. However, these are investigational drugs so there may be side effects we don't yet know about and that could happen. KLH injection can cause redness, itching and swelling of the skin at the site of injection, but these effects normally don't last more than 3-4 days. Imiquimod challenge can cause redness, itching, pain, tingling and skin peeling where the imiquimod has been applied. Blisters can cause discoloration of the skin, which usually disappears after a few weeks. However, in rare cases the discoloration can stay present for months to years.

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

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

Who is funding the study?
Evelo Biosciences (USA)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05682222

Clinical Trials Information System (CTIS)
2022-000975-37

Protocol serial number
CHDR2158

Study information

Scientific Title
A Phase I, randomized, double-blind, placebo-controlled, multiple-dose platform study investigating the immunopharmacology of EDP1815 and EDP2939

Study objectives

Both EDP1815 and EDP2939 exert an immunomodulatory effect which will significantly attenuate the dermal immune reactions to KLH and imiquimod challenge.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/05/2022, Stichting Stichting Beoordeling Ethiek Biomedisch Onderzoek (BEBO) (Doctor Nassaulaan 10, 9401 HK Assen, The Netherlands; +31 (0)592 405871; info@stbebo.nl), ref: NL81037.056.22

Primary study design
Interventional

Study design
Single-center randomized double-blind placebo-controlled multiple-dose platform trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
KLH and imiquimod induced skin inflammation in healthy volunteers

Interventions
The active drug will be EDP1815 in Cohorts 1 and 2, and EDP2939 in Cohorts 3 and 4. In all cohorts, subjects will be randomized 2:1 to receive active or placebo treatment. The study drug will be administered daily from Day 1 up until Day 60 through oral self-administration; on clinic visit days, the study drug will be administered at the clinic.

An unblinded statistician generates a randomization list (active:placebo = 2:1). Study drug will be dispensed by an unblinded pharmacist. The randomization list will be made available to the pharmacist preparing the study drug, and to statisticians or programmers involved in preparing blinded summaries, graphs and listings. All other study staff and participants will be blinded until the database is locked.

Cohorts 1 and 2 will take one capsule EDP1815 per day (dose_ 8 $x10^{12}$ cells) for a duration of 60 days. Cohort 1 will receive capsules with normal enteric coating, cohort 2 will receive capsules with an early release coating. Cohorts 3 and 4 will take one capsule EDP2939 per day (dose cohort 3_ 3.9 $x10^{12}$ eTPN, dose cohort 4 maximal 7.5 $x10^{13}$ eTPN, both with early release coatings) for a duration of 60 days.

Subjects will be present on Day -1 for initial baseline procedures, and again on Day 1 for remaining baseline procedures and initial dosing of study drug, and to receive instructions on study drug storage and dosing at home. Subjects will present to the Centre for Human Drug Research (CHDR) on days 8, 22, and 36 to receive intramuscular KLH immunisations. Subjects will present on Day 57 to receive intradermal KLH administration and to start topical administration of Imiquimod. All study visits will consist of ambulatory visits. Imiquimod will also be administered on days 58 and 59.

The follow-up visit will be 12 to 16 days after the last dose of the study drug.

KLH-challenge: KLH will be administered by intramuscular injection. The KLH challenge will be performed by intradermal administration.
Imiquimod-challenge: imiquimod will be administered topically.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
EDP1815, EDP2939

Primary outcome(s)
KLH-induced immune reaction after intradermal re-challenge, measured as basal flow (laser speckle contrast imaging [LSCI]) at 24 h

Key secondary outcome(s)
1. KLH-induced immune reaction after intradermal re-challenge, measured as basal flow (LSCI) at 4 h, 48 h and 72 h
2. KLH-induced immune reaction after intradermal re-challenge, measured as flare (LSCI) at 4 h, 24 h, 48 h and 72 h
3. KLH-induced immune reaction after intradermal re-challenge, measured as erythema (multispectral imaging) at 4 h, 24 h, 48 h and 72 h
4. Specific B-cell response to KLH, measured as anti-KLH IgM and IgG at 1, 22, 36 and 57 days
5. IMQ-induced immune reaction, measured as basal flow (LSCI) at 24 h, 48 h and 72 h
6. IMQ-induced immune reaction, measured as flare (LSCI) at 24 h, 48 h and 72 h
7. IMQ-induced immune reaction, measured as erythema (multispectral imaging) at 24 h, 48 h and 72 h

Completion date
23/05/2023

Eligibility

Key inclusion criteria
1. Capable of giving signed informed consent, and willing to comply with requirements of the study
2. Age 18 years to 45 years, inclusive
3. Body mass index of 18 to 35 kg/m2, inclusive
4. Caucasian
5. Healthy based on medical history, physical examination, blood pressure, ECG and blood and urine laboratory tests

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
38

Key exclusion criteria
1. Use of Aldara® (imiquimod cream) within 3 weeks prior to the study
2. Has previously received Immucothel® or KLH
3. Allergy to Alhydrogel® or Aldara® (imiquimod cream)
4. Current or recurrent skin diseases affecting the arms or back, or extensive tattoos in these areas
5. Previous diagnosis of psoriasis
6. History of pathological scar formation (e.g. keloid scar)
7. History of skin cancer (basal cell carcinoma, squamous cell carcinoma, melanoma)
8. Significant bowel disease (e.g. inflammatory bowel disease, coeliac disease)
9. Currently has an infection or has needed antibiotics within 6 weeks before the study
10. Current smoker of more than 5 cigarettes per day
11. Tanning due to sunbathing, excessive sun exposure or a tanning booth within 3 weeks before the start of the study
12. History of schistosomiasis (infection with Schistosoma parasite)

Date of first enrolment
20/05/2022

Date of final enrolment
01/07/2023

Locations

Countries of recruitment
Netherlands

Study participating centre
Centre for Human Drug Research
Zernikedreef 8
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Sponsor information

Organisation
Evelo Biosciences

Funder(s)

Funder type
Industry

Funder Name
Evelo Biosciences

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to proprietary reasons.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		15/05/2024	24/05/2024	Yes	No