A phase 1, randomized, double-blind, placebo-controlled, multiple dose platform study investigating the immunopharmacology of EDP1815 and EDP2939

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Primary• To evaluate the effect of EDP1815 (same dose using EC1 and EC2 capsules) and EDP2939 (two dose levels using EC2 capsules) on the immune system.Secondary• To evaluate the effect of EDP1815 (same dose using EC1 and EC2 capsules) and EDP2939 (...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON51644

Source
ToetsingOnline

Brief title
Evaluation of the Immunopharmacology of EDP1815 and EDP2939

Condition

- Autoimmune disorders

Synonym
Autoimmune disease

Research involving
Human

Sponsors and support

Primary sponsor: Evelo Biosciences
Source(s) of monetary or material Support: Biotech industry

Intervention

Keyword: Immunopharmacology, IMQ, KLH, Prevotella histicola

Outcome measures

Primary outcome

• KLH-induced immune reaction, after intradermal re-challenge, measured as basal flow (LSCI) at 24 hours (h).

Secondary outcome

• KLH-induced immune reaction, after intradermal re-challenge, measured as basal flow (LSCI) at 4h, 48h and 72h.

• KLH-induced immune reaction, after intradermal re-challenge, measured as flare (LSCI) at 4h, 24h, 48h and 72h.

• KLH-induced immune reaction, after intradermal re-challenge, measured as erythema (multispectral imaging) at 4h, 24h, 48h and 72h.

• Specific B-cell response to KLH, measured as anti-KLH IgM and IgG

• IMQ-induced immune reaction, measured as basal flow (LSCI) at 24h, 48h and 72h.

• IMQ-induced immune reaction, measured as flare (LSCI) at 24h, 48h and 72h.

• IMQ-induced immune reaction, measured as erythema (multispectral imaging) at 24h, 48h and 72h.

• Serious adverse event (SAE) and adverse event (AE) incidents

• Clinical safety laboratory measurements

• Electrocardiogram (ECG) measurements

• Vital sign measurements

• Physical examination

• Gut microbiota composition in stool samples

- 16S RNA sequencing

Study description

Background summary

Keyhole Limpet Hemocyanin (KLH) and imiquimod (IMQ) challenges in healthy volunteers represent promising methodologies for the evaluation of novel, immunomodulatory therapeutics.

EDP1815 and EDP2939 are novel therapeutic agents that aim to modulate systemic inflammation by targeting the small intestinal immunological axis (SINTAXTM) without systemic drug exposure.

This study, EDP1815-105, will evaluate the pharmacodynamic effects on KLH and IMQ challenge of EDP1815 in enteric coated capsules utilizing two coating levels, enteric coating level 1 (EC1 - approximately 58 mg dry weight enteric coat, original release); as used in study EDP1815-102) and a thinner enteric coating level 2 (EC2 - approximately 14 mg dry weight enteric coat, earlier release). Subsequently, the pharmacodynamic effects on the KLH and IMQ challenge of EDP2939 at two dose levels in capsules with EC2 will be evaluated.

Study objective

Primary
• To evaluate the effect of EDP1815 (same dose using EC1 and EC2 capsules) and EDP2939 (two dose levels using EC2 capsules) on the immune system.

Secondary
• To evaluate the effect of EDP1815 (same dose using EC1 and EC2 capsules) and EDP2939 (two dose levels using EC2 capsules) on the immune system.
• To evaluate the safety and tolerability of EDP1815 in two enteric coated

capsule dosage forms.
• To evaluate the safety and tolerability of EDP2939 at different doses

Study design

This is a single-center, randomized, double-blind, placebo-controlled, platform trial to evaluate the effects of EDP1815 and EDP2939 on the systemic immune system, using KLH and IMQ challenges.

Intervention

Cohort 1: EDP1815, 1 capsule QD, 8x10^10 cells per capsule (EC1)
Cohort 2: EDP1815, 1 capsule QD, 8x10^10 cells per capsule (EC2)
Cohort 3: EDP2939, 1 capsule QD, 3.9x10^12 EV per capsule (EC2).
Cohort 4: EDP2939, 1 capsule QD, up to 7.5x1013 EV per capsule (EC2). Dose will be confirmed based on interim safety review of multiple dose escalation part of EDP2939-101

All subjects will undergo 3 KLH intramuscular administrations, 1 intradermal KLH administration, and 3 consecutive days of topical IMQ administration.

Study burden and risks

The study will be conducted in healthy volunteers. Both the KLH challenge and IMQ challenge have been conducted in healthy volunteers before.
Participants in this study are healthy volunteers and are not expected to experience therapeutic benefit from exposure to EDP1815 or EDP2939.
EDP1815 is a pharmaceutical preparation of a single strain of P. histicola, a commensal found in all human populations studied to date. EDP1815 drug-substance has viability of <0.02% and is not genetically modified. While P. histicola is a human commensal, it is a potentially pathogenic micro-organism. Most frequently reported are urinary tract infections with a relatively mild clinical course, in most cases in immune-compromised patients, who are not part of the current protocol. P. histicola and EDP1815 specifically have been tested and found to be sensitive for various antibiotics, which will be administered in the current protocol if necessary.
Across the Phase 1 and 2 studies to date, EDP1815 has demonstrated a safety profile similar to placebo at doses up to 1.28 x1012 cells per day for durations up to 8 weeks (cohort 8 of study EDP1815-101), and up to 8x1011 cells per day for 16 weeks (e.g. in psoriasis phase 2 study EDP1815-201). There have been no drug-related serious adverse events, no SUSARs and no adverse events of severe intensity. No subjects required cessation of dosing due to a drug-related AE.
EDP2939 comprises EVs from EDP1815, and thereby is non-viable and does not include the parent microbe. EDP1815 contains both the parent microbe and EVs (EDP2939) hence the risk profile of EDP2939 is expected to be similar to

EDP1815. Doses of EDP2939 to be used in the current study will be qualified by prior Phase 1 safety data from EDP2939-101.
The study design and challenge methodology to be used in the current study has been used previously in many other CHDR studies, and is accepted by scientists and regulatory authorities.

For a structured risk assessment see Section 10.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Capable of giving signed informed consent which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol. Obtained prior to any screening procedures and in accordance with national, local, institutional guidelines.

2. Age >= 18 years to 45 years, inclusive.
3. Participant has a body mass index of >= 18 kg/m2 to <= 35 kg/m2 at Screening.
6. The participant has clinical laboratory evaluations (including clinical chemistry, haematology, and complete urine analysis) within the reference range for the testing laboratory, unless the results are deemed not to be clinically significant by the investigator (1 repeat test is permitted).
7. Fitzpatrick skin type I-III (Caucasian).
8. 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 -1.

Exclusion criteria

9. The participant has used Aldara® (imiquimod cream) within 3 weeks prior to the baseline visit or plans to use it during the course of the study.
10. Previous known exposure to Immucothel® or KLH.
12. The participant has a history of hypersensitivity or allergies to Prevotella (or Prevotella containing probiotics) including any associated excipients for EDP1815 or EDP2939, or has a history of hypersensitivity or allergies to placebo capsule/powder (magnesium stearate, microcrystalline cellulose, colloidal silicon dioxide, hydroxypropylmethylcellulose, or mannitol) or to the hard capsule shells (hydroxylpropylmethylcellulose and titanium dioxide), or has a known allergy against Alhydrogel®, or has a known allergy against Aldara® (imiquimod cream).
16. The participant has any current and / or recurrent pathologically, clinically significant skin condition at the treatment area (i.e., atopic dermatitis), including tattoos. Treatment area includes the forearms and back.
19. 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.
20. Diagnosed with psoriasis.
21. History of skin cancer (basal cell carcinoma, squamous cell carcinoma, melanoma).
22. Tanning due to sunbathing, excessive sun exposure or a tanning booth within 3 weeks before start of treatment (Day 1) and for the duration of the study.
23. History of Schistosomiasis (infection with Schistosoma parasite).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-05-2022
Enrollment:	72
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aldara 5%®
Generic name:	Imiquimod
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Immucothel

Ethics review

Approved WMO Date:	14-04-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-05-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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
EudraCT	EUCTR2022-000975-37-NL
CCMO	NL81037.056.22