A phase 1, double-blind, randomised, placebo-controlled multiple dose study investigating the immunopharmacology of EDP1066 with multiple formulations

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Primary* To evaluate the effect of EDP1066 in multiple formulations on the systemic immune system.Secondary* To evaluate the safety and tolerability of EDP1066 in multiple formulations.

Ethical review	Approved WMO
Status	Completed
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON48298

Source
ToetsingOnline

Brief title
MAD immunopharmacology study of EDP1066 with multiple formulations

Condition

- Immune disorders NEC

Synonym
Auto immune diseases

Research involving
Human

Sponsors and support

Primary sponsor: Evelo Biosciences Inc.

Source(s) of monetary or material Support: Evelo Biosciences Inc.

Intervention

Keyword: Auto immune disorders, EDP1066, KLH antigen challenge

Outcome measures

Primary outcome

o KLH challenge

* Serum anti-KLH IgM and IgG titres

* LSCI * basal flow and flare

* multispectral imaging * CIELAB colour level a* and Haemoglobin average level

* Ex-vivo lymphocyte activation

o Whole blood ex-vivo PHA and LPS challenges with cytokine release as read-out

measured by MSD.

o Circulating regulatory T cells and B cell subsets

Secondary outcome

o Treatment-emergent (serious) adverse events ((S)AEs).

o Clinical laboratory tests

* Haematology

* Chemistry

* Urinalysis

o Vital signs

* Pulse Rate (bpm)

* Systolic blood pressure (mmHg)

* Diastolic blood pressure (mmHg)

o ECG

* Heart Rate (HR) (bpm), PR, QRS, QT, QTcF

o Physical examination

o Bristol stool scale

o Stool questionnaire

o Blood immunological markers

* Cytokines e.g. TNF-*, IFN-*, IL-1*, IL-4, IL-5, IL-6, IL-8, IL-10, IL-13

* Immunoglobulins e.g. IgG (including individual subclasses IgG1 to IgG4), IgM,

IgA

* Leukocyte subsets e.g. CD3+, CD4+, CD8+, CD19+, NK-cells and CD14+

o Specific markers of GI integrity

* Faecal calprotectin

o EDP1066 prevalence in stool samples (transit time and persistence)

* Strain-specific PCR

o Faecal microbiome composition

* 16S RNA sequencing

Study description

Background summary

Over the past decades, evidence has emerged for an interplay between the gut microbial flora (microbiome) and the (systemic) immune system. Alteration in the composition of the gut microbiome has been associated with the presence of several (auto)inflammatory diseases. Evelo Biosciences has identified and selected individual microbial strains of human commensal bacteria based on their properties to modulate the systemic immune system to use as therapeutics for auto-immune diseases e.g. psoriasis and eczema. These individual microbial strains are called monoclonal microbials. These microbials are expected to be restricted to the gut lumen and interact locally with immune cells, inducing a systemic immunomodulatory effect. If they are capable of modulating multiple

immune pathways in humans, as different preclinical studies are suggesting, they have the potential to become an attractive therapeutic strategy in patients with (auto) inflammatory diseases, either as monotherapy or in combination with other agents.

Study objective

Primary
* To evaluate the effect of EDP1066 in multiple formulations on the systemic immune system.
Secondary
* To evaluate the safety and tolerability of EDP1066 in multiple formulations.

Study design

This is a single centre, double-blind, randomised placebo-controlled trial to evaluate the effect of EDP1066 on the systemic immune system, using a KLH challenge.

Intervention

EDP1066
KLH

Study burden and risks

EDP1066 is a natural organism which has been used in probiotic formulations, food production and dairy manufacturing. It is a gram-positive bacterium sensitive to the major classes of antibiotics, e.g. penicillins and cephalosporins. There have been rare case reports of infections reported in the literature, although these have been responsive to standard antibiotic therapy. Similar doses of Lactococcus species have been given as probiotics without any tolerability issues being reported, providing further confidence that EDP1066 will be well tolerated. The evidence available so far suggests EDP1066 will be very well tolerated and is being investigated for its potential benefit in chronic immunoinflammatory disorders. The initial conditions being tested are mild to moderate psoriasis and mild to moderate atopic dermatitis. A well tolerated oral therapy could offer significant benefit in both of these conditions and at present it is anticipated that EDP1066 would be used in established but early disease before the intervention of biologic therapies is required.
The study design has been used previously in many FIH studies, and is accepted by scientists and regulatory authorities. All study drug administrations will be done in the clinic under medical supervision. The subjects receiving any study drug will remain in the clinic for at least 48 hours after their first study drug administration. Thus, the subjects can be closely monitored for any

adverse signs during the different treatments. Therefore, providing the protocol is adhered to, careful observation and medical management will minimize any associated risk in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Participants are eligible to be included in the study only if all of the following criteria apply:
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 60 years, inclusive.

3. Participant has a body mass index of * 18 kg/m2 to * 35 kg/m2 at Screening.
4. Contraception:
a. Male participants:
* A male participant must agree to use contraception as indicated in Section 4.5.1 during their participation in this study and for a period of 90 days after the last dose and refrain from donating sperm during this period.
b. Female participants:
* A female participant is eligible to participate if she is not pregnant, does not plan to become pregnant during the study, not breastfeeding, and at least 1 of the following conditions applies:
i. Not a woman of child-bearing potential (WOCBP)
OR
ii. A WOCBP who agrees to follow the contraceptive guidance during their participation in this study as indicated in Section 4.5.1 and for at least 3 complete menstrual cycles (*90 days) after last EDP1066 dose.
5. CRP * 10 mg/L and faecal calprotectin * 150 mcg/g faeces. Exceedings of these thresholds may be allowed by the investigator if deemed clinically irrelevant.
6. Participant has clinical laboratory evaluations (including clinical chemistry, haematology, and complete urinalysis) 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. Participants who are overtly healthy as determined by medical evaluation including medical history, physical examination, laboratory tests, and cardiac monitoring at Screening and on Day 1.
8. Participant has the ability to communicate well with the Investigator in the Dutch language and willing to comply with the study restrictions.
9. Subject needs to have sufficient space in a refrigerator to store the IMP during the ambulant dosing phase.

Exclusion criteria

1. Participant has received live attenuated vaccination within 42 days prior to Screening or intends to have vaccinations during the course of the study.
2. Participant has received any investigational drug or experimental procedure within 90 days or 5 half-lives, whichever is longer, prior to study intervention administration or participant was enrolled in an investigational drug or device study within 90 days prior to first EDP1066 dosing.
3. Participant requires treatment with an anti-inflammatory drug or prophylactic antibiotics for any reason during the study period. Paracetamol will be permitted for use as an antipyretic and/or analgesic (maximum of 4 grams/day in any 24-hour period).
4. Participant has an active infection (e.g. sepsis, pneumonia, abscess) or recurrent infection, or has had an infection requiring antibiotic treatment within 42 days prior to Investigational Medicinal Product (IMP) administration.

5. Participant is diagnosed with tuberculosis (TB, as per positive skin test (Mantoux) or IFN-* release assay), or history of TB, or latent TB, or recent contact with TB (patient); having travelled to countries where TB is endemic within 56 days of planned drug administration or planning to travel to countries where TB is endemic from the moment of drug administration until 90 days after the end of the study.
6. Participant has renal or liver impairment, defined as:
a. For women, serum creatinine level * 125 *mol/L; for men, * 135 *mol/L
b. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) * 1.5 x upper limit of normal (ULN), or
c. Alkaline phosphatase (ALP) and/or bilirubin > 1.5 x ULN
Exceedings of these thresholds may be allowed by the investigator if deemed clinically irrelevant.
7. Participant has active neoplastic disease or history of neoplastic disease within 5 years of Screening (except for basal or squamous cell carcinoma of the skin or carcinoma in situ that has been definitively treated with standard of care).
8. Impaired cardiac function or clinically significant cardiac diseases, including any of the following:
a. Unstable angina or acute myocardial infarction * 90 days prior to Screening;
b. Clinically significant heart disease (e.g. symptomatic congestive heart failure [e.g. >New York Heart Association [NYHA] Class 2]; uncontrolled arrhythmia, or hypertension; history of labile hypertension or poor compliance with an antihypertensive regimen.
9. Participant with a positive screening result for hepatitis B surface antigen, anti-hepatitis B core, hepatitis C, or HIV.
10. Participants with gastrointestinal tract disease (e.g. short bowel syndrome, diarrhoea predominant irritable bowel syndrome [IBS], celiac disease) that could interfere with the subject*s safety or pharmacodynamic effect of the monoclonal microbial.
11. Serious psychiatric or medical conditions that, in the opinion of the investigator, could interfere with treatment, compliance, or the ability to give consent.
12. Participant has a history of hypersensitivity or allergies to Lactococcus (or Lactococcus containing probiotics) including any associated excipients, 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 (hydroxyl propyl methyl cellulose and titanium dioxide), or has a known allergy against Alhydrogel®.
13. Participant has a history of Schistosomiasis (infection with Schistosoma parasite).
14. Participant has taken any over-the-counter (OTC) medication (with the exception of paracetamol and anti-histamines) within 14 days prior to Baseline (Day -1) or any prescription medications or nutraceuticals (e.g. supplements including high doses of probiotics and prebiotics, as usually found in capsules/tablets/powders) within 28 days prior to Baseline (Day -1) or

anticipates an inability to abstain from these products for the duration of the study period. Note that probiotic and prebiotic foods e.g. yoghurts that contain low doses are allowed.
15. Participant used probiotic capsules within 14 days prior to screening.
16. Participant has a significant history of drug abuse or regular use of illicit drugs or a history of alcohol abuse within 1 year prior to Screening.
17. Participant uses more than 10 cigarettes per day and/or is unable to refrain from cigarettes or tobacco use or other nicotine-containing products (e.g., patches) during 4 consecutive days.
18. Participant has donated more than 400 mL of blood or blood products within 90 days prior to Baseline (Day -1) or plans to donate blood during the study.
19. Participant has a diastolic blood pressure *50 or *90 mm Hg, or a systolic blood pressure *105 or *140 mm Hg at Screening or Baseline (Day -1) unless deemed to be not clinically significant by the investigator.
20. Participant has had an acute, clinically significant illness or major surgery within 30 days prior to screening.

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:	Completed
Start date (anticipated):	08-02-2019
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	EDP1066

Generic name:	N.A.

Ethics review

Approved WMO Date:	30-01-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-02-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-02-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-02-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-07-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-10-2019
Application type:	Amendment

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

ID: 27726
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2019-000166-38-NL
CCMO	NL68765.056.19
Other	NL7519

Study results

Date completed:	03-01-2020
Results posted:	01-04-2021

First publication
24-03-2021