Multiple ascending dose KLH antigen challenge study of EDP1815

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This study will investigate the potential of EDP1815 to modify the immune system through a Keyhole Limpet Haemocyanin (KLH) challenge. Furthermore, safety and tolerability of multiple oral doses of the monoclonal microbial EDP1815 will be assessed...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20845

Bron
Nationaal Trial Register

Verkorte titel
CHDR1829

Aandoening

Auto immune diseases

Ondersteuning

Primaire sponsor: Evelo Biosciences Inc.
Overige ondersteuning: Evelo Bioscience Inc.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

* KLH challenge
o Delayed type hypersensitivity after

intradermal KLH re-challenge. Response characterization by Laser Speckle Contrast Imaging and erythema by Antera 3D imaging
o Serology: anti-KLH IgM and IgG
o Ex vivo lymphocyte activation upon KLH re-challenge. Response characterization by ELISPOT.
* (Changes in) regulatory T cells
* Blood chemokine and cytokine levels

Toelichting onderzoek

Achtergrond van het onderzoek

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. These individual microbial strains are called monoclonal microbials. Since these monoclonal microbials are human commensal organisms they are likely to be well-tolerated and in addition are restricted to the gut when orally administered. 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.
EDP1815 is a monoclonal microbial of the species Prevotella histicola isolated from a subject in remission from coeliac disease (gluten free diet). Prevotella are natural human commensal organisms, commonly found on oral, nasopharyngeal, gastrointestinal, and genito-urinary mucosal surfaces. Preclinical studies using EDP1815 have been carried out across a range of human and mouse cell in vitro assays, as well as in 5 key in vivo models, which all support the use of this agent in the treatment of autoimmune diseases (See D1 Investigators Brochure in submission dossier)
In vitro, EDP1815 has been found to stimulate secretion of antiinflammatory cytokines such as interleukin (IL) 10, IL-27, and IL-1RA, from human macrophages and dendritic cells, whilst not inducing significant levels of pro inflammatory cytokines such as IL-17, IL-12, interferon gamma (IFN-γ) and granulocyte-macrophage colony stimulating factor (GM-CSF).
In vivo, EDP1815 has shown evidence of efficacy in the delayed type hypersensitivity (DTH) assay which is very similar to the KLH challenge assay included in this protocol. In addition to the DTH assay EDP1815 has shown beneficial effects in the dextran sulphate sodium (DSS) colitis, experimental allergic encephalomyelitis (EAE), fluorescein isothiocyanate

(FITC) cutaneous hypersensitivity, and collagen-induced arthritis (CIA) models of immunoinflammatory disease. No potentially related adverse effects were observed in the animals used in these experiments with daily dosing of up to 42 days. These data suggest that treatment with this monoclonal microbial strain of P. histicola could provide benefit in a range of auto-immune conditions including psoriasis, multiple sclerosis and rheumatoid arthritis.
EDP1815-101 is the first in human (FIH) study that has been conducted by an independent clinical research organization (CRO) in the United Kingdom (UK) with EDP1815 to date. Overall EDP1815 is considered safe and well tolerated in the first 4 cohorts of EDP1815-101 covering a dose range which will be evaluated in this study.
Please refer to the Development Safety Update Report (DSUR, included as L3 document in this Clinical Trial Application (CTA)) for a detailed description of the EDP1815-101 safety data.
There is preclinical evidence that exposure of the monoclonal microbial (EDP1815) to different parts of the GI tract are important for the mechanism of action and may affect the response to EDP 1815. Different formulations of EDP1815 are expected to result in monoclonal microbial exposure at different regions of the gastrointestinal tract. For this reason, the current study will compare different EDP1815 formulations.
The present study will test the following hypotheses:
- EDP1815 in powder formulation, administered via enteric coated capsules, induces a systemic immunomodulatory effect.
- EDP1815 in a mini-tablet formulation, administered via noncoated capsules, induces a systemic immunomodulatory effect.
This study will evaluate the effect of EDP1815 on the Keyhole Limpet Haemocyanin (KLH) challenge that was previously developed by CHDR. Furthermore, safety and tolerability of multiple oral doses of the monoclonal microbial EDP1815 will be assessed in healthy volunteers.

Doel van het onderzoek

This study will investigate the potential of EDP1815 to modify the immune system through a Keyhole Limpet Haemocyanin (KLH) challenge. Furthermore, safety and tolerability of multiple oral doses of the monoclonal microbial EDP1815 will be assessed in healthy volunteers.

Onderzoeksopzet

Day -1 – Day 40

Onderzoeksproduct en/of interventie

EPD1815 and antigen challenge

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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 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, 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 and for at least 1 complete menstrual cycle (≥30 days) after last dose.
5. CRP ≤ 10 mg/L and faecal calprotectin ≤ 150 mcg/g faeces
6. The 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. Subject needs to have sufficient space in a refrigerator to store the IMP during the ambulant dosing phase.
9. Participant has the ability to communicate well with the Investigator in the Dutch language and willing to comply with the study restrictions.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Female participant who is pregnant, or plans to become pregnant during the study, or breastfeeding, or sexually active with child-bearing potential who is not using a medically accepted birth control method.
2. Participant has received live attenuated vaccination within 6 weeks prior to Screening or intends to have vaccinations during the course of the study.
3. Participant has received any investigational drug or experimental procedure within 90 days or 5 half-lives, whichever is longer, prior to study intervention administration.
4. Participant was enrolled in an investigational drug or device study within 3 months prior to first dosing.
5. Participant requires treatment with an anti-inflammatory drug 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).
6. Participant has an active infection (e.g. sepsis, pneumonia, abscess) or recurrent infection, or has had an infection requiring antibiotic treatment within 6 weeks prior to Investigational Medicinal Product (IMP) administration.
7. Participant is diagnosed with tuberculosis (TB, as per positive skin test (Mantoux) or IFN-γ release assay), or history of TB, or latent TB, or recent contact with TB (patient); having travelled to countries where TB is endemic within eight weeks of planned drug administration or planning to travel to countries where TB is endemic from the
moment of drug administration until three months after the end of the study.
8. Patient requires prophylactic antibiotics for any reason

9. Participant has renal or liver impairment, defined as:
a. For women, serum creatinine level ≥ 125 µmol/L; for men, ≥ 135 µmol/L
b. An estimated creatinine clearance (MDRD formula) <60 mL/min
c. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≥ 1.5 x upper limit of normal (ULN), or
d. Alkaline phosphatase (ALP) and/or bilirubin > 2.5 x ULN
10. 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).
11. Impaired cardiac function or clinically significant cardiac diseases, including any of the following:
a. Unstable angina or acute myocardial infarction ≤ 3 months 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.
12. Participant with a positive screening result for hepatitis B surface antigen, anti-hepatitis B core, hepatitis C, or HIV.
13. 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.
14. Serious psychiatric or medical conditions that, in the opinion of the investigator, could interfere with treatment, compliance, or the ability to give consent.
15. The participant has a history of hypersensitivity or allergies to Prevotella (or Prevotella containing probiotics) including any associated excipients, or has a history of hypersensitivity or allergies to placebo capsule/powder (magnesium stearate and cellulose) or to the hard capsule shells (hydroxyl propyl methyl cellulose and titanium dioxide), or has a known allergy against Alhydrogel®.
16. Participant has a history of Schistosomiasis (infection with Schistosoma parasite).
17. The 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.
18. The participant uses probiotic capsules within 2 weeks prior to screening.
19. The 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.

20. The 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.
21. The participant intends to donate sperm during the course of this study and for a period of 90 days after the last dose.
22. The 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.
23. The 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.
24. The participant has had an acute, clinically significant illness or major surgery within 30 days prior to screening.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-01-2020
Aantal proefpersonen:	48
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Toelichting
N.A.

Ethische beoordeling

Positief advies

Datum:	20-05-2020
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 49769
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8676
CCMO	NL67464.056.18
OMON	NL-OMON49769

Resultaten

Samenvatting resultaten
N.A.