A double blind, placebo controlled Phase 2 dose ranging study of the effects of ARA 290 on corneal nerve fiber density and neuropathic symptoms of patients with sarcoidosis.

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The primary objective of this double blind study is to determine the effects of 1 mg, 4 mg, or 8 mg of ARA 290 administered subcutaneously for 28 consecutive days versus placebo on corneal nerve fiber density

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

Samenvatting

ID

NL-OMON23963

Bron
NTR

Verkorte titel
DOSARA

Aandoening

sarcoidosis (sarcoidose)
neuropathy (neuropathie)
pain (pijn)
eye exams (oogonderzoek)

Ondersteuning

Primaire sponsor: ARAIM Pharmaceuticals Inc
Overige ondersteuning: ARAIM Pharmaceuticals Inc

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The study primary endpoint is:
 change in corneal nerve fiber density at day 28 versus baseline

Toelichting onderzoek

Achtergrond van het onderzoek

Subjects will be initially seen at the research center/clinical site for a screening visit after informed consent is signed to collect demographic and medical information, measure vital signs, perform a physical examination, blood collection for general chemistry and hematology, measure corneal nerve fiber density, and complete questionnaires required for screening (BPI, RAND-36) and the 6-minute walk test.
Within 28 days of screening and after confirmation of initial eligibility, the subjects return to the research center for the start of the treatment period. Vital signs will be measured, and concomitant medication assessed. The subject will complete the BPI, RAND-36, modified COMPASS-31, FAS, NPSI, and SFNSL questionnaires. After eligibility is re-confirmed, subjects will be randomized to one
of the four treatment groups. A baseline corneal nerve fiber density will be obtained, a skin biopsy obtained from the ankle for determination of IENFD, the 6 minute walk test performed, and quantitative sensory testing and cardiac autonomic reflex testing will be performed. Candida and mumps antigens will be placed intradermally to test for anergy (subjects will self-evaluate injection site 48 hrs after placement.) Baseline blood sample for anti-ARA 290 antibodies will be obtained. Subjects will then receive the first injection at the research site, be trained for self-injection, receive a diary card and questionnaires to complete at home, and receive sufficient study medication for 2 weeks. Immediately following the first SC injection, an ECG will be obtained at 10 minutes post dose (peak plasma levels of ARA 290 occur at 6 minutes) to assess for potential changes in the QT interval. After the first injection, the subject is required to stay at the research center for 1 hour post dose for safety observation and any adverse events will be recorded.
Thereafter, the subjects will self-administer the study medication daily at home using individual vials and disposable insulin needles and syringes. They will revisit the clinic or be visited by one of the investigators every 14 ± 2 days of dosing during which a physical examination will be performed, vital signs, and blood samples collected, questionnaires completed and adverse events and

concomitant medication assessed. During each contact event the patient will return their completed diary cards/questionnaires, and used/unused study medication vials (if applicable) and will receive a new diary card/questionnaires and study medication supply (if applicable).
During the dosing and follow-up periods study personnel will contact the subjects by telephone bi-weekly, not on weeks when visiting the clinic, to assess for potential safety issues and confirm that questionnaires and diary cards have been filled out appropriately. During the follow-up period, questionnaires will be completed bi-weekly.
Subjects will visit the clinic after 28 ± 2 days of dosing, where the assessments listed above will be conducted, including a repeat anergy skin panel and excepting the anergy panel, again at day 56 ± 2 (an up to 2 day variance for all assigned visit days will be allowable).

Doel van het onderzoek

The primary objective of this double blind study is to determine the effects of 1 mg, 4 mg, or 8 mg of ARA 290 administered subcutaneously for 28 consecutive days versus placebo on corneal nerve fiber density

Onderzoeksopzet

The screening period is maximum 28 days. If greater than 28 days elapses, potential subjects will be rescreened.
The duration of the study will be 16 weeks: 4 weeks of daily self-administered SC dosing of ARA 290/placebo (study days 1-28) followed by a 12 week follow up period

Onderzoeksproduct en/of interventie

ARA 290 (1, 4 or 8 mg) or placebo injected subcutaneously daily for 28 consecutive days

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

The subjects will have to present the following criteria:

Established diagnosis of sarcoidosis with any of the following two criteria:

1) Score of 4 or greater on Brief Pain Inventory “pain now” or “average pain” questions (BPI; 0 (least discomfort)-10 (worst discomfort))

2) Discomfort defined as distal pain/discomfort plus one of the following: 1) dysesthesia, 2) burning/painful feet worsening at night, or 3) intolerance of sheets or clothes touching the legs or feetAND either of the following two criteria

1) Corneal nerve fiber density reduced compared to normal (i.e., greater than 1 standard deviation less than the mean of a normative population)
2) A previous skin biopsy (obtained within the prior 2 years) showing a reduced intraepidermal nerve fiber density ((i.e., greater than 1 standard deviation less than the mean of a normal age and gender relevant population)

In addition, subjects must:

 Be able to read and understand the written consent form, complete studyrelated procedures, and communicate with the study staff

 Be willing to comply with study restrictions

 Be willing to check in with the study center via the telephone

 Between 18 and 70 years of age (inclusive)

 Body Mass Index (BMI) < 35 kg/m2 (inclusive)

 If female of childbearing potential, a negative urine pregnancy test at screening and acceptable contraception will be maintained during the screening and dosing period and 1 month beyond. Acceptable contraception consists of hormonal methods such as oral, implantable, injectable, or transdermal contraceptives for a minimum of 1 full cycle (based on the patient’s usual menstrual cycle period) before study entry, intrauterine device (IUD), or double-barrier method (condoms, sponge, diaphragm, or vaginal ring with spermicidal jellies or cream).

 Able to complete self-administered questionnaires (RAND-36, SFNSL, BPI, COMPASS-31, FAS, NPSI)

 Refrigerator at home for storage of study medication.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

The subjects should not present any of the following criteria:

 Clinically relevant abnormal history of physical and mental health other than conditions related to sarcoidosis, as determined by medical history taking (as judged by the investigator)

 Clinically relevant abnormal laboratory results, vital signs, or physical findings other than conditions related to sarcoidosis (as judged by the investigator) or could interfere with conduct of 6-minute walk assessment

 Known clinically relevant abnormalities in ECG (as judged by the investigator)

 Illicit drug abuse or excessive alcohol consumption (as judged by the investigator)

 History of serious malignancy within the last 5 years other than a basal cell or squamous cell carcinoma that has been removed

 History of fainting (as judged by the investigator)

 History of severe allergies, or has had an anaphylactic reaction or significant intolerability to prescription or non-prescription drugs or food (as judged by the investigator)

 Anti-TNF therapy or other biological anti-inflammatory agents administered

within the 6 months prior to screening.

 Use of erythropoiesis stimulating agents within the two months prior to screening or during the trial

 Participation in an investigational drug trial in the 3 months prior to administration of the initial dose of study drug or more than 4 times in the calendar year preceding study enrollment

 Inadequate venous accessibility as judged by clinicians (physician or nurse)

 Inability or unwillingness to self-administer ARA 290 via subcutaneous injections (or not have access to home health care for assistance in administration)

 If female, pregnant or breast-feeding

 Any other condition that in the opinion of the investigator would complicate or compromise the study, or the well-being of the patient

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-01-2014
Aantal proefpersonen:	64
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	07-11-2013
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL4017
NTR-old	NTR4260
Ander register	P13.173 : DOSARA
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A