A pilot study towards a therapy with prednisolone encapsulated liposomes for the treatment of Graves* Orbitopathy with reduced systemic steroid exposure

Published: 10-04-2017
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To demonstrate that Nanocort is safe and effectively reduces the inflammatory signs and symptoms of active GO.

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

Summary

ID

NL-OMON45340

Source
ToetsingOnline

Brief title
GO Nanocort

Condition

- Eye disorders NEC

Synonym
Graves' orbitopathy

Research involving
Human

Sponsors and support

Primary sponsor: Oogziekenhuis Rotterdam
Source(s) of monetary or material Support: Enceladus Pharmaceuticals,Rotterdamse

Stichting Blindenbelangen

Intervention

Keyword: Graves' orbitopathy, Liposomal steroids, Reduced systemic steroid exposure

Outcome measures

Primary outcome

Number of patients with a predefined response to treatment.

Secondary outcome

See protocol.

Study description

Background summary

The mainstay of treatment for patients with moderate to severe Graves* Orbitopathy (GO) currently consists of various dose schemes of intravenous (IV) methylprednisolone or high doses oral prednisone. To avoid the frequent and potentially serious adverse effects of such treatment, new immunomodulating therapies are required. In a small study, IV administration of long-circulating liposomal prednisolone (Nanocort, LCLP) has been shown effective in rheumatoid arthritis without causing the typical glucocorticoid-related adverse events (AEs). It is hypothesized that GO can also be effectively treated with LCLP and that the number of AEs will be reduced.

Study objective

To demonstrate that Nanocort is safe and effectively reduces the inflammatory signs and symptoms of active GO.

Study design

Open label, multicentre, dose-escalating study (phase I/II).

Intervention

The first 10 subjects in this trial will be treated with 150 mg/infusion of Nanocort administered IV at week 0 and 2. Infusion will take approximately 2.5 hours. If three or more of these patients respond to treatment, another cohort

of 10 subjects will be treated with 150 mg/infusion of Nanocort administered IV at week 0, 2 and (if applicable) 4.

Study burden and risks

The incidence of infusion reactions to liposomes (empty placebo as well as drug-loaded) is not unlike that for other colloidal formulations and biologics: 5-10%. AEs (possibly) associated with Nanocort appear to be manageable. Compared to conventional therapy, the study regimen (i.e. treatment and control visits together) involves reduced burden (12 hospital visits versus 8) and reduced steroid dose (total 4500/7500 mg methylprednisolone versus 300/450 mg Nanocort). In consequence of the lower steroid dose, it has to be expected that the incidence of AEs which are associated with sytemic steroid exposure will be less.

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

1. Male or female * 18 years old.
2. Informed consent.
3. Patients are able and willing to complete the study (12 months follow-up).
4. Active GO, defined as Clinical Activity Score (CAS) * 3.
5. Moderate to severe GO (Bartalena et al. 2016):
6. Euthyroidism for at least 3 months with antithyroid drugs or following thyroidectomy, or 6 months following radioiodine administration.

Exclusion criteria

1. Sight threatening GO due to optic neuropathy (decrease of (pinhole) vision, visual field loss, prolonged VEP, diminished colour vision) or severe keratopathy.
2. Any concurrent illness, disability or clinically significant abnormality that may, as judged by the investigator, affect the interpretation of clinical efficacy or safety data or prevent the subject from safely completing the assessments required by the protocol.
3. Current participation in another interventional clinical trial (with subjects having received an investigational drug within 30 days prior to the baseline visit).
4. Treatment with oral, rectal or injectable (including intra-articular) glucocorticoids within 6 weeks prior to baseline visit. Inhaled glucocorticoids are allowed. Topical steroids are allowed, however subjects should not have received more than 100 gram of a mild to moderate topical corticosteroid cream per week, 50 gram of a potent corticosteroid cream per week or 30 gram of a very potent topical corticosteroid cream per week in the 4 weeks prior to the baseline visit.
5. Patients who are unlikely to adequately comply with the trial*s procedures (due for instance to medical conditions likely to require an extended interruption or discontinuation, history of substance abuse or noncompliance).
6. Women who are lactating, pregnant (positive pregnancy test at screening) or planning to become pregnant during the course of the study.
7. Unwillingness to use reliable and acceptable contraceptive methods untill 3 months after last study medication except for female patients who are surgically sterile (bilateral tubal ligation, bilateral oophorectomy or hysterectomy) or at least 1 year postmenopausal
8. Uncontrolled Diabetes Mellitus.
9. History of a psychiatric disease (psychosis, depression, mania).
10. History of or active hepatitis or Human immunodeficiency virus.
11. Abnormal hepatic function (ALT/AST or bilirubin > 2 x upper limit of normal) at screening.
12. Abnormal renal function (Blood Urea Nitrogen or creatinine >1.25 x upper limit of normal) at screening.
13. Signs of active infection, requiring systemic treatment.
14. Major surgery within the 60 Days prior to screening or planned surgery during study period.
15. Malignant disease, unless cured.

16. Clinically significant out-of-range values on hematology panel, at discretion of the PI.
17. Poor peripheral venous access (as per Investigator or site personnel opinion).
18. Current substance abuse or alcohol abuse.
19. Contraindications for MRI.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-11-2017
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nanocort
Generic name:	long-circulating liposomal prednisolone (LCLP)

Ethics review

Approved WMO

Date:	10-04-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	20-07-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-01-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-03-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-04-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-10-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-11-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-04-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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: 24926
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2017-001158-33-NL
CCMO	NL61298.078.17
OMON	NL-OMON24926