PROSPECTIVE, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PHASE III STUDY EVALUATING EFFICACY AND SAFETY OF OCTAGAM 10% IN PATIENTS WITH DERMATOMYOSITIS

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Primary Objective:The primary objective of this study is to provide confirmatory data on the beneficial effect of 2.0 g/kg of Octagam 10% given every 4 weeks compared with placebo in subjects with active DM based on the percentage of responders at...

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

Summary

ID

NL-OMON46776

Source
ToetsingOnline

Brief title
(ProDERM Study)

Condition

- Autoimmune disorders
- Muscle disorders

Synonym
Dermatomyositis, DM

Research involving
Human

Sponsors and support

Primary sponsor: Octapharma Pharmazeutika Produktionsges m.b.H.
Source(s) of monetary or material Support: by Octapharma

Intervention

Keyword: Dermatomyositis, Octagam 10%

Outcome measures

Primary outcome

Primary Efficacy Endpoints:

* Proportion of responders in the 2.0 g/kg Octagam 10% and placebo arms at Week

16. A responder is defined as a subject with an increase from baseline (Week 0)

of *20 points on the Total Improvement Score (TIS).

Safety Endpoints:

Safety (throughout the entire First and Extension Period):

* Occurrence of all adverse events with particular emphasis on thromboembolic

events (TEEs) and hemolytic transfusion reactions (HTRs).

* Vital signs (blood pressure, heart rate, body temperature and respiratory

rate).

* Physical examination (at Screening and every 12 weeks from Week 4 on).

* Laboratory parameters (hematology, clinical chemistry).

Safety (at Baseline and end of Extension Period):

* Tests for viral safety.

* Pregnancy test, if applicable.

Secondary outcome

SecondaryEfficacy Endpoints:

* Proportion of TIS responders by improvement category (minimal, moderate,

major) at Week 16 and Week 40.

* Mean change from baseline (Week 0) to end of First Period (Week 16) in the

modified Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI).

* Mean change from end of First Period (Week 16) to end of Extension Period

(Week 40) in the modified CDASI.

* Mean change from Baseline (Week 0) to end of First Period (Week 16) and

Extension Period (Week 40) in:

o SF-36v2 Health Survey;

o Individual 6 CSM used for TIS calculation.

* Mean change in TIS from Baseline (Week 0) to end of First Period (Week 16)

and from Baseline (Week 0) to end of Extension Period (Week 40).

* Time to minimal, moderate and major improvement in TIS.

* Time to confirmed deterioration in the First Period and overall.

Study description

Background summary

Octagam 10% is a solution for intravenous administration, which contains human antibodies also called immunoglobulins. It is manufactured by Octapharma. Octagam 10% got its first license in May 2008 and is now approved in 55 countries worldwide.

Intravenous human immunoglobulins (IVIGs) are increasingly used in the treatment of patients with a variety of autoimmune and inflammatory neurological disorders. In a previous study with 15 patients having dermatomyositis (DM), the use of IVIGs has shown positive results. So far, no studies have been performed with Octagam 10% in the treatment of DM.

Dermatomyositis is a rare disease, characterized by inflammation of the muscles and the skin. The muscle inflammation leads to muscle weaknesses, for example in the legs and the arms. The skin inflammation leads to skin rash.

The mechanism of action of immunoglobulins in DM has not been fully cleared up; however, IVIGs have become part of a recommended second-line treatment option for patients with DM.

Study objective

Primary Objective:
The primary objective of this study is to provide confirmatory data on the beneficial effect of 2.0 g/kg of Octagam 10% given every 4 weeks compared with placebo in subjects with active DM based on the percentage of responders at Week 16.

Secondary Objectives:
The secondary objectives of this study are
* to evaluate the beneficial effect of Octagam 10% in subjects with active DM by assessing different parameters and scores at Week 16 and Week 40;
* to confirm the sustained benefit of treatment with Octagam 10% by assessing the primary response measures at Week 40;
* to evaluate the safety and tolerability of Octagam 10% in subjects with DM.

Study design

Prospective, parallel group, double-blind, randomized, placebo-controlled, multicenter Phase III study with a controlled 16-week efficacy period followed by a 24-week open-label extension period.

Intervention

First Period (Octagam 10% vs. placebo in double-blind design): 2.0 g/kg (20 mL/kg) Octagam 10% or 20 mL/kg placebo given over 2 to 5 days at 4-week intervals (in total 4 infusion cycles).

Extension Period: 2.0 g/kg (20 mL/kg) Octagam 10% given over 2 to 5 days at 4-week intervals (in total 6 infusion cycles). At Week 28, subjects who are stable on 2.0 g/kg Octagam 10% can be switched to 1.0 g/kg (10 mL/kg) Octagam 10%, at the discretion of the investigator.

Study burden and risks

There will be physical discomfort due to intravenous infusion. Next to this, several quality of life questionnaires needs to be completed. This could cause

psychological discomfort.

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.Subjects with diagnosis of definite or probable DM according to the Bohan and Peter criteria.;2.Subjects under treatment with corticosteroids and/or maximally 2 immune-suppressants and being on stable therapy for at least 4 weeks (see Section 4.2.1) OR Subjects with previous failure of response or previous intolerance to corticosteroid and at least 1 additional immunosuppressive drug, and with steroid/immunosuppressive drugs washed out as per Section 4.2.1 (Table 2). ;3. Subjects with active disease, assessed and agreed upon by an independent adjudication committee. being on stable therapy for at least 4 weeks.;4. Manual Muscle Testing-8 (MMT-8) score <142, with at least 2 other abnormal Core Set Measures (CSM) (Visual Analogue Scale [VAS] of patient global activity *2 cm,

physician*s global disease activity *2 cm, extra-muscular activity *2 cm; at least one muscle enzyme >1.5 times upper limit of normal, Health Assessment Questionnaire *0.25).;5. Males or females * 18 to < 80 years of age.;6. Voluntarily given, fully informed written consent obtained from subject before any study-related procedures are conducted.;7. Subject must be capable to understand and comply with the relevant aspects of the study protocol.

Exclusion criteria

1. Cancer-associated myositis, defined as the diagnosis of myositis within 2 years of the diagnosis of cancer (except basal or squamous cell skin cancer or carcinoma in situ of the cervix that has been excised and cured and at least 1 or 5 years, respectively have passed since excision).;2. Evidence of active malignant disease or malignancies diagnosed within the previous 5 years (including hematological malignancies and solid tumors) or breast cancer diagnosed within the previous 10 years.;3. Subjects with overlap myositis (except for overlap with Sjögren*s syndrome), connective tissue disease associated DM, inclusion body myositis, polymyositis, juvenile dermatomyositis or drug-induced myopathy.;4. Subjects with immune-mediated necrotizing myopathy with absence of typical DM rash.;5. Subjects with generalized, severe musculoskeletal conditions other than DM that prevent a sufficient assessment of the subject by the physician.;6. Subjects who have received IgG treatment within the last 6 months before enrolment.;7. Subjects who received blood or plasma-derived products (other than IgG) or plasma exchange within the last 3 months before enrolment.;8. Subjects starting or planning to start a physical therapy*directed exercise regimen during the trial.;9. Cardiac insufficiency (New York Heart Association III/IV), cardiomyopathy, significant cardiac dysrhythmia requiring treatment, unstable or advanced ischemic heart disease.;10. Severe liver disease, with signs of ascites and hepatic encephalopathy.;11. Severe kidney disease (as defined by estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m2).;12. Known hepatitis B, hepatitis C or HIV infection.;13. Subjects with a history of deep vein thrombosis within the last year prior to study enrollment or pulmonary embolism ever.;14. Body mass index *40 kg/m2.;15. Medical conditions whose symptoms and effects could alter protein catabolism and/or IgG utilization (e.g. protein-losing enteropathies, nephrotic syndrome).;16. Known IgA deficiency with antibodies to IgA.;17. History of hypersensitivity, anaphylaxis or severe systemic response to immuno-globulin, blood or plasma derived products or any component of Octagam 10%.;18. Known blood hyperviscosity, or other hypercoagulable states.;19. Subjects with a history of drug abuse within the past 5 years prior to study enrollment.;20. Subjects unable or unwilling to understand or comply with the study protocol.;21. Participating in another interventional clinical study with investigational treatment within 3 months prior to study enrollment.;22.Women who are breast feeding, pregnant, or planning to become pregnant, or are unwilling to apply an effective birth control method (such as implants, injectables, combined oral contraceptives, some intrauterine devices [IUDs], sexual abstinence or vasectomized partner) up to four weeks after the last IMP infusion.;23.Subjects who are accommodated in an institution or care facility based on an official directive or court order.;24.Subjects who are in any way dependent on the Sponsor, Investigator or Study Site.;25.Subjects who received forbidden medication within the washout period as defined in Section 4.2.2 (Table 3).

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-07-2018
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Octagam 10%
Generic name:	Immune Globulin Intravenous, Human 10%
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	24-01-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-06-2018
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-11-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2016-002902-37-NL
CCMO	NL64255.018.17