ISRCTN11520709 https://doi.org/10.1186/ISRCTN11520709

Efficacy and safety of Octanorm in patients with dermatomyositis

Submission date
25/06/2018

Recruitment status
Stopped

Registration date
18/09/2018

Overall study status
Stopped

Last Edited
07/12/2018

Condition category
Musculoskeletal Diseases

- [ ] Prospectively registered
- [ ] Protocol
- [ ] Statistical analysis plan
- [ ] Results
- [ ] Individual participant data
- [ ] Record updated in last year

Plain English summary of protocol

Background and study aims
This trial is being carried out to investigate the efficacy, safety, and tolerability of subcutaneous human immunoglobulin (Octanorm) in patients with dermatomyositis (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.
This will be the first clinical study with Octanorm in patients with dermatomyositis although a couple of clinical trials with Octanorm in patients with primary immunodeficiency (PID) have been conducted at several locations in Europe, Russia, Canada and USA; In total 59 patients have been treated and received 2666 infusions of Octanorm. Recently, Canada was the first country to license Octanorm in PID.

Who can participate?
Dermatomyositis must have been diagnosed in accordance with international guidelines and the patient should have responded to intravenous immunoglobulin (IVIG) therapy within GAM10-08 study (clinical study conducted by Octapharma to assess efficacy and safety of Octagam 10% (IVIG) in patients with DM) or to any other commercially available IVIG, based on the opinion of the patient´s physician.

What does the study involve?
Participants are randomly assigned 1:1 into two groups, receiving either octanorm or placebo. Octanorm, manufactured by Octapharma, is a solution for subcutaneous (SC) administration, which contains human antibodies also called immunoglobulins. “Subcutaneous” means under the skin.
Intravenous (IV) administration of immunoglobulins have become part of a recommended second-line treatment option for patients with DM. Immunoglobulins administered subcutaneously are likely to show the same efficacy as those administered by IV route.

What are the possible benefits and risks of participating?
Despite its well-established safety profile, intravenous treatment often leads to undesired adverse reactions. Due to the slower administration of the medication it is expected that subcutaneous treatment has a lower incidence of systemic adverse events. As a participant of

the clinical study patients will be placed under careful medical observation. Participation may also bring scientific benefit and therapeutic benefit for other current or future DM patients. Risks of participating involve the minor risks associated with repeated blood tests, such as pain, bruising or infection

Where is the study run from?
This study is performed in various countries at about 45 sites worldwide. It is expected that approximately 78 patients will take part in this study. The participation in this clinical study will last for about 35 week per patient.

When is study starting and how long is it expected to run for?
Study duration:June 2018 until May 2020

Who is funding the study
Octapharma Pharmazeutika Produktionsges.m.b.H., Vienna
Main Contact: Tatiana Lavrova (tatiana.lavrova@octapharma.com), Global Clinical Project Management

Contact information

Type(s)
Scientific

Contact name
Mrs Tatiana Lavrova

Contact details
Octapharma Pharmazeutika Produktionsges.m.b.H.
Oberlaaer Str. 235 | A-1100 Vienna, Austria
Vienna
Austria
1100

Type(s)
Scientific

Contact name
Mrs Hemma Juch

Contact details
Octapharma Pharmazeutika Produktionsges.m.b.H.
Oberlaaer Str. 235 | A-1100 Vienna, Austria
Vienna
Austria
1100

Additional identifiers

Clinical Trials Information System (CTIS)
2017-002710-31

Protocol serial number
SCGAM-02

Study information

Scientific Title
Double-blind, randomized, placebo-controlled phase III study evaluating efficacy and safety of subcutaneous human immune globulin (Octanorm) in patients with dermatomyositis

Study objectives
There is a difference in the proportions of patients with clinically important deterioration in the Octanorm arm (Po) versus the placebo arm (Pp)

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Ethik-Kommission der Medizin, Fakultät der Georg-August Universität Göttingen, Göttingen, 20/08/2018, 34/3/18
2. Central Ethics Committee of the Faculty Hospital Kralovske, Prague, 27/06/2018, MEK/09/0 /2018
3. Comisia Nationala de Bioetica a Medicamentului si a Dispozitivelor Medicale (National Bioethics Committee for Medicines and Medical Devices), Bucharest, 16/07/2018, 31S-16.07.2018
4. Egészségügyi Tudományos Tanács Klinikai Farmakológiai Etikai Bizottsága (Medical Research Council Ethics Committee for Clinical Pharmacology), Budapest, 28/06/2018, 32252-0/2018-EKL
5. Komisja Bioetyczna przy Narodowym Instytucie Geriatrii, Reumatologii i Rehabilitacji w Warszawie, Warsaw, approval expected 31/08/2018
6. Council of Ethics at the Ministry of Health of Russia, Moscow, 12/07/2018, Ministry of Health CEC Case Number: 4069 298-20-1-ES, Extract #169 (Internal Number 53244)

Primary study design
Interventional

Study design
Double-blind randomized placebo-controlled phase III trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Dermatomyositis

Interventions
All subjects qualified to participate in the study at baseline will be block randomized to one of the two treatment arms by an electronic IRT tool. The randomization will apply a randomization ratio of 1:1 with respect to Octanorm and placebo. If a subject is randomized to receive placebo, the same volume with the same infusion rate as would have been applied if the subject was randomized to 0.5 g/kg Octanorm 16.5% will be used.
Octanorm or placebo will be administered subcutaneously every week (±2 days) using a syringe driver for precise infusion rates. The total dose/volume of a weekly infusion will be calculated on

the basis of body weight. The weekly infusion will be performed in two separate sessions (equivalent to one infusion cycle for a given weekly administration). An infusion cycle comprises both sessions to be administered on one or two days, either on the same day or on two consecutive days or with maximum 1 day in between the two sessions.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Octanorm (16.5% human immune globulin)

Primary outcome(s)
1. Muscle strength assessed using MMT-8 (manual muscle testing of 8 designated muscles tested bilaterally [potential score 0-150]) at week 32
2. Cutaneous disease activity assessed using Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) at week 32
3. Disease activity at week 32 assessed using Physician's Global Disease Activity on a visual analog scale (VAS) assessing global disease activity from “No evidence of disease activity” to “Extremely active or severe disease activity”, with disease activity being defined as potentially reversible pathology or physiology resulting from the myositis)

Key secondary outcome(s)
4. Extra-muscular disease activity at baseline and week 32 assessed using Myositis Disease Activity Assessment Tool (MDAAT), a combined tool that captures the physician’s assessment of disease activity of various organ systems using a scale from 0 = “Not present in the last 4 weeks” to 4 = “New - in the last 4 weeks (compared to the previous 4 weeks)” and a VAS.
5. Muscle damage assessed using blood aldolase, creatine kinase, alanine aminotransferase, aspartate aminotransferase and lactate dehydrogenase levels at baseline and week 32
6. Disability assessed using Health Assessment Questionnaire (HAQ) at baseline and week 32. HAQ is a generic rather than a disease-specific instrument; consisting of 8 sections: dressing, arising, eating, walking, hygiene, reach, grip, and activities. There are 2 or 3 questions for each section. Scoring within each section is from 0 [without any difficulty] to 3 [unable to do]. For each section the score given to that section is the worst score within the section. The 8 scores of the 8 sections are summed and divided by 8.
7. Patient-reported health assessed using SF-36 v2 Health Survey at baseline and week 32. The SF-36 is a multi-purpose, short-form health survey with only 36 questions. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures and a preference-based health utility index.
8. Improvement in patient-reported health assessed using Total Improvement Score (TIS) at week 32.
9. Time to clinically important deterioration defined as worsening of Core Set Measures and/or CDASI during the treatment period (Weeks 0, 4, 8, 12,16, 20, 24 and 28)
10. List of deviations from protocol requirements relating to home treatment: (e.g. dosing, timing) documented at weeks 4, 8,12, 16, 20, 24 and 28
11. Occurrence of all adverse events with particular emphasis on thromboembolic events (TEEs) and haemolytic transfusion reactions (HTRs) documented at weeks 0, 4, 8, 12,16, 20, 24, 28 and 32
12. Local injection site reactions documented at weeks 0, 4, 8, 12, 16, 20, 24, 28 and 32

13. Vital signs (blood pressure, heart rate, body temperature and respiratory rate) documented at weeks -2 to 0, 0, 4, 8, 12, 16, 20, 24, 28 and 32
14. Physical examination documented at weeks -2 to 0, 0, 4, 8, 12, 16, 20, 24, 28 and 32
15. Laboratory parameters (hematology, clinical chemistry, urinalysis) documented at weeks -2 to 0, 0, 4, 8, 12, 16, 20, 24, 28 and 32
16. Tests for viral safety at baseline and end of treatment period
17. Pregnancy test, if applicable, at baseline and end of treatment period

Completion date
31/03/2020

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Diagnosis of definite or probable DM according to the Bohan and Peter criteria
2. Responded to IGIV (intravenous immunoglobulin) treatment as assessed by the treating physician and on a stable dose for at least 3 months on 2 g/kg bodyweight (+/- 10%).
3. If on other medication(s) for the treatment of DM (immunosuppressants, corticosteroids):
3.1. Receiving these medication(s) at the start of IGIV treatment in the first place
3.2. Receiving these medication(s) for at least 3 months prior to study enrolment and at a stable dose for at least 4 weeks prior to study enrolment
4. MMT-8 score ≥144, with at least 3 of the 5 other core set measures to be normal or near normal as per the following criteria:
4.1. Visual Analogue Scale (VAS) of patient global disease activity ≤2 cm
4.2. Physician’s global disease activity ≤2 cm,
4.3. Extra-muscular disease activity ≤2 cm
4.4. No muscle enzyme >4x upper limit of normal due to myositis
4.5. Health Assessment Questionnaire (HAQ) ≤0.25.
5. Aged ≥18 to <80 years
6. Voluntarily given, fully informed written consent obtained from subject before any study-related procedures are conducted
7. Capable and willing to understand and comply with the relevant aspects of the study protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key 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. Subjects >5 years (>10 years for breast cancer) of cancer diagnosis who have been treated and are in remission are allowed
3. Overlap myositis (except for overlap with Sjögren's syndrome), connective tissue disease associated DM, inclusion body myositis, polymyositis or drug-induced myopathy
4. Immune-mediated necrotizing myopathy with absence of typical DM rash
5. Generalized, severe musculoskeletal conditions other than DM that prevent a sufficient assessment of the subject by the physician
6. Received blood or plasma-derived products (other than IGIV) or plasma exchange within the last 3 months before enrolment
7. Receiving permitted concomitant medications exceeding the maximally allowed conditions as above
8. Received non-permitted concomitant medications within the washout periods
9. Starting or planning to start a physical therapy–directed exercise regimen during the trial. Subjects on stable physical therapy for >4 weeks are allowed but the regimen should remain the same throughout the trial
10. Cardiac insufficiency (New York Heart Association III/IV), cardiomyopathy, significant cardiac dysrhythmia requiring treatment, unstable or advanced ischemic heart disease
11. Severe liver disease, with signs of ascites and hepatic encephalopathy
12. Severe kidney disease (as defined by estimated glomerular filtration rate (eGFR) < 30 ml/min /1.73 m2)
13. Known hepatitis B, hepatitis C or HIV infection
14. History of deep vein thrombosis within the last year prior to study enrolment or pulmonary embolism ever
15. Body mass index >40 kg/m2 and/or body weight >120 kg
16. Medical conditions whose symptoms and effects could alter protein catabolism and/or IgG utilization (e.g. protein-losing enteropathies, nephrotic syndrome)
17. Known IgA deficiency with antibodies to IgA
18. History of hypersensitivity, anaphylaxis or severe systemic response to immunoglobulin, blood or plasma derived products or any component of Octanorm 16.5% such as polysorbate 80 or to sodium chloride
19. Known blood hyperviscosity, or other hypercoagulable states
20. Subjects with a history of drug abuse within the past 5 years prior to study enrolment
21. Participating in another interventional clinical study with investigational treatment within 3 months prior to study enrolment. Subjects who participated in the Octagam 10% Dermatomyositis Study (GAM10-08) can be included
22. Women who are breast feeding, pregnant, or planning to become pregnant, or are unwilling to apply an effective birth control method up to 4 weeks after the last Octagam infusion received

Date of first enrolment

02/08/2018

Date of final enrolment

30/09/2019

Locations

Countries of recruitment
Czech Republic

Germany

Hungary

Netherlands

Poland

Romania

Russian Federation

United States of America

Study participating centre
UNIVERSITY OF DEBRECEN DEPARTMENT OF INTERNAL MEDICINE III
Móricz Zs. Krt. 22
Debrecen
Hungary
H-4032

Study participating centre
UNIVERSITY OF SZEGED, ALBERT SZENT-GYÖRGYI MEDICAL CENTER
DEPARTMENT OF DERMATOLOGY AND ALLERGOLOGY
Korányi Fasor 6
Szeged
Hungary
H-6720

Study participating centre
UNIVERSITY MEDICAL CENTER GÖTTINGEN DEPARTMENT OF NEUROLOGY
Robert-Koch-Str.40
Göttingen
Germany
37075

Study participating centre

UNIKLINIKUM MÜNSTER, KLINIK FÜR HAUTKRANKHEITEN
Von Esmarch-Str. 58
Münster
Germany
48149

Study participating centre
NARODOWY INSTYTUT GERIATRII, REUMATOLOGII I REHABILITACJI
Klinika I Poliklinika Układowych Chorób Tkanki Łącznej
Spartanska 1
Warszawa
Poland
02-637

Study participating centre
CENTRUM MEDYCZNE PLEJADY
Ul. Tadeusza Szafrana 5d/u2, U4, U5
Krakow
Poland
30-363

Study participating centre
REVMATOLOGICKÝ ÚSTAV
Na Slupi 450/4
Prague
Czech Republic
128 50

Study participating centre
EMERGENCY COUNTY CLINICAL HOSPITAL
Clinicilor Str. 4-6
Cluj Napoca
Romania
400006

Study participating centre
SPITALUL CLINIC JUDETEAN MURES
12, Gheorghe Doja Str.
Targu-Mures
Romania
540342

Study participating centre
SPITALUL CLINIC "SF. MARIA"
37-39, Ion Mihalache Blvd
Bucharest
Romania
011172

Study participating centre
CAMPUS CHARITÉ MITTE, UNIVERSITÄTSMEDIZIN BERLIN, ALLERGIE-CENTRUM-CHARITÉ,
KLINIK FÜR DERMATOLOGIE, VENEROLOGIE UND ALLERGOLOGIE
Charitéplatz 1
Berlin, 10117
Germany
10117

Study participating centre
KLINIK FÜR DERMATOLOGIE UND ALLERGOLOGIE UNIVERSITÄTSKLINIKUM GIEßEN UND MARBURG GMBH,
STANDORT MARBURG
Baldingerstraße
Marburg, 35043
Germany
35043

Study participating centre
SEMMELWEIS UNIVERSITY, FACULTY OF MEDICINE DEPARTMENT OF DERMATOLOGY, VENEREOLOGY AND DERMATOONCOLOGY
Maria U.41
Budapest, H-1085
Hungary
H-1085

Study participating centre
LLC "AVA-PETER"
22-24 P.A Premises 50-h, Nevsky Prospect
St-Petersburg, 191186
St-Petersburg, 191186
Russian Federation
191186

Study participating centre
V.A. NASSONOVA RESEARCH RHEUMATOLOGY INSTITUTE
V.A. NASSONOVA RESEARCH RHEUMATOLOGY INSTITUTE
34a Kashirskoe Shosse
Moscow, 115522
Moscow, 115522
Russian Federation
115522

Study participating centre
I.M. SECHENOV FIRST MOSCOW STATE MEDICAL UNIVERSITY Rheumatology Department Of Clinici Of Nephrology
11/5 Rossolimo Str
Moscow, 119992
Moscow, 119992
Russian Federation
119992

Study participating centre
ORENBURG STATE MEDICAL UNIVERSITY BASED ON REGIONAL CLINICAL HOSPITAL
23 Aksakova
Orenburg, 460018
Orenburg, 460018
Russian Federation
460018

Sponsor information

Organisation
Octapharma Pharmazeutika Produktionsges.m.b.H.

ROR
https://ror.org/022k50n33

Funder(s)

Funder type
Not defined

Funder Name
Octapharma Pharmazeutika Produktionsges.m.b.H.

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Not provided at time of registration