# Efficacy and safety of Octanorm in patients with dermatomyositis

Submission date 25/06/2018	<b>Recruitment status</b> Stopped	<ul> <li>Prospectively registered</li> <li>Protocol</li> </ul>
<b>Registration date</b> 18/09/2018	<b>Overall study status</b> Stopped	<ul> <li>Statistical analysis plan</li> <li>Results</li> </ul>
Last Edited 07/12/2018	<b>Condition category</b> Musculoskeletal Diseases	<ul> <li>Individual participant data</li> <li>Record updated in last year</li> </ul>

### 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**

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# Additional identifiers

**EudraCT/CTIS number** 2017-002710-31

### **IRAS number**

ClinicalTrials.gov number

Secondary identifying numbers 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

 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
 Egészségügyi Tudományos Tanács Klinikai Farmakológiai Etikai Bizottsága (Medical Research Council Ethics Committee for Clinical Pharmacology), Budapest, 28/06/2018, 32252-0/2018-EKL
 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)

### Study design

Double-blind randomized placebo-controlled phase III trial

### Primary study design

Interventional

## Secondary study design

Randomised controlled trial

**Study setting(s)** Hospital

**Study type(s)** Treatment

### Participant information sheet

Not available in web format, please use contact details to request a participant information sheet.

### 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 measure

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)

### Secondary outcome measures

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

### Overall study start date

19/04/2018

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  $\leq 2$  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 studyrelated procedures are conducted

7. Capable and willing to understand and comply with the relevant aspects of the study protocol

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

# Target number of participants

In total, 78 adult male or female subjects with DM who have responded to treatment with intravenous immunoglobulin, and have been on a stable dose of 2g/kg BW (+/- 10%) for at least 3 months will be enrolled into the study

## 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.

### Sponsor details

Oberlaaer Str. 235 A-1100 Vienna, Austria Vienna Austria 1100

**Sponsor type** Industry

ROR https://ror.org/022k50n33

# Funder(s)

Funder type Not defined

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

# **Results and Publications**

**Publication and dissemination plan** Planned publication in a high-impact peer-reviewed journal

# Intention to publish date 31/03/2020

### 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