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Efficacy and safety of L0133 in the treatment of dermatomyositis and polymyositis: prospective, randomised, double-blind, placebo-controlled study

Submission date 23/10/2006	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 21/12/2006	**Overall study status** Completed	
Last Edited 01/10/2012	**Condition category** Skin and Connective Tissue Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

L00133 IV 301 (ORF)

Study information

Scientific Title

Study objectives
Primary objective:
To assess the efficacy of the L0133 product as adjunctive treatment to conventional glucocorticosteroids (GS) and immunosuppressors (IS) in dermatomyositis (DM) and polymyositis (PM) patients with insufficient improvement of muscle strength.

Secondary objective:
To assess the overall safety profile of the intravenous immunoglobulin (IVIg) product in DM and PM patients.

As of 18/01/2008 this record was updated. Changes are written under the relevant sections under the above update date. Please also note that the anticipated end date of this trial has been extended; the initial anticipated end date of this trial was 21/03/2008.

As of 14/08/2009 this record was again updated; all updates can be found under the relevant field with the above update date. At this time, the anticipated end date was also updated; the previous anticipated end date of this trial was 31/08/2009.

As of 09/12/2010 this record was again updated; all updates can be found under the relevant field with the above update date. At this time, the anticipated end date was also updated; the previous anticipated end date of this trial was 31/07/2010.

Please note that as of 01/10/2012, the anticipated end date of this trial was updated from 31/12 /2012 to 06/09/2011. This was the final completion date of the study.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Positive opinions from the Ethics Committees in:
1. Austria: approved on 25/01/2007
2. France: approved on 06/03/2006
3. Germany: approved on 18/07/2006
4. Italy: Ancona site approved on 20/07/2006

Added 14/08/2009:
5. Italy: Pisa site approved on 18/09/2008

Added 09/12/2010:
6. Hungary: approved on 21/01/2010
7. Czech Republic: approved on 16/12/2009
8. Mexico: approved on 22/01/2010

Study design

Run-in period: observational study; period I: randomised, double-blind, placebo-controlled, two-parallel groups design; period II: open-labelled, non comparative, one-arm design

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Dermatomyositis (DM) and polymyositis (PM)

Interventions
The study will comprise three periods:
1. Run-in period: observational period, in which patients under conventional therapies (GS, IS) will be followed. Only patients with an insufficient improvement on muscle strength will be allowed to enter Period I.
2. Period I: randomised, double-blind, placebo-controlled, two-parallel groups design (stratification between DM and PM patients).
3. Period II: open-labelled, non comparative, one-arm design.

1. L0133 product: 2 g/Kg (40 ml/Kg) IV per month, delivered in two consecutive days (1 g/Kg daily or 20 ml/Kg daily) during period I and period II
2. Placebo: 40 ml/Kg IV per month, delivered in two consecutive days (20 mL/Kg daily) during period I only

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Prednisone, methotrexate, intravenous immunoglobulin product (L0133)

Primary outcome measure
1. Muscle strength intensity, as defined by the BMRC.
2. Treatment response will be defined as an improvement from baseline of BMRC score at the end of Period I.

Secondary outcome measures
1. Time course evaluation of muscle strength using BMRC index (run-in period, Period I and Period II).

2. Physical function recorded by the patients, as measured by the Health Assessment Questionnaire (HAQ) scale.
3. Visual Analogue Scale (VAS) global disease activity made by the Investigators and the patients
4. Serum activity of muscle enzymes - Measurement outcome as defined by International Myositis Assessment and Clinical Studies Group (IMACS).
5. Cutaneous signs severity, according to the modified three-point scale from Göttfried
6. Other organ involvement (cardiac, pharyngeal, gastro-intestinal, joint, pulmonary, others) assessed by the Investigators, using clinical and paraclinical examinations.
7. Consumption of prednisone during the run-in period, Period I and Period II.
8. Consumption of IS during period II.
9. Routine blood laboratory tests (haematology, chemistry).
10. Adverse events.

Overall study start date
21/09/2006

Completion date
06/09/2011

Eligibility

Key inclusion criteria
Current inclusion criteria as of 14/08/2009:
1. Male or female patients of at least 18 years of age
2. Patients fulfilling the diagnostic criteria (definite or probable) of the European Neuromuscular Committee (ENMC) for idiopathic DM and PM
3.1. Patients with an active DM or PM disease who received conventional therapies for at least 14 weeks: oral prednisone 1 mg/kg per day for at least 4 weeks, with or without immunosuppressors (IS), followed by IS at stable dose and prednisone for at least 10 weeks, or
3.2. Patients with a contra-indication or a major side-effect to prednisone or methotrexate/other IS, or
3.3. Patients under biotherapy with a documented deterioration of their British Medical Research Council (BMRC) score, or
3.4. DM patients under biotherapy having a documented deterioration of their cutaneous signs, or
3.5. Patients under biotherapy with an onset of visceral involvement
4. Patients with no significant improvement of muscle strength under conventional therapy
5. Patients with BMRC index between 24 and 72 at baseline

Previous inclusion criteria as of 18/01/2008:
1. Male or female patients of at least 18 years of age
2. Patients fulfilling the diagnostic criteria (definite or probable) of the European Neuromuscular Committee (ENMC) for idiopathic DM and PM
3. Patients with an active DM or PM disease who received conventional therapies for at least 14 weeks: oral prednisone 1 mg/Kg per day, immunosuppressors at stable dosage
4. Patients with no significant improvement of muscle strength under conventional therapy, i.e. with an improvement of their muscle British Medical Research Council (BMRC) index of less than 18 points at baseline compared to the beginning of the run-in period
5. Patients with BMRC index between 32 and 64 at baseline

Initial inclusion criteria:
1. Male or female patients of at least 18 years of age
2. Patients fulfilling the diagnostic criteria (definite or probable) of the European Neuromuscular Committee (ENMC) for idiopathic DM and PM
3. Patients with an active DM or PM disease who received conventional therapies for at least 18 weeks: oral prednisone 1 mg/Kg per day, Methotrexate 15 mg per week
4. Patients with no significant improvement of muscle strength under conventional therapy, i.e. with an improvement of their muscle British Medical Research Council (BMRC) index of less than 18 points at baseline compared to the beginning of the run-in period
5. Patients with BMRC index between 32 and 64 at baseline

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
44 patients

Key exclusion criteria
Current exclusion criteria as of 14/08/2009:
1. Pregnant women, nursing mothers and women of childbearing potential with no reliable contraception
2. Patients who do not fulfil the ENMC diagnostic criteria (definite or probable) of idiopathic DM and PM
3. Patients with a diagnosis of paraneoplasic DM or PM
4. Juvenile DM and PM (age less than 18 years)
5. DM patients with no muscle involvement
6. Patients with life expectancy of less than three months
7. Patients whose muscle strength is responsive to conventional therapy, i.e. with an improvement of at least 18 points of their BMRC index at baseline compared to the beginning of the run-in period if BMRC below 40,5 at first run-in period assessment, 12 points if BMRC between 40.5 and 56 included at first run-in period assessment and 8 points if BMRC over 56 at first run-in period assessment
8. Patients with an BMRC index of less than 24 or more than 72
9. Patients having received a bolus of methylprednisone within three weeks prior to study entry
10. Patients with a known allergy to one of the ingredients of the IVIg test product
11. Patients with decompensated cardiac insufficiency or any other inter-current condition that may alter the study conduct
12. Patients with positive Coomb's test at baseline

Previous exclusion criteria as of 18/01/2008:
1. Pregnant women, nursing mothers and women of childbearing potential with no reliable

contraception
2. Patients who do not fulfil the ENMC diagnostic criteria (definite or probable) of idiopathic DM and PM
3. Patients with a diagnosis of paraneoplasic DM or PM
4. Juvenile DM and PM (age less than 18 years)
5. DM patients with no muscle involvement
6. Patients with life expectancy of less than three months
7. Patients with severe forms of DM and PM: pharyngeal, cardiac or pulmonary involvement
8. Patients without conventional treatments as first-line therapy for at least 14 weeks: oral prednisone 1 mg/Kg per day, immunosuppressors at stable dosage
9. Patients whose muscle strength is responsive to conventional therapy, i.e. with an improvement of at least 18 points of their BMRC index at baseline compared to the beginning of the run-in period
10. Patients with a BMRC index of less than 32 or more than 64
11. Patients having received a bolus of methylprednisone within three months prior to study entry
12. Patients with a known allergy to one of the ingredients of the IVIg test product
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8. Patients without conventional treatments as first-line therapy: prednisone 1 mg/Kg daily Methotrexate 15 mg per week)
9. Patients whose muscle strength is responsive to conventional therapy, i.e. with an improvement of at least 18 points of their BMRC index at baseline compared to the beginning of the run-in period
10. Patients with a BMRC index of less than 32 or more than 64
11. Patients having received a bolus of methylprednisone within three months prior to study entry
12. Patients with a known allergy to one of the ingredients of the IVIg test product
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14. Patients with positive Coomb's test at baseline

Date of first enrolment
21/09/2006

Date of final enrolment
06/09/2011

Locations

Countries of recruitment
Austria

Czech Republic

France

Germany

Hungary

Italy

Mexico

Study participating centre
ORFAGEN,
Toulouse Cedex 1
France
31 035

Sponsor information

Organisation
Orfagen (France)

Sponsor details
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3, avenue Hubert Curien
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Sponsor type
Industry

Website
http://www.orfagen.com

Funder(s)

Funder type
Industry

Funder Name
Orfagen (France)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration