Clinical trial results:
A randomised, double-blind, placebo-controlled proof-of concept study of the efficacy of gevokizumab 60mg subcutaneously every 4 weeks over 24 weeks in the treatment of patients with polymyositis, dermatomyositis or necrotizing autoimmune myopathy disease

Summary

EudraCT number	2012-005772-34
Trial protocol	IT SE DE CZ GB ES HU BE GR
Global end of trial date	25 November 2015

Results information

Result version number	v1 (current)
This version publication date	09 November 2016
First version publication date	09 November 2016

Trial information

Trial identification

Sponsor protocol code	CL2-78989-010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1139-6207

Notes:

Sponsors

Sponsor organisation name	Institut de Recherches Internationales Servier
Sponsor organisation address	50 rue Carnot, Suresnes, France, 92284
Public contact	Clinical Studies Department, Institut de Recherches Internationales Servier, +33 1 55 72 43 66, clinicaltrials@servier.com
Scientific contact	Clinical Studies Department, Institut de Recherches Internationales Servier, +33 1 55 72 43 66, clinicaltrials@servier.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 November 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 November 2015
Global end of trial reached?	Yes
Global end of trial date	25 November 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Evaluate the efficacy and safety of gevokizumab in adult patients with polymyositis (PM) or dermatomyositis (DM) or necrotizing autoimmune myopathy (NAM) intolerant or resistant or dependent to systemic oral corticosteroids.

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice standards, ethical principles stated in the Declaration of Helsinki and applicable regulatory requirements. After the subject has ended his/her participation in the trial, the investigator provided appropriate medication and/or arranged access to appropriate care for the patient.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 September 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Brazil: 7
Worldwide total number of subjects	27
EEA total number of subjects	20

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	27
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male/female, age ≥ 18 years with probable or definite polymyositis, dermatomyositis, or necrotizing autoimmune myopathy diagnosed according to 119th ENMC classification, intolerant/resistant/dependent to systemic oral corticosteroids, duration ≤ 10 years, active disease with MMT-8 score on proximal muscles and neck flexors no greater than 85/110

Period 1

Period 1 title	double-blind treatment period (W0-W24)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Gevokizumab 60mg

Arm description:

Gevokizumab 60mg [W0-W24]

Arm type	Experimental
Investigational medicinal product name	Gevokizumab
Investigational medicinal product code	S78989
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One subcutaneous injection of Gevokizumab 60 mg every 4 weeks (Q4W) from W0 to W20 in the first period of the study (for a total of 6 injections).

Arm title	Placebo

Arm description:

Placebo [W0-W24]

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One subcutaneous injection of Placebo every 4 weeks (Q4W) from W0 to W20 in the first period of the study (for a total of 6 injections).

Number of subjects in period 1	Gevokizumab 60mg	Placebo
Started	14	13
Completed	7	10
Not completed	7	3
Adverse event, non-fatal	1	-
Non-medical reason	6	3

Period 2

Period 2 title	open label period (W24-W48)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Gevokizumab 60mg

Arm description:

Gevokizumab 60mg (W24-W48)

Arm type	Experimental
Investigational medicinal product name	Gevokizumab
Investigational medicinal product code	S78989
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One subcutaneous injection of Gevokizumab 60 mg every 4 weeks (Q4W) from W24 to W44 in the second period of the study (for a total of 6 injections).

Number of subjects in period 2[1]	Gevokizumab 60mg
Started	15
Completed	6
Not completed	9
Non-medical reasons	9

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Two patients did not enter the open-label period as they had stopped the IMP before W24 and continued in the study without treatment until W24.

Baseline characteristics

Reporting groups	
Reporting group title	Gevokizumab 60mg
Reporting group description: Gevokizumab 60mg [W0-W24]	
Reporting group title	Placebo
Reporting group description: Placebo [W0-W24]	

Reporting group values	Gevokizumab 60mg	Placebo	Total
Number of subjects	14	13	27
Age categorical Units: Subjects			
Adults (18-64 years)	14	13	27
Age continuous Units: years			
arithmetic mean	46.1	46.4	
standard deviation	± 9.7	± 11.5	-
Gender categorical Units: Subjects			
Female	9	10	19
Male	5	3	8

End points

End points reporting groups

Reporting group title	Gevokizumab 60mg
Reporting group description: Gevokizumab 60mg [W0-W24]	
Reporting group title	Placebo
Reporting group description: Placebo [W0-W24]	
Reporting group title	Gevokizumab 60mg
Reporting group description: Gevokizumab 60mg (W24-W48)	

Primary: clinical improvement during the double-blind treatment period

End point title	clinical improvement during the double-blind treatment

End point description:

Clinical improvement was defined according to the Manual Muscle Testing (MMT-8) on the proximal muscles and neck flexors score as an increase of 15% or more in the score (with no clinical worsening during the double-blind treatment period).

End point type	Primary

End point timeframe:

Clinical improvement at W24 (or LOCF) during the double-blind treatment period.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: In the specific context of the study (study discontinued due to general strategic and business reasons unrelated to safety), it was decided to not perform the efficacy analyses planned in the study protocol.

End point values	Gevokizumab 60mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: number of patients				
Improvement = No	9	6		
Improvement = Yes	5	7		
All	14	13		

Statistical analyses

No statistical analyses for this end point

Primary: clinical improvement during the double-blind treatment period in Dermatomyositis patients

End point title	clinical improvement during the double-blind treatment period in Dermatomyositis patients[2]

End point description:

Clinical improvement was defined according to the Manual Muscle Testing (MMT-8) on the proximal

muscles and neck flexors score as an increase of 15% or more in the score (with no clinical worsening during the double-blind treatment period).

End point type	Primary

End point timeframe:

Clinical improvement at W24 (or LOCF) during the double-blind treatment period.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: In the specific context of the study (study discontinued due to general strategic and business reasons unrelated to safety), it was decided to not perform the efficacy analyses planned in the study protocol.

End point values	Gevokizumab 60mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: number of patients				
Improvement = No	5	5		
Improvement = Yes	3	4		
All	8	9		

Statistical analyses

No statistical analyses for this end point

Primary: clinical improvement during the double-blind treatment period in Necrotizing Autoimmune Myopathy patients

End point title	clinical improvement during the double-blind treatment period in Necrotizing Autoimmune Myopathy patients[3]

End point description:

Clinical improvement was defined according to the Manual Muscle Testing (MMT-8) on the proximal muscles and neck flexors score as an increase of 15% or more in the score (with no clinical worsening during the double-blind treatment period).

End point type	Primary

End point timeframe:

Clinical improvement at W24 (or LOCF) during the double-blind treatment period.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: In the specific context of the study (study discontinued due to general strategic and business reasons unrelated to safety), it was decided to not perform the efficacy analyses planned in the study protocol.

End point values	Gevokizumab 60mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: number of patients				
Improvement = No	2	1		
Improvement = Yes	1	1		
All	3	2		

Statistical analyses

No statistical analyses for this end point

Primary: clinical improvement during the double-blind treatment period in Polymyositis patients

End point title	clinical improvement during the double-blind treatment period in Polymyositis patients[4]

End point description:

Clinical improvement was defined according to the Manual Muscle Testing (MMT-8) on the proximal muscles and neck flexors score as an increase of 15% or more in the score (with no clinical worsening during the double-blind treatment period).

End point type	Primary

End point timeframe:

Clinical improvement at W24 (or LOCF) during the double-blind treatment period.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: In the specific context of the study (study discontinued due to general strategic and business reasons unrelated to safety), it was decided to not perform the efficacy analyses planned in the study protocol.

End point values	Gevokizumab 60mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: number of patients				
Improvement = No	2	0		
Improvement = Yes	1	2		
All	3	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Over the double blind treatment period (W0-W24): all adverse events which occurred, worsened or became serious between the first IMP intake date (included) during the double-blind treatment and the first IMP intake date during open-label period (excluded)

Adverse event reporting additional description:

Over the open label period: All adverse events occurring after W24 (included)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	Gevokizumab 60mg [W0-W24]
Reporting group description: -	
Reporting group title	Gevokizumab 60mg [W24-W48]
Reporting group description: -	
Reporting group title	Placebo [W0-W24]
Reporting group description: -	

Serious adverse events	Gevokizumab 60mg [W0-W24]	Gevokizumab 60mg [W24-W48]	Placebo [W0-W24]
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 14 (21.43%)	1 / 15 (6.67%)	1 / 13 (7.69%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian adenoma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Coagulopathy			

subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphopenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Polymyositis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pharyngeal abscess			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			

subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Gevokizumab 60mg [W0-W24]	Gevokizumab 60mg [W24-W48]	Placebo [W0-W24]
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 14 (78.57%)	7 / 15 (46.67%)	10 / 13 (76.92%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Keratoacanthoma			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Melanocytic naevus			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	3	0	0
Pyrexia			

subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Bartholinitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Dyspnoea exertional			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Weight increased			

subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Accidental exposure to product			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Head injury			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Rib fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Headache			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	1 / 13 (7.69%)
occurrences (all)	1	1	2
Migraine			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			

subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Eye disorders			
Scleral haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatomyositis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Erythema			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Photosensitivity reaction			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pruritus allergic			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Swelling face			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	2	0	1
Chondrocalcinosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Muscle fatigue			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Myalgia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Osteoarthritis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Tenosynovitis			

subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Dengue fever			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Escherichia urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	2
Herpes virus infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Molluscum contagiosum			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	4	0	1
Pneumonia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Sinusitis bacterial			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0

Upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Urinary tract infection bacterial			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hypertriglyceridaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Hypo HDL cholesterolaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 April 2013	Concerned all centres in all countries. The main changes were: - To document that in the event of anaphylaxis, the study drug was to be stopped immediately and permanently. - To update the selection criteria No. 11, regarding patients with a positive interferon-γ-released assay (IGRA). - A new selection criteria had been added for patients considered as exposed to tuberculosis. - A new section in the protocol for having a benefit/risk assessment for the current clinical study had been added. - To add a new paragraph in the protocol (in order to warrant the patient's safety), related to the therapeutic monitoring of therapies with a narrow therapeutic index being CYP450 and/or transporter substrates when initiating gevokizumab treatment.
20 September 2013	Concerned all centres in all countries. The main objective of this Amendment was to add an open label treatment period of 24 weeks after the end of the planned double-blind 24-week period.
12 June 2014	Concerned all centres in all countries. The main changes were: - Eligibility requirements for patients with indeterminate QuantiFERON®-TB test result at Selection visit: no evidence of active Tuberculosis (TB), agreement of a TB expert was to be obtained, - Eligibility requirements for patients with positive QuantiFERON®-TB test result at Selection visit: precision on the duration of the prophylactic TB treatment, - Modified selection criteria: disease duration ≤ 10 years, - Modified selection criteria: if CK and/or Aldolase ≤ 2 ULN and neither muscle biopsy nor Magnetic Resonance Imaging (MRI) ≤ 3 months was available, a MRI was authorized for the assessment of disease activity (edema and inflammatory changes). In this case the delay between selection and inclusion visit could be more than to 2 weeks, - Modified non selection criteria: the re-selection of a patient was authorized (no more than once) in case of a change in his clinical situation or of an infection or personal reason that temporarily avoided his inclusion, - Non participation of France to the open-label period of the study, due to Ethics Committee refusal for amended protocol n°2 (20 Septembre 2013), - For German sites only: additional safety measurements at visits W36 and W44 in order to satisfy Ethics Committee requirements for amended protocol n°2 (20 Septembre 2013), - For the United Kingdom (UK), the chest X-ray at W24 should not be performed in line with UK usual practice, for patients who performed the open-label period, - New laboratory (Biostorage) was added to the "Non sponsor parties" for the storage of pharmacogenomics, other omics and retrospective analysis samples at the end of the study,

04 February 2015	Concerned all centres in all countries. The main changes were the following: - Modification in the definition of corticoresistance and corticodependence to be in compliance with current clinical practice. - Deletion of the criterion "Disease diagnosis duration < 10 years". Disease duration became indefinite. - To allow the selection/inclusion of patients with dermatomyositis (DM) sine dermatitis (DM without cutaneous signs). These patients were initially not eligible, but as the disease is well-described in the literature and is a sub-group of DM, and in order to extend the possibility of an alternative treatment to this population in need, the efficacy of gevokizumab could also be assessed in this disease within the framework of the study. For these patients, the diagnosis should have been confirmed by the Adjudication Committee of the study before the inclusion of the patient. - Extension of the study population to patients with necrotizing autoimmune myopathy (NAM).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
22 September 2015	The study was prematurely discontinued due to strategic and business reasons unrelated to safety	-

Notes:

Limitations and caveats

None reported