Clinical trial results:
An Open-label, Non-controlled, Phase II Study to Evaluate the Safety, Pharmacodynamics, Pharmacokinetics, Efficacy and Conditions of Use of ARGX-113 in Patients with Mild to Moderate Pemphigus (Vulgaris or Foliaceus)

Summary

EudraCT number	2017-002333-40
Trial protocol	DE HU IT RO
Global end of trial date	28 October 2020

Results information

Result version number	v1 (current)
This version publication date	13 November 2021
First version publication date	13 November 2021

Trial information

Trial identification

Sponsor protocol code	ARGX-113-1701

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03334058
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	argenx BV
Sponsor organisation address	Industriepark Zwijnaarde 7, Zwijnaarde, Belgium, 9052
Public contact	Regulatory Manager, argenx BV, regulatory@argenx.com
Scientific contact	Regulatory Manager, argenx BV, regulatory@argenx.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	28 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of efgartigimod in Pemphigus Vulgaris (PV) and Pemphigus Foliaceus (PF) subjects.

Protection of trial subjects:

This study was performed according to the International Conference on Harmonisation of Good Clinical Practice, the principles of the Declaration of Helsinki, and other applicable local ethical and legal requirements.

Background therapy:

Relapsing subjects under tapered prednisone therapy were kept in the study at the same dosage during the Induction treatment period. Then prednisone dosage could be tapered from the beginning of the Maintenance treatment period (Visit 5) up to study end (Follow-up Visit 3), according to standard of care (SoC). Newly diagnosed subjects or relapsing subjects off therapy, who were already on a first course of oral prednisone and for whom efgartigimod monotherapy was considered not clinically acceptable, were kept at the same dosage during the Induction treatment period. From the beginning of the Maintenance treatment period (Visit 5) up to study end (Follow-up Visit 3), prednisone dosage could be tapered according to SoC. Newly diagnosed subjects naïve to any treatment and relapsing subjects off therapy, or with a first course of oral prednisone (≤ 4 weeks), for whom an initial period of efgartigimod monotherapy was judged clinically acceptable, were not administered any SoC (e.g. oral prednisone). Any adjuvant conventional immunosuppressant (e.g. mycophenolate mofetil, azathioprine) was discontinued at any time during the screening period.
SoC in additional Cohort 4:
• All subjects off therapy were associated with oral prednisone 20 mg/day at baseline. In relapsing subjects who were under oral prednisone therapy at tapered dose, oral prednisone was maintained at the same dosage, while any adjuvant conventional immunosuppressant was discontinued at any time during the screening period.
• Oral prednisone dose could be tapered as of end of consolidation (EoC) (the time at which no new lesions have developed for a minimum of 2 weeks, and approximately 80% of lesions have healed).
For all subjects with a clinically active disease (e.g. worsening of the clinical signs) upon Investigator's judgment, a rescue treatment of oral prednisone could be implemented at any post-baseline visit.

Evidence for comparator: -

Actual start date of recruitment	02 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Ukraine: 5
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Italy: 8

Worldwide total number of subjects	34
EEA total number of subjects	25

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 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	27
From 65 to 84 years	6
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This Phase 2 study was conducted in subjects with mild to moderate PV or PF at 17 centers worldwide. Of the 53 subjects who were screened, 19 subjects were screen failures and 34 subjects were enrolled.

Pre-assignment

Screening details:

The study comprised a screening period of up to 3 weeks, treatment periods ranging from 9 to 34 weeks, and a treatment-free follow-up period of 8 (Cohort 1) or 10 weeks (Cohorts 2-4).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 (10 mg/kg)

Arm description:

Efgartigimod intravenous (IV) 10 milligrams per kilogram (mg/kg) was administered as 4 weekly infusions during the induction period and during the maintenance period at weeks 2 and 6.

Arm type	Experimental
Investigational medicinal product name	Efgartigimod
Investigational medicinal product code	ARGX-113
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Efgartigimod (10 mg/kg), 250 milliliter (mL) was infused IV over a period of 2 hours. Subjects remained at the site for 2 hours minimum after the end of infusion during these visits as part of routine safety monitoring.

Arm title	Cohort 2 (10 mg/kg)

Arm description:

Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period once every 2 weeks (q2w) for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	Efgartigimod
Investigational medicinal product code	ARGX-113
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Efgartigimod (10 mg/kg), 250 mL was infused IV over a period of 2 hours. Subjects remained at the site for 2 hours minimum after the end of infusion during these visits as part of routine safety monitoring.

Arm title	Cohort 3 (10 mg/kg)

Arm description:

Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period q2w for 12 weeks.

Arm type	Experimental

Investigational medicinal product name	Efgartigimod
Investigational medicinal product code	ARGX-113
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Efgartigimod (10 mg/kg), 250 mL was infused IV over a period of 2 hours. Subjects remained at the site for 2 hours minimum after the end of infusion during these visits as part of routine safety monitoring.

Arm title	Cohort 4 (25 mg/kg)

Arm description:

Efgartigimod IV 25 mg/kg was administered as 5 weekly infusions (minimum) during the induction period until EoC, and during the maintenance period q2w until Week 34.

Arm type	Experimental
Investigational medicinal product name	Efgartigimod
Investigational medicinal product code	ARGX-113
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Efgartigimod (25 mg/kg), 250 mL was infused IV over a period of 2 hours. Subjects remained at the site for 2 hours minimum after the end of infusion during these visits as part of routine safety monitoring.

Number of subjects in period 1	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)
Started	6	5	8
Completed	3	2	7
Not completed	3	3	1
Other	1	-	-
Investigator termination	2	3	-
Withdrawal of informed consent	-	-	1
Lost to follow-up	-	-	-

Number of subjects in period 1	Cohort 4 (25 mg/kg)
Started	15
Completed	10
Not completed	5
Other	-
Investigator termination	2
Withdrawal of informed consent	2
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 (10 mg/kg)
Reporting group description:	
Efgartigimod intravenous (IV) 10 milligrams per kilogram (mg/kg) was administered as 4 weekly infusions during the induction period and during the maintenance period at weeks 2 and 6.	
Reporting group title	Cohort 2 (10 mg/kg)
Reporting group description:	
Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period once every 2 weeks (q2w) for 8 weeks.	
Reporting group title	Cohort 3 (10 mg/kg)
Reporting group description:	
Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period q2w for 12 weeks.	
Reporting group title	Cohort 4 (25 mg/kg)
Reporting group description:	
Efgartigimod IV 25 mg/kg was administered as 5 weekly infusions (minimum) during the induction period until EoC, and during the maintenance period q2w until Week 34.	

Reporting group values	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)
Number of subjects	6	5	8
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	42.0	64.6	46.9
full range (min-max)	29 to 63	43 to 78	30 to 65
Gender categorical Units: Subjects			
Female	3	4	7
Male	3	1	1
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	6	5	8
Race Units: Subjects			
White	6	5	8
Black or African American	0	0	0
Asian	0	0	0
American Indian or Alaska	0	0	0
Native	0	0	0
Native Hawaiian or Other	0	0	0
Pacific Islander	0	0	0
Multiple Race	0	0	0
Pemphigus Type Units: Subjects			
PV: Mucosal-dominant	1	3	3

PV: Mucocutaneous	4	2	4
PV: Cutaneous	1	0	0
PF	0	0	1

Reporting group values	Cohort 4 (25 mg/kg)	Total	
Number of subjects	15	34	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	53.3		
full range (min-max)	22 to 85	-	
Gender categorical Units: Subjects			
Female	8	22	
Male	7	12	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	15	34	
Race Units: Subjects			
White	14	33	
Black or African American	0	0	
Asian	1	1	
American Indian or Alaska	0	0	
Native	0	0	
Native Hawaiian or Other	0	0	
Pacific Islander	0	0	
Multiple Race	0	0	
Pemphigus Type Units: Subjects			
PV: Mucosal-dominant	2	9	
PV: Mucocutaneous	4	14	
PV: Cutaneous	2	3	
PF	7	8	

End points

End points reporting groups

Reporting group title	Cohort 1 (10 mg/kg)
Reporting group description:	
Efgartigimod intravenous (IV) 10 milligrams per kilogram (mg/kg) was administered as 4 weekly infusions during the induction period and during the maintenance period at weeks 2 and 6.	
Reporting group title	Cohort 2 (10 mg/kg)
Reporting group description:	
Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period once every 2 weeks (q2w) for 8 weeks.	
Reporting group title	Cohort 3 (10 mg/kg)
Reporting group description:	
Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period q2w for 12 weeks.	
Reporting group title	Cohort 4 (25 mg/kg)
Reporting group description:	
Efgartigimod IV 25 mg/kg was administered as 5 weekly infusions (minimum) during the induction period until EoC, and during the maintenance period q2w until Week 34.	
Subject analysis set title	Cohorts 1-3
Subject analysis set type	Full analysis
Subject analysis set description:	
Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period in Cohorts 1, 2, and 3; and during the maintenance period at weeks 2 and 6 (Cohort 1), q2w for 8 weeks (Cohort 2), and q2w for 12 weeks (Cohort 3).	
Subject analysis set title	Cohorts 1-4
Subject analysis set type	Full analysis
Subject analysis set description:	
Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period in Cohorts 1, 2, and 3; and during the maintenance period at weeks 2 and 6 (Cohort 1), q2w for 8 weeks (Cohort 2), and q2w for 12 weeks (Cohort 3). Efgartigimod IV 25 mg/kg was administered as 5 weekly infusions (minimum) during the induction period until EoC in Cohort 4; and during the maintenance period q2w until Week 34.	

Primary: Number of Subjects who Experienced Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects who Experienced Treatment-emergent Adverse Events (TEAEs)[1]
End point description:	
A TEAE was an undesirable event not present prior to medical treatment, or an already present event that worsened either in intensity or frequency following the treatment. A serious adverse event (SAE), experience or reaction, was any untoward medical occurrence (whether considered to be related to investigational medicinal product [IMP] or not) that at any dose: • Resulted in death; • Was life-threatening; • Required in subject hospitalization or prolongation of existing hospitalization; • Resulted in persistent or significant disability or incapacity; • Was a congenital abnormality or birth defect; • Medically significant events, which did not meet any of the criteria above, but may have jeopardized the subject and may have required medical or surgical intervention to prevent one of the other serious outcomes listed in the definition above. The Safety analysis set (SAS) included all enrolled subjects who received at least 1 dose of efgartigimod.	
End point type	Primary
End point timeframe:	
From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks	

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: No additional statistical analysis was prespecified for this end point.

End point values	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)	Cohort 4 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	8	15
Units: subjects				
TEAE	6	4	6	13
SAE	1	1	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Vital Sign Measurements

End point title	Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Vital Sign Measurements[2]

End point description:

At each visit, vital signs (supine blood pressure, pulse rate, and oral body temperature) were assessed. Supine blood pressure and pulse rate were measured using standard equipment after approximately 10 minutes in a supine position.

The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.

End point type	Primary

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

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: No additional statistical analysis was prespecified for this end point.

End point values	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)	Cohort 4 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	8	15
Units: subjects	1	0	0	2

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Electrocardiograms (ECG)

End point title	Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Electrocardiograms (ECG)[3]

End point description:

ECG was taken at a paper speed of 25 millimeter/second and should be obtained with the subject in the supine position after they have rested in this position for at approximately 10 minutes. Three consecutive ECG recordings was taken with an interval of approximately 5 minutes at each occasion to obtain reliable and interpretable data. The ECG parameters that were collected are heart rate, PR, QRS, QT whereas QTcF was calculated.

The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.

End point type	Primary

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

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: No additional statistical analysis was prespecified for this end point.

End point values	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)	Cohort 4 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	8	15
Units: subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Physical Examinations (Cohorts 1-3)

End point title	Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Physical Examinations (Cohorts 1-3)[4][5]

End point description:

At each visit, physical examinations were carried out. Only physical examinations and visits where a clinically significant change from baseline occurred are included below. A clinically significant change from baseline was defined as a change from normal or abnormal (not clinically significant) to abnormal (clinically significant) post-baseline. The complete physical examination included an assessment of general appearance, skin, head and neck (including ears, eyes, nose and throat), lymph nodes, thyroid, musculoskeletal/extremities, abdomen, breast, and cardiovascular, respiratory, neurological, and genital/rectal systems.

The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.

End point type	Primary

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

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: No additional statistical analysis was prespecified for this end point.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

End point values	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	8	
Units: subjects				
Head and Neck: Day 15	1	0	0	
Respiratory: Day 15	1	0	0	
Musculoskeletal/Extremities: Day 22	0	1	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Physical Examinations (Cohort 4)

End point title	Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Physical Examinations (Cohort 4)[6][7]

End point description:

At each visit, physical examinations were carried out. Only physical examinations and visits where a clinically significant change from baseline occurred are included below. A clinically significant change from baseline was defined as a change from normal or abnormal (not clinically significant) to abnormal (clinically significant) post-baseline. The complete physical examination included an assessment of general appearance, skin, head and neck (including ears, eyes, nose and throat), lymph nodes, thyroid, musculoskeletal/extremities, abdomen, breast, and cardiovascular, respiratory, neurological, and genital/rectal systems.

The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.

End point type	Primary

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

[6] - 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: No additional statistical analysis was prespecified for this end point.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

End point values	Cohort 4 (25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: subjects				
Abdomen: Day 99	1			
General Appearance: Day 211	1			
General Appearance: Day 239	1			
General Appearance: Day 260	1			
General Appearance: Day 281	1			
General Appearance: Day 309	1			
Genital/Rectal: Day 85	1			
Genital/Rectal: Day 99	1			
Genital/Rectal: Day 190	1			
Genital/Rectal: Day 204	1			

Genital/Rectal: Day 218	1			
Genital/Rectal: Day 232	1			
Genital/Rectal: Day 246	1			
Genital/Rectal: Day 274	1			
Genital/Rectal: Day 288	1			
Genital/Rectal: Day 323	1			
Head and Neck: Day 78	1			
Head and Neck: Day 120	1			
Head and Neck: Day 134	1			
Head and Neck: Day 148	1			
Head and Neck: Day 162	1			
Head and Neck: Day 176	1			
Head and Neck: Day 190	1			
Head and Neck: Day 204	1			
Head and Neck: Day 218	1			
Head and Neck: Day 232	1			
Head and Neck: Day 253	1			
Head and Neck: Day 274	1			
Head and Neck: Day 302	1			
Neurological: Day 127	1			
Neurological: Day 141	1			
Neurological: Day 155	1			
Neurological: Day 169	1			
Neurological: Day 183	1			
Neurological: Day 197	1			
Neurological: Day 211	1			
Neurological: Day 225	1			
Neurological: Day 239	1			
Neurological: Day 253	1			
Neurological: Day 288	1			
Neurological: Day 309	1			
Respiratory: Day 50	1			
Respiratory: Day 85	1			
Respiratory: Day 127	1			
Respiratory: Day 141	1			
Respiratory: Day 155	1			
Respiratory: Day 169	1			
Respiratory: Day 183	1			
Respiratory: Day 197	1			
Respiratory: Day 211	1			
Respiratory: Day 225	1			
Respiratory: Day 239	1			
Respiratory: Day 253	1			
Respiratory: Day 288	1			
Respiratory: Day 309	1			
Skin: Day 211	1			
Skin: Day 239	1			
Skin: Day 260	1			
Skin: Day 281	1			
Skin: Day 309	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Clinical Laboratory Evaluations

End point title	Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Clinical Laboratory Evaluations[8]

End point description:

At each visit, routine blood samples were taken for determination of:
• Hematology: hemoglobin, hematocrit, mean corpuscular volume, red blood cell count, platelet count, white blood cell count with differential;
• Blood chemistry: sodium, potassium, calcium, glucose, creatinine, creatinine clearance, blood urea nitrogen, alanine aminotransferase, aspartate aminotransferase, total bilirubin, gamma-glutamyl transferase, C-reactive protein, alkaline phosphatase, lactate dehydrogenase, uric acid, total protein and albumin.
Urinalysis was performed by dipstick method and included: color, clarity/appearance, specific gravity, pH, protein, glucose, ketones, blood, bilirubin, urobilinogen, nitrite, leukocyte esterase, and microscopic examination including red blood cells, white blood cells, cast crystals, and bacteria.

Subjects need to be fasting for at least 8 hours prior to blood glucose assessment. The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.

End point type	Primary

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

[8] - 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: No additional statistical analysis was prespecified for this end point.

End point values	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)	Cohort 4 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	8	15
Units: subjects	0	0	3	3

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline in Serum Levels of Total Immunoglobulin G (IgG) (Cohorts 1-3)

End point title	Mean Percentage Change from Baseline in Serum Levels of Total Immunoglobulin G (IgG) (Cohorts 1-3)[9]

End point description:

Levels of total IgG were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

Baseline (Day 1), end of Induction Period (Day 29), end of Maintenance Period (Cohort 1: Day 64; Cohort 2: Day 78; Cohort 3: Day 106), and end of Treatment-free Follow-up (Cohort 1: Day 120; Cohort 2: Day 148; Cohort 3: Day 176)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

End point values	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3[10]	3[11]	7[12]	
Units: percentage change (%)				
arithmetic mean (standard error)				
End of Induction Period (n = 2, 3, 7)	-55.00 (± 1.400)	-67.90 (± 3.005)	-63.44 (± 3.192)	
End of Maintenance Period (n = 3, 3, 7)	-4.37 (± 4.834)	-50.67 (± 3.176)	-49.21 (± 3.782)	
End of Treatment-free Follow-up (n = 3, 2, 7)	23.30 (± 13.141)	-9.65 (± 21.550)	-8.54 (± 6.762)	

Notes:

[10] - 'n' in category title denotes number of subjects analyzed for that category.

[11] - 'n' in category title denotes number of subjects analyzed for that category.

[12] - 'n' in category title denotes number of subjects analyzed for that category.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline in Serum Levels of Total IgG (Cohort 4)

End point title	Mean Percentage Change from Baseline in Serum Levels of Total IgG (Cohort 4)[13]

End point description:

Levels of total IgG were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and End of Induction Period (Day 29)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

End point values	Cohort 4 (25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage change (%)				
arithmetic mean (standard error)	-63.53 (± 3.285)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline in Serum Levels of IgG Subtypes (IgG1, IgG2, IgG3, IgG4) (Cohorts 1-3)

End point title	Mean Percentage Change from Baseline in Serum Levels of IgG Subtypes (IgG1, IgG2, IgG3, IgG4) (Cohorts 1-3)[14]

End point description:

Levels of IgG subtypes (IgG1, IgG2, IgG3, IgG4) were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

Baseline (Day 1), end of Induction Period (Day 29), and the end of Maintenance Period (Cohort 1: Day 64; Cohort 2: Day 78; Cohort 3: Day 106), and end of Treatment-free Follow-up (Cohort 1: Day 120; Cohort 2: Day 148; Cohort 3: Day 176)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

End point values	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	7	
Units: percentage change (%)				
arithmetic mean (standard error)				
IgG1: End of Induction Period	-45.83 (± 13.715)	-69.47 (± 1.785)	-69.14 (± 3.051)	
IgG1: End of Maintenance Period	-7.83 (± 5.210)	-48.63 (± 1.281)	-55.67 (± 3.907)	
IgG2: End of Induction Period	-45.00 (± 12.501)	-63.70 (± 5.524)	-57.11 (± 2.474)	
IgG2: End of Maintenance Period	-25.63 (± 6.542)	-50.17 (± 1.185)	-49.33 (± 3.729)	
IgG3: End of Induction Period	-43.07 (± 16.689)	-70.30 (± 1.320)	-65.43 (± 4.153)	
IgG3: End of Maintenance Period	-4.37 (± 1.354)	-45.67 (± 1.955)	-45.36 (± 5.201)	
IgG4: End of Induction Period	-40.43 (± 8.842)	-61.07 (± 5.374)	-56.80 (± 5.382)	
IgG4: End of Maintenance Period	7.17 (± 12.856)	1.97 (± 58.640)	-46.94 (± 5.862)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline in Serum Levels of IgG Subtypes (IgG1, IgG2, IgG3, IgG4) (Cohort 4)

End point title	Mean Percentage Change from Baseline in Serum Levels of IgG Subtypes (IgG1, IgG2, IgG3, IgG4) (Cohort 4)[15]

End point description:

Levels of IgG subtypes (IgG1, IgG2, IgG3, IgG4) were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and End of Induction Period (Day 29)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

End point values	Cohort 4 (25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage change (%)				
arithmetic mean (standard error)				
IgG1: End of Induction Period	-66.95 (± 3.067)			
IgG2: End of Induction Period	-62.54 (± 2.722)			
IgG3: End of Induction Period	-69.15 (± 2.753)			
IgG4: End of Induction Period	-55.85 (± 4.986)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-1 Autoantibodies (Cohorts 1-3)

End point title	Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-1 Autoantibodies (Cohorts 1-3)[16]

End point description:

Levels of anti-desmoglein-1 were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC. '99999' denotes standard error could not be calculated as only one subject was analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1), end of Induction Period (Day 29), end of Maintenance Period (Cohort 1: Day 64; Cohort 2: Day 78; Cohort 3: Day 106), and end of Treatment-free Follow-up (Cohort 1: Day 120; Cohort 2: Day 148; Cohort 3: Day 176)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

End point values	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1[17]	2[18]	4[19]	
Units: percentage change (%)				
arithmetic mean (standard error)				
End of Induction Period (n = 1, 2, 4)	-64.70 (± 99999)	11.85 (± 82.050)	-50.08 (± 22.920)	
End of Maintenance Period (n = 1, 1, 4)	-14.10 (± 99999)	-88.80 (± 99999)	-50.23 (± 19.924)	
End of Treatment-free Follow-up (n = 1, 1, 4)	25.60 (± 99999)	-88.20 (± 99999)	-30.13 (± 51.025)	

Notes:

[17] - 'n' in category title denotes number of subjects analyzed for that category.

[18] - 'n' in category title denotes number of subjects analyzed for that category.

[19] - 'n' in category title denotes number of subjects analyzed for that category.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-1 Autoantibodies (Cohort 4)

End point title	Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-1 Autoantibodies (Cohort 4)[20]

End point description:

Levels of anti-desmoglein-1 were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and End of Induction Period (Day 29)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

End point values	Cohort 4 (25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: percentage change (%)				
arithmetic mean (standard error)	-57.81 (± 7.701)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-3 Autoantibodies (Cohorts 1-3)

End point title	Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-3 Autoantibodies (Cohorts 1-3)[21]

End point description:

Levels of anti-desmoglein-3 were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

Baseline (Day 1), end of Induction Period (Day 29), and the end of Maintenance Period (Cohort 1: Day 64; Cohort 2: Day 78; Cohort 3: Day 106), and end of Treatment-free Follow-up (Cohort 1: Day 120; Cohort 2: Day 148; Cohort 3: Day 176)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

End point values	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3[22]	3[23]	6[24]	
Units: percentage change (%)				
arithmetic mean (standard error)				
End of Induction Period (n = 3, 3, 6)	-20.77 (± 4.100)	-56.90 (± 12.468)	-52.63 (± 12.314)	
End of Maintenance Period (n = 3, 3, 6)	72.27 (± 79.268)	-48.37 (± 19.804)	-40.62 (± 17.492)	
End of Treatment-free Follow-up (n = 3, 2, 6)	213.03 (± 155.219)	-59.45 (± 25.050)	-46.52 (± 4.873)	

Notes:

[22] - 'n' in category title denotes number of subjects analyzed for that category.

[23] - 'n' in category title denotes number of subjects analyzed for that category.

[24] - 'n' in category title denotes number of subjects analyzed for that category.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-3 Autoantibodies (Cohort 4)

End point title	Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-3 Autoantibodies (Cohort 4)[25]

End point description:

Levels of anti-desmoglein-3 were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and End of Induction Period (Day 29)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

End point values	Cohort 4 (25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage change (%)				
arithmetic mean (standard error)	-35.32 (± 11.279)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline in Pemphigus Disease Area Index (PDAI) (Cohorts 1-3)

End point title	Mean Percentage Change from Baseline in Pemphigus Disease Area Index (PDAI) (Cohorts 1-3)[26]

End point description:

PDAI is a cutaneous and mucosal disease activity assessment performed by investigator based on evaluation of lesions. The score was weighted for the number and size of lesions with score of 0 (absent) to 10 (> 3 lesions, and/or at least one lesion > 16 cm diameter or entire area) given for skin at 12 anatomic locations, scalp, and mucous membrane showing disease activity (erosions/blisters or new erythema). Damage from post inflammatory hyperpigmentation or erythema from the resolving lesions was scored separately from the main score as absent (0) or present (1) for each body area or scalp resulting in a score of 0 to 12 and 0 to 1. The PDAI total activity score ranged from 0 to 263, with 250 points representing disease activity (120 points for skin activity; 10 points for scalp activity; 120 points for mucosal activity) and 13 points representing disease damage. Higher total activity scores indicate more severe pemphigus symptoms. The Efficacy Analysis Set.

End point type	Secondary

End point timeframe:

Baseline (Day 1), end of Induction Period (Day 29), and the end of Maintenance Period (Cohort 1: Day 64; Cohort 2: Day 78; Cohort 3: Day 106), and end of Treatment-free Follow-up (Cohort 1: Day 120; Cohort 2: Day 148; Cohort 3: Day 176)

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

End point values	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3[27]	3[28]	7[29]	
Units: percentage change (%)				
arithmetic mean (standard error)				
End of Induction Period (n = 3, 3, 7)	-53.77 (± 10.791)	88.20 (± 161.816)	-58.26 (± 24.617)	
End of Maintenance Period (n = 3, 3, 7)	-23.83 (± 17.629)	-56.20 (± 24.906)	-15.49 (± 69.638)	

End of Treatment-free Follow-up (n = 3, 2, 7)	9.90 (± 46.279)	-76.30 (± 6.300)	-37.86 (± 45.237)	

Notes:

[27] - 'n' in category title denotes number of subjects analyzed for that category.

[28] - 'n' in category title denotes number of subjects analyzed for that category.

[29] - 'n' in category title denotes number of subjects analyzed for that category.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage Change from Baseline in PDAI (Cohort 4)

End point title	Mean Percentage Change from Baseline in PDAI (Cohort 4)[30]

End point description:

PDAI is a cutaneous and mucosal disease activity assessment performed by investigator based on evaluation of lesions. The score was weighted for the number and size of lesions with score of 0 (absent) to 10 (> 3 lesions, and/or at least one lesion > 16 cm diameter or entire area) given for skin at 12 anatomic locations, scalp, and mucous membrane showing disease activity (erosions/blisters or new erythema). Damage from post inflammatory hyperpigmentation or erythema from the resolving lesions was scored separately from the main score as absent (0) or present (1) for each body area or scalp resulting in a score of 0 to 12 and 0 to 1. The PDAI total activity score ranged from 0 to 263, with 250 points representing disease activity (120 points for skin activity; 10 points for scalp activity; 120 points for mucosal activity) and 13 points representing disease damage. Higher total activity scores indicate more severe pemphigus symptoms. The Efficacy Analysis Set.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and End of Induction Period (Day 29)

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

End point values	Cohort 4 (25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: percentage change (%)				
arithmetic mean (standard error)	-55.16 (± 5.474)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to Disease Control (DC)

End point title	Median Time to Disease Control (DC)[31]

End point description:

Time to DC, defined as when new lesions cease to form and established lesions begin to heal, evaluated from visit 2 until control was achieved. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis for Cohorts 1-3 is pooled using a subject analysis set.

End point values	Cohort 4 (25 mg/kg)	Cohorts 1-3		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	16		
Units: days				
median (full range (min-max))	29 (6 to 64)	15 (8 to 92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to EoC (Cohort 4)

End point title	Median Time to EoC (Cohort 4)[32]

End point description:

Time to EoC was defined as the time at which no new lesions have developed for a minimum of 2 weeks, and approximately 80% of lesions have healed. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis was prespecified for Cohort 4 only.

End point values	Cohort 4 (25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: days				
median (full range (min-max))	43 (34 to 99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time Until Relapse

End point title	Median Time Until Relapse[33]

End point description:

Time until relapse, relapse being defined as the appearance of 3 or more new lesions a month that do

not heal spontaneously within 1 week, or as the extension of established lesions, evaluated from any visit after DC. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis for Cohorts 1-3 is pooled using a subject analysis set.

End point values	Cohort 4 (25 mg/kg)	Cohorts 1-3		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	14[34]	14		
Units: days				
median (full range (min-max))	82 (63 to 211)	141 (10 to 169)		

Notes:

[34] - Median value represents the lower 95% confidence interval as the median could not be calculated.

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to Complete Clinical Remission (CR) (Cohort 4)

End point title	Median Time to Complete Clinical Remission (CR) (Cohort 4)[35]

End point description:

Time to calculated and Investigator-assessed CR, with CR being defined as the absence of new lesions and complete healing of established lesions for Cohort 4. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis was prespecified for Cohort 4 only.

End point values	Cohort 4 (25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: days				
median (full range (min-max))				
Calculated CR	72 (41 to 287)			
Investigator-assessed CR	92 (41 to 287)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to Complete CR Under Minimal Therapy (Cohort 4)

End point title	Median Time to Complete CR Under Minimal Therapy (Cohort 4)[36]

End point description:

CR under minimal therapy was defined as a prednisone dose of 10 mg/day or less for at least 8 weeks. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

End point type	Secondary

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistical analysis was prespecified for Cohort 4 only.

End point values	Cohort 4 (25 mg/kg)	Cohorts 1-3		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	0[37]	0[38]		
Units: days				
median (full range (min-max))	(to)	(to)		

Notes:

[37] - No data was collected for this end point.

[38] - No data was collected for this end point.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Maximum Serum Concentration (Cmax) of Efgartigimod (Cohorts 1-3)

End point title	Mean Maximum Serum Concentration (Cmax) of Efgartigimod (Cohorts 1-3)

End point description:

In order to assess the pharmacokinetic (PK) parameters of efgartigimod, blood samples were collected from each subject at each visit from Baseline. Concentrations of serum efgartigimod were determined using a validated assay. The PK Analysis Set included all subjects in the SAS who have at least one evaluable time-point of efgartigimod PK concentration data. No PK parameters were derived from Cohort 4.

End point type	Secondary

End point timeframe:

Within 30 minutes prior to start of infusion for the predose sample and within 30 minutes after end of infusion for the postdose sample at Baseline (Day 1) and Days 8, 15, 22, 36, 50, 64, 78, 92, and 106

End point values	Cohorts 1-3			
Subject group type	Subject analysis set			
Number of subjects analysed	19[39]			
Units: micrograms (µg)/mL				
arithmetic mean (standard deviation)				
Day 1 (n = 19)	168.748 (± 74.4491)			
Day 8 (n = 19)	171.079 (± 51.0213)			
Day 15 (n = 17)	147.829 (± 55.9076)			
Day 22 (n = 15)	209.147 (± 212.4485)			
Day 36 (n = 11)	173.209 (± 49.3980)			
Day 50 (n = 10)	164.590 (± 59.4498)			
Day 64 (n = 12)	229.333 (± 251.7157)			
Day 78 (n = 10)	227.100 (± 189.2784)			
Day 92 (n = 7)	195.286 (± 73.6698)			
Day 106 (n = 7)	168.071 (± 80.1428)			

Notes:

[39] - 'n' in category title denotes number of subjects analyzed for that category.

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time to Cmax (Tmax) of Efgartigimod (Cohorts 1-3)

End point title	Median Time to Cmax (Tmax) of Efgartigimod (Cohorts 1-3)

End point description:

In order to assess the PK parameters of efgartigimod, blood samples were collected from each subject at each visit from Baseline. Concentrations of serum efgartigimod were determined using a validated assay. The PK Analysis Set included all subjects in the SAS who have at least one evaluable time-point of efgartigimod PK concentration data. No PK parameters were derived from Cohort 4.

End point type	Secondary

End point timeframe:

Within 30 minutes prior to start of infusion for the predose sample and within 30 minutes after end of infusion for the postdose sample at Baseline (Day 1) and Days 8, 15, 22, 36, 50, 64, 78, 92, and 106

End point values	Cohorts 1-3			
Subject group type	Subject analysis set			
Number of subjects analysed	19[40]			
Units: hours (h)				
median (full range (min-max))				
Day 1 (n = 19)	2.500 (2.50 to 2.50)			
Day 8 (n = 19)	2.317 (2.03 to 2.55)			

Day 15 (n = 17)	2.250 (2.03 to 2.50)			
Day 22 (n = 15)	2.300 (2.13 to 2.50)			
Day 36 (n = 11)	2.250 (2.05 to 2.50)			
Day 50 (n = 10)	2.267 (2.08 to 2.50)			
Day 64 (n = 12)	2.450 (2.08 to 3.33)			
Day 78 (n = 10)	2.425 (2.08 to 2.50)			
Day 92 (n = 7)	2.333 (2.08 to 2.50)			
Day 106 (n = 7)	2.283 (2.08 to 2.50)			

Notes:

[40] - 'n' in category title denotes number of subjects analyzed for that category.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Concentration of Efgartigimod at the End of the Dosing Interval (Ctrough) (Cohorts 1-3)

End point title	Mean Concentration of Efgartigimod at the End of the Dosing Interval (Ctrough) (Cohorts 1-3)

End point description:

In order to assess the PK parameters of efgartigimod, blood samples were collected from each subject at each visit from Baseline. Concentrations of serum efgartigimod were determined using a validated assay. The PK Analysis Set included all subjects in the SAS who have at least one evaluable time-point of efgartigimod PK concentration data. No PK parameters were derived from Cohort 4.

End point type	Secondary

End point timeframe:

Within 30 minutes prior to start of infusion for the predose sample and within 30 minutes after end of infusion for the postdose sample on Days 8, 15, 22, 36, 50, 64, 78, 92, and 106

End point values	Cohorts 1-3			
Subject group type	Subject analysis set			
Number of subjects analysed	19[41]			
Units: µg/mL				
arithmetic mean (standard deviation)				
Day 8 (n = 19)	9.395 (± 5.2388)			
Day 15 (n = 18)	10.742 (± 5.9878)			
Day 22 (n = 15)	11.164 (± 7.5341)			
Day 29 (n = 14)	12.993 (± 6.5653)			
Day 36 (n = 12)	3.519 (± 2.3757)			
Day 50 (n = 10)	3.044 (± 2.1179)			

Day 64 (n = 12)	1.883 (± 1.8393)			
Day 78 (n = 10)	3.257 (± 1.9766)			
Day 92 (n = 7)	2.581 (± 1.2742)			
Day 106 (n = 7)	2.469 (± 1.5568)			

Notes:

[41] - 'n' in category title denotes number of subjects analyzed for that category.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Experiencing Postdose Antidrug Antibodies (ADA) to Efgartigimod

End point title	Number of Subjects Experiencing Postdose Antidrug Antibodies (ADA) to Efgartigimod

End point description:

In Cohorts 1-3, blood samples to assess ADA were collected at Baseline, Visit 3, Visit 5, all Maintenance treatment visits, Follow-up 1, Follow-up 2 and Follow-up 3. In Cohort 4, blood samples to assess ADA were collected at Baseline, then biweekly until End of Treatment, and at each Follow-up visit. The Full Analysis Set included all subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

End point values	Cohorts 1-4			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: subjects	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks	
Adverse event reporting additional description:	
The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Cohort 1 (10 mg/kg)
Reporting group description:	
Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period at weeks 2 and 6.	
Reporting group title	Cohort 2 (10 mg/kg)
Reporting group description:	
Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period once q2w for 8 weeks.	
Reporting group title	Cohort 3 (10 mg/kg)
Reporting group description:	
Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period q2w for 12 weeks.	
Reporting group title	Cohort 4 (25 mg/kg)
Reporting group description:	
Efgartigimod IV 25 mg/kg was administered as 5 weekly infusions (minimum) during the induction period until EoC, and during the maintenance period q2w until Week 34.	

Serious adverse events	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Tibia fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 8 (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
Infections and infestations			
Pneumonia			

subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (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

Serious adverse events	Cohort 4 (25 mg/kg)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Tibia fracture			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1 (10 mg/kg)	Cohort 2 (10 mg/kg)	Cohort 3 (10 mg/kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	3 / 5 (60.00%)	6 / 8 (75.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Infusion site swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hernia pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Nasal dryness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Respiratory failure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cystatin C increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Traumatic ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Neutrophilia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Anaemia macrocytic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Excessive cerumen production			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Middle ear inflammation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Blindness transient			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Dyspepsia			

subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oral disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Rash erythematous			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Renal cyst			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Renal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Rhinitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Impetigo			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Pustule			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Bacteriuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Candida infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pulpitis dental			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Sialoadenitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

Non-serious adverse events	Cohort 4 (25 mg/kg)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 15 (86.67%)		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	4		
Pyrexia			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Infusion site swelling subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Hernia pain subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Nasal dryness subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Cough subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Respiratory failure subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	2 / 15 (13.33%) 2		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Blood creatine phosphokinase			

increased subjects affected / exposed occurrences (all) Blood creatinine increased subjects affected / exposed occurrences (all) Weight increased subjects affected / exposed occurrences (all) Cystatin C increased subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1		
Injury, poisoning and procedural complications Traumatic ulcer subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1 3 / 15 (20.00%) 3 1 / 15 (6.67%) 1 0 / 15 (0.00%) 0		
Blood and lymphatic system disorders Anaemia			

subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Neutrophilia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Anaemia macrocytic			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Excessive cerumen production			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Middle ear inflammation			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Eye disorders			
Blindness transient			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Nausea			

subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Gastrointestinal disorder subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Oral pain subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Toothache subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Oral disorder subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Alopecia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Psoriasis subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Pruritus subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Rash erythematous subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Urticaria subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Renal and urinary disorders Renal cyst			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Renal pain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Endocrine disorders			
Cushingoid			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Rhinitis			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	3		
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Gastroenteritis			

subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Impetigo				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Pustule				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Bacteriuria				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Candida infection				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Oral herpes				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Conjunctivitis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Folliculitis				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Pulpitis dental				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Respiratory tract infection				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Sialoadenitis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Tonsillitis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Skin infection				

subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Tooth infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 October 2017	The following sections of the protocol were updated: - Schedule of Assessments - Section 5.1 Summary of Study Design - Section 5.3 Selection of Study Population - Section 5.3.1 Inclusion Criteria - Section 5.3.2 Exclusion Criteria - Section 6.3.4 Visit 6 and Visit 7 (Maintenance treatment period) - Section 6.6 Unscheduled Visit - Section 8.1.2.2 Other Laboratory Assessments - Section 9.2 Quality Control of Data - Section 10.2 Statistical Methods
28 February 2018	The following sections of the protocol were updated: - Section 3.1 Primary Objectives - Section 5.3 Selection of Study Population - Synopsis Section 5.3.1 Inclusion Criteria - Synopsis Methodology - Section 11.4 Patient Data Protection
11 June 2018	The following sections of the protocol were updated: - Section 5.1 Summary of Study Design - Schedule of Assessments - Section 5.3.1 Inclusion Criteria - Section 5.3.6 Sample Size Increase - Section 7.7 Prior and Concomitant Treatments - Section 7.8.1 Rescue Therapy - Section 8.1.2.2 Other Laboratory Assessments
06 February 2019	The following sections of the protocol were updated: - Section 3 Study Objectives - Section 4.2 Secondary endpoints - Section 5.1 Summary of Study Design - Section 5.3.6 Sample Size Increase - Section 5.3.1 Inclusion Criteria - Section 5.3.8 Screen Failures and Rescreening - Section 6.2 Screening - Sections 6.4, 6.5.1, 8.1.2.2 Assessments - Section 7.1 Treatments Administered - Section 7.7 Prior and Concomitant Treatments - Section 7.8.1 Rescue Therapy - Section 8.1.2.2 Other Laboratory Assessments - Section 8.5 Antidrug Antibodies - Section 10.4 Interim Analysis
26 June 2019	The following sections of the protocol were updated: - Section 6.4.2 Visit 2 to EoC - Section 7.1 Treatments Administered

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported