Clinical trial results:
A randomized, active-controlled, open-label, multicenter proof-of concept study of intravitreal LFG316 in patients with active non-infectious intermediate-, posterior-, or panuveitis requiring systemic immunosuppressive therapy

Summary

EudraCT number	2011-003254-90
Trial protocol	GB
Global end of trial date	24 August 2017

Results information

Result version number	v1 (current)
This version publication date	31 August 2018
First version publication date	31 August 2018

Trial information

Trial identification

Sponsor protocol code	CLFG316A2204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01526889
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.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	24 August 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of intravitreal LFG316 on the protocol defined, Day 85 response rate in eyes of patients who met the inclusion criteria.
The above objective applied to the study eye only. A response was defined by any one of the following criteria in the study eye:

- An improvement of 2 or more steps in vitreous haze, relative to baseline, or
- An improvement of 10 or more letters in visual acuity, relative to baseline, or
- An improvement of 2 or more steps in anterior chamber cells score, relative to baseline or
- Absence of chorioretinal lesions as determined by the investigator

Remission (complete response) was defined as any patient who had a vitreous haze score of 0 or 0.5 and who had an anterior chamber cell score of 0 and no chorioretinal lesions in the study eye and was off all immune modulatory therapy (systemic, corticosteroids and topical), without any worsening of uveitis during the trial.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 December 2012
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	United Kingdom: 6
Country: Number of subjects enrolled	United States: 19
Worldwide total number of subjects	25
EEA total number of subjects	6

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)	23
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Approximately 24 patients were planned to be enrolled. A total of 25 patients were randomized (18 patients in LFG316 group and 7 patients in conventional therapy group).

Period 1

Period 1 title	Treatment period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	LFG316

Arm description:

LFG316 administered intravitreally

Arm type	Experimental
Investigational medicinal product name	LFG316
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

The LFG316 solution for injection was a liquid solution.

Arm title	Conventional Therapy

Arm description:

Conventional treatment was selected by the investigator.

Arm type	Active comparator
Investigational medicinal product name	Conventional therapy on site at the discretion of the investigator
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection, Coated tablet, Eye drops, suspension
Routes of administration	Intravitreal use, Intravascular use , Oral use, Subcutaneous use, Intravenous use, Ophthalmic use

Dosage and administration details:

Depending on the conventional medications given, the dosage and administration varied (at the discretion of the investigator).

Number of subjects in period 1	LFG316	Conventional Therapy
Started	18	7
Completed	16	7
Not completed	2	0
Adverse event, non-fatal	2	-

Period 2

Period 2 title	Treatment extension period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	LFG316_extension period

Arm description:

LFG316 administered intravitreally

Arm type	Experimental
Investigational medicinal product name	LFG316
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

The LFG316 solution for injection was a liquid solution.

Number of subjects in period 2[1]	LFG316_extension period
Started	5
Completed	4
Not completed	1
Administrative problems	1

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: Only five patients in the LFG316 group entered the treatment extension period.

Baseline characteristics

Reporting groups	
Reporting group title	LFG316
Reporting group description:	
LFG316 administered intravitreally	
Reporting group title	Conventional Therapy
Reporting group description:	
Conventional treatment was selected by the investigator.	

Reporting group values	LFG316	Conventional Therapy	Total
Number of subjects	18	7	25
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	16	7	23
From 65-84 years	2	0	2
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	45.3	39.1	
standard deviation	± 14.84	± 14.89	-
Sex: Female, Male Units: Subjects			
Female	7	4	11
Male	11	3	14
Race/Ethnicity, Customized Units: Subjects			
Caucasian	17	6	23
Black	1	1	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	0	2
Not Hispanic or Latino	16	7	23
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	LFG316
Reporting group description: LFG316 administered intravitreally	
Reporting group title	Conventional Therapy
Reporting group description: Conventional treatment was selected by the investigator.	
Reporting group title	LFG316_extension period
Reporting group description: LFG316 administered intravitreally	

Primary: Number of participants with response rate for the individual response criteria - in the study eye

End point title	Number of participants with response rate for the individual response criteria - in the study eye[1]

End point description:

Response rate as defined by: 1) An improvement of 2 or more steps in vitreous haze, relative to baseline OR 2) An improvement of 10 or more letters in visual acuity (VA), relative to baseline OR 3) An improvement of 2 or more steps in anterior chamber cells (ACC) score, relative to baseline OR 4) Absence of chorioretinal lesions as determined by the investigator

End point type	Primary

End point timeframe:

Day 85 (end of study)

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: descriptive statistics

End point values	LFG316	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	7		
Units: Participants				
Improvement of vitreous haze ≥2 steps (N=15,6)	3	3		
Improvement of VA ≥ 10 letters (N=15,6)	0	1		
Improvement of ACC score ≥2 steps (N=7, 1)	0	0		
Resolution of chorioretinal lesions (N= 3, 0)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with remission rate in study eye - treatment period

End point title	Number of participants with remission rate in study eye - treatment period[2]

End point description:

Remission (complete response) was defined as any patient who had: - a vitreous haze score of 0 or 0.5 in the study eye, AND - an anterior chamber cell score of 0, AND - no chorioretinal lesions in the study eye, AND - was off all immune modulatory therapy (systemic, corticosteroids and topical), AND - without any worsening of uveitis during the trial.

End point type	Primary

End point timeframe:

Day 85 (end of study)

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: descriptive statistics

End point values	LFG316	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	7		
Units: Participants	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with vitreous haze score in study eye - treatment period

End point title	Number of participants with vitreous haze score in study eye - treatment period

End point description:

Vitreous haze score: 0, 0.5/Trace, 1+, 2+, 3+, 4+

End point type	Secondary

End point timeframe:

Day 2, 8, 15, 29, 43, 57 and, 85 (end of the study)

End point values	LFG316	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	7		
Units: Participants				
Day 2|0	0	0		
Day 8|0	0	0		
Day 15|0	2	1		
Day 29|0	0	3		
Day 43|0	6	2		
Day 57|0	5	2		
Day 85 (end of study)|0	2	1		
Day 2|0.5/Trace	2	1		
Day 8|0.5/Trace	1	0		

Day 15|0.5/Trace	3	1		
Day 29|0.5/Trace	4	1		
Day 43|0.5/Trace	1	3		
Day 57|0.5/Trace	5	2		
Day 85 (end of study)|0.5/Trace	6	3		
Day 2|1+	10	4		
Day 8|1+	4	1		
Day 15|1+	6	4		
Day 29|1+	10	3		
Day 43|1+	6	1		
Day 57|1+	4	3		
Day 85 (end of study)|1+	3	2		
Day 2|2+	1	1		
Day 8|2+	0	0		
Day 15|2+	3	1		
Day 29|2+	0	0		
Day 43|2+	0	0		
Day 57|2+	0	0		
Day 85 (end of study)|2+	3	0		
Day 2|3+	2	1		
Day 8|3+	1	0		
Day 15|3+	0	0		
Day 29|3+	0	0		
Day 43|3+	0	0		
Day 57|3+	0	0		
Day 85 (end of study)|3+	1	0		
Day 2|4+	0	0		
Day 8|4+	0	0		
Day 15|4+	2	0		
Day 29|4+	1	0		
Day 43|4+	1	0		
Day 57|4+	0	0		
Day 85 (end of study)|4+	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Best corrected visual acuity (BCVA) in study eye - treatment period

End point title	Mean Best corrected visual acuity (BCVA) in study eye - treatment period

End point description:

Visual acuity were measured using Early Treatment Diabetic Retinopathy Study (ETDRS) eye charts under ETDRS conditions. ETDRS best-corrected visual acuity was obtained in each eye separately under certified ETDRS conditions. This assessment was to be performed prior to pupil dilation. The number of letters read correctly (for each eye) was recorded

End point type	Secondary

End point timeframe:

Day 2, 8, 15, 29, 43, 57 and, 85 (end of the study)

End point values	LFG316	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	7		
Units: Mean BCVA				
arithmetic mean (standard deviation)				
Day 2	72.5 (± 19.36)	76.1 (± 0.7)		
Day 8	80.5 (± 11.69)	79.0 (± 79)		
Day 15	68.8 (± 18.53)	78.9 (± 9.10)		
Day 29	70.3 (± 19.39)	79.6 (± 9.47)		
Day 43	65.5 (± 24.45)	77.3 (± 9.07)		
Day 57	72.6 (± 14.79)	80.1 (± 10.35)		
Day 85	72.1 (± 15.53)	76.7 (± 10.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with macular edema in study eye - treatment period

End point title	Number of patients with macular edema in study eye - treatment period
End point description:	
Macular edema is a sign of uveitis.	
End point type	Secondary
End point timeframe:	
Day 85 (end of study)	

End point values	LFG316	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	3		
Units: Participants				
Day 2	2	1		
Day 8	1	1		
Day 15	3	0		
Day 29	2	0		
Day 43	2	0		
Day 57	2	0		
Day 85 (end of study)	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with chorioretinal lesions in study eye - treatment period

End point title	Number of patients with chorioretinal lesions in study eye - treatment period

End point description:

Chorioretinal lesions is a sign of uveitis.

End point type	Secondary

End point timeframe:

Day 2, 8, 15, 29, 43, 57 and, 85 (end of the study)

End point values	LFG316	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	3		
Units: Participants				
Day 2	3	0		
Day 8	2	0		
Day 15	4	0		
Day 29	5	0		
Day 43	4	0		
Day 57	5	1		
Day 85 (end of study)	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with anterior chamber cells score in study eye - treatment period

End point title	Number of participants with anterior chamber cells score in study eye - treatment period

End point description:

anterior chamber cells score (ACCS) with the scores being 0 (≤ 1 cell), 0.5 (1 to 5 aqueous cells), 1 (6 to 15 aqueous cells), 2 (16 to 25 aqueous cells), 3 (26 to 50 aqueous cells), 4 (>50 aqueous cells).

End point type	Secondary

End point timeframe:

Day 2, 8, 15, 29, 43, 57 and, 85 (end of the study)

End point values	LFG316	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	3		
Units: Participants				
Day 2|0; <1 cell	2	0		
Day 8|0; <1 cell	2	0		
Day 15|0; <1 cell	3	1		
Day 29|0; <1 cell	2	1		
Day 43|0; <1 cell	5	1		
Day 57|0; <1 cell	5	1		
Day 85|0; <1 cell	4	3		
Day 2|0.5; 1-5 cells	4	1		
Day 8|0.5; 1-5 cells	4	1		
Day 15|0.5; 1-5 cells	4	0		
Day 29|0.5; 1-5 cells	5	0		
Day 43|0.5; 1-5 cells	0	0		
Day 57|0.5; 1-5 cells	1	1		
Day 85|0.5; 1-5 cells	5	0		
Day 2|1; 6-15 cells	1	0		
Day 8|1; 6-15 cells	0	0		
Day 15|1; 6-15 cells	1	0		
Day 29|1; 6-15 cells	0	0		
Day 43|1; 6-15 cells	1	0		
Day 57|1; 6-15 cells	2	0		
Day 85|1; 6-15 cells	0	0		
Day 2|2; 16-25 cells	0	0		
Day 8|2; 16-25 cells	0	0		
Day 15|2; 16-25 cells	0	0		
Day 29|2; 16-25 cells	0	0		
Day 43|2; 16-25 cells	1	0		
Day 57|2; 16-25 cells	0	0		
Day 85|2; 16-25 cells	0	0		
Day 2|3; 26-50 cells	0	0		
Day 8|3; 26-50 cells	0	0		
Day 15|3; 26-50 cells	0	0		
Day 29|3; 26-50 cells	0	0		
Day 43|3; 26-50 cells	0	0		
Day 57|3; 26-50 cells	0	0		
Day 85|3; 26-50 cells	0	0		
Day 2|4; >50 cells	0	0		
Day 8|4; >50 cells	0	0		
Day 15|4; >50 cells	0	0		
Day 29|4; >50 cells	0	0		
Day 43|4; >50 cells	0	0		
Day 57|4; >50 cells	0	0		
Day 85|4; >50 cells	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with or without anti-LFG316 antibodies

End point title	Number of Participants with or without anti-LFG316

End point description:

Blood will be collected at each visit for the profiling of serum drug concentrations. The summary of immunogenicity (IG) by visit . The immunogenicity data (presence/absence of anti-LFG316 antibodies [anti-drug antibodies]). NO: No immunogenicity; YES: Positive immunogenicity.
with = w/
without = w/o
antibodies = Ab
EOS = end of study
EOE = end of extension

End point type	Secondary

End point timeframe:

Throughout the study (treatment and extension period)

Notes:

[3] - 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: descriptive statistics

End point values	LFG316			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Participants				
Day 1|participants w/ anti-LFG316 Ab	3			
Day 29|participants w/ anti-LFG316 Ab	3			
Day 85 (EOS)|participants w/ anti-LFG316 Ab	2			
Day 169|participants w/ anti-LFG316 Ab	1			
Day 253|participants w/ anti-LFG316 Ab	0			
EOE period|participants w/ anti-LFG316 Ab	1			
Day 1|participants w/o anti-LFG316 Ab	12			
Day 29|participants w/o anti-LFG316 Ab	10			
Day 85 (EOS)|participants w/o anti-LFG316 Ab	9			
Day 169|participants w/o anti-LFG316 Ab	1			
Day 253|participants w/o anti-LFG316 Ab	1			
EOE period|participants w/o anti-LFG316 Ab	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percent Change in Total C5 Concentrations in serum - treatment period

End point title	Mean Percent Change in Total C5 Concentrations in serum - treatment period

End point description:

Percent change from baseline (using each patient’s pre-dose value as baseline) in total C5 concentrations.

End point type	Secondary

End point timeframe:

Day 2, 8, 15, 29, 43, 57 and, 85 (end of the study)

End point values	LFG316	Conventional Therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	7		
Units: percent change in C5				
arithmetic mean (standard deviation)				
Day 2	6.80 (± 14.5)	1.02 (± 5.69)		
Day 15	8.21 (± 15.3)	-1.27 (± 19.7)		
Day 29	10.6 (± 17.4)	-8.33 (± 17.5)		
Day 43	8.38 (± 13.4)	6.46 (± 18.6)		
Day 57	6.73 (± 12.0)	5.98 (± 40.9)		
Day 85	3.21 (± 22.1)	1.28 (± 31.3)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All AEs reported in this record are from date of First Patient First Treatment until Last Patient Last Visit) up to approximately 5 years.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	LFG316

Reporting group description:

LF G316 administered intravitreally

Reporting group title	Conventional therapy

Reporting group description:

Conventional therapy

Serious adverse events	LFG316	Conventional therapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinopathy proliferative			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Mycotic endophthalmitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	LFG316	Conventional therapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 18 (61.11%)	5 / 7 (71.43%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Blood pressure increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Intraocular pressure increased			
subjects affected / exposed	3 / 18 (16.67%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Optic nerve cup/disc ratio increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Conjunctival haemorrhage			
subjects affected / exposed	4 / 18 (22.22%)	0 / 7 (0.00%)	
occurrences (all)	5	0	

Conjunctival hyperaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Cystoid macular oedema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Eye pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Hypotony of eye			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Macular fibrosis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Ocular hypertension			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Uveitis			
subjects affected / exposed	4 / 18 (22.22%)	0 / 7 (0.00%)	
occurrences (all)	5	0	
Visual impairment			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Vitreous floaters			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			

Myalgia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Giardiasis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Oral candidiasis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Tooth infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 18 (11.11%)	1 / 7 (14.29%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 January 2012	This amendment was necessary to address a request from the MHRA. This included modification of the study stopping criteria making them absolute.
18 January 2012	During the course of this trial, a liquid formulation of LFG316 became available and was to be the primary formulation for use in future clinical investigation with LFG316. The CLFG316A2204 protocol at that time only referenced the LFG316 lyophilized powder formulation which was no longer being produced. To assure continuity in study conduct, this amendment included the option to use either formulation with relevant sections updated to reflect this change.
08 July 2014	Due to the difficulty of recruiting patients with multi-focal Choroiditis (MFC), the study population was expanded to include patients with active non-infectious intermediate-, posterior- or panuveitis (NIU) in at least one eye, requiring intensification of systemic immunosuppressive therapy. The Inclusion and Exclusion criteria were modified to reflect this broader uveitis population. The requirement for a score of vitreous haze of 2 was reduced to 1+ at Screening. The study stopping criteria were modified to align with other protocols in the LFG316 program. Safety data from recently completed intravenous and intravitreal studies of LFG316 was added. With respect to planned study assessments, the frequency of fundus photography was reduced as this was no longer necessary to follow the progression of disease. With the shift away from patients with MFC and need to monitor neovascularization, the inclusion of fluorescein angiography was removed. Spectral domain optical coherence tomography (OCT) was added at key time points before and after administration of LFG316 in order to profile the incidence and explore the effect of LFG316 administration on disease pathology such as CME, ERMs and vitreomacular traction associated with NIU. Overall, in consideration of these proposed changes, the risk/benefit profile of LFG316 in patients with NIU was expected to be the same as with the previous MFC population.
22 December 2014	This amendment was necessary to address a request from the UK Health Authority (MHRA). This included an update of the protocol to harmonize with the new Reference Safety Information (RSI) section in the current Investigator's Brochure. With this update, the risk-benefit for patients with NIU remained the same.
07 September 2015	This amendment was implemented to allow a wider range of patients with uveitis the ability to participate in the study, and if they responded, to enable the patients to receive intravitreal LFG316 treatment for a longer period of time. To achieve these, the inclusion criteria and primary endpoint were updated and patients randomized to LFG316, who met the criteria for 'responder' and were willing to continue, were allowed to remain on therapy for an additional 6 months. The secondary endpoints were also updated to measure the mean changes in BCVA, vitreous haze score, anterior chamber cell score, and central retinal thickness and to assess the proportion of responders up to Day 281. To simplify the decision making for potential continuation, the primary endpoint was moved to Day 85 from Day 57. In addition, clarifications to the Exclusion criteria as well as an exploratory objective were proposed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported