Clinical trial results:
A Phase 2, randomized, double-blind placebo-controlled study to test the efficacy and safety of KPL-301 in giant cell arteritis

Summary

EudraCT number	2018-001003-36
Trial protocol	EE GB DE ES NL BE SI IT HR
Global end of trial date	25 November 2020

Results information

Result version number	v1
This version publication date	13 December 2021
First version publication date	13 December 2021

Trial information

Trial identification

Sponsor protocol code	KPL-301-C001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03827018
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Kiniksa Pharmaceuticals, Ltd.
Sponsor organisation address	Clarendon House 2 Church Street, Hamilton, Bermuda, HM 11
Public contact	Kiniksa Medical Information Group, Kiniksa Pharmaceuticals, Ltd. (Hamilton, Bermuda), Kiniksa Pharmaceuticals, Ltd. (Hamilton, Bermuda) c/o Kiniksa Pharmaceuticals Corp. , 1 7814319100, medinfo@kiniksa.com
Scientific contact	Kiniksa Medical Information Group, Kiniksa Pharmaceuticals, Ltd. (Hamilton, Bermuda), Kiniksa Pharmaceuticals, Ltd. (Hamilton, Bermuda) c/o Kiniksa Pharmaceuticals Corp. , 1 7814319100, medinfo@kiniksa.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	30 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 November 2020
Global end of trial reached?	Yes
Global end of trial date	25 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to evaluate the efficacy of KPL-301 versus placebo, coadministered with a 26-week steroid taper, for maintaining sustained remission for 26 weeks in subjects with new-onset or relapsing/refractory giant cell arteritis (GCA).
Secondary objectives of the trial were:
a) To evaluate the effect of KPL-301 vs placebo on cumulative corticosteroid dose.
b) To evaluate the effect of KPL-301 vs placebo on health-related quality of life (HRQoL).
c) To evaluate the safety and tolerability of KPL-301.
d) To evaluate the pharmacokinetics (PK) of KPL-301.

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, and applicable International Council for/Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines, and applicable country and local laws and regulations. Subjects were informed that their participation was voluntary. Subjects or their legally authorized representative were required to sign a statement of informed consent that met the requirements of 21 Code of Federal Regulations 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act requirements, where applicable, and the IRB/IEC or study center.

Background therapy:

All subjects received an unblinded 26-week oral prednisone taper according to a standardized tapering protocol. The oral steroid taper was self-administered by study subjects on a daily basis.

Evidence for comparator: -

Actual start date of recruitment	20 September 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Slovenia: 2
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Estonia: 8
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Ireland: 2

Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Serbia: 7
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	70
EEA total number of subjects	44

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)	18
From 65 to 84 years	51
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Subjects who met all of the inclusion criteria and none of the exclusion criteria were enrolled into the study. Eligible subjects entered the double-blind treatment period after randomization 3:2 to blinded treatment with KPL-301 150 mg or placebo administered subcutaneously (SC) every other week (every 2 weeks).

Pre-assignment

Screening details:

The study consisted of a screening period up to 6 weeks. Potential subjects were screened for meeting study-specified diagnostic criteria for GCA. Prior to first administration of KPL-301 or placebo, all subjects were required to have achieved remission.

Period 1

Period 1 title	Base Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

This was a double-blind study in which KPL-301 and placebo were identical in appearance/viscosity. Neither the subject nor any of the investigator or sponsor staff who were involved in the treatment or clinical evaluation of the subjects were aware of the treatment received.

Arms

Are arms mutually exclusive?	Yes
Arm title	KPL-301 150mg

Arm description:

Treatment with KPL-301 150 mg administered subcutaneously (SC) every other week (every 2 weeks). KPL-301 was coadministered with a 26-week corticosteroid taper.

Arm type	Experimental
Investigational medicinal product name	KPL-301
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects randomized to KPL-301 received 150 mg every other week by SC injection coadministered with a 26-week steroid taper.

Arm title	Placebo

Arm description:

Treatment with placebo administered subcutaneously (SC) every other week (every 2 weeks). Placebo was coadministered with a 26-week corticosteroid taper.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects randomized to Placebo received sterile, clear, colorless, free from visible particles liquid product identical in appearance/viscosity to the KPL-301 every other week by SC injection coadministered with a 26-week steroid taper.

Number of subjects in period 1	KPL-301 150mg	Placebo
Started	42	28
Completed	31	12
Not completed	11	16
Consent withdrawn by subject	2	2
Adverse event, non-fatal	1	1
Lack of efficacy	8	12
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	KPL-301 150mg
Reporting group description:	
Treatment with KPL-301 150 mg administered subcutaneously (SC) every other week (every 2 weeks). KPL-301 was coadministered with a 26-week corticosteroid taper.	
Reporting group title	Placebo
Reporting group description:	
Treatment with placebo administered subcutaneously (SC) every other week (every 2 weeks). Placebo was coadministered with a 26-week corticosteroid taper.	

Reporting group values	KPL-301 150mg	Placebo	Total
Number of subjects	42	28	70
Age categorical Units: Subjects			
Adults (18-64 years)	9	9	18
From 65-84 years	33	18	51
85 years and over	0	1	1
Age continuous Units: years			
median	69.5	72	
full range (min-max)	52 to 84	55 to 85	-
Gender categorical Units: Subjects			
Female	32	18	50
Male	10	10	20

Subject analysis sets	
Subject analysis set title	mITT Analysis Set
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomized subjects who received at least 1 dose of KPL-301 or placebo and at least had 1 assessment in the Double-blind Treatment period. Efficacy analyses were based on the Modified intent-to-treat (mITT) analysis set. All analyses based on mITT were based on each subject's randomized treatment assignment.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized subjects who took at least 1 dose of KPL-301 or placebo. Safety analyses were based on the medication that was actually administered to each subject.	
Subject analysis set title	Per Protocol Analysis Set
Subject analysis set type	Per protocol
Subject analysis set description:	
All mITT subjects without important protocol deviations deemed to impact efficacy or ethical conduct.	
Subject analysis set title	PK Analysis Set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects who received at least 1 dose of KPL-301 and had sufficient KPL-301 concentration data for calculation of KPL-301 PK parameters were included in the PK analysis set.	

Reporting group values	mITT Analysis Set	Safety Analysis Set	Per Protocol Analysis Set
Number of subjects	70	70	67
Age categorical Units: Subjects			
Adults (18-64 years)	18	18	
From 65-84 years	51	51	
85 years and over	1	1	
Age continuous Units: years			
median	70	70	
full range (min-max)	52 to 85	52 to 85	
Gender categorical Units: Subjects			
Female	50	50	
Male	20	20	

Reporting group values	PK Analysis Set		
Number of subjects	70		
Age categorical Units: Subjects			
Adults (18-64 years)	18		
From 65-84 years	51		
85 years and over	1		
Age continuous Units: years			
median	70		
full range (min-max)	52 to 85		
Gender categorical Units: Subjects			
Female	50		
Male	20		

End points

End points reporting groups

Reporting group title	KPL-301 150mg

Reporting group description:

Treatment with KPL-301 150 mg administered subcutaneously (SC) every other week (every 2 weeks). KPL-301 was coadministered with a 26-week corticosteroid taper.

Reporting group title	Placebo

Reporting group description:

Treatment with placebo administered subcutaneously (SC) every other week (every 2 weeks). Placebo was coadministered with a 26-week corticosteroid taper.

Subject analysis set title	mITT Analysis Set
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All randomized subjects who received at least 1 dose of KPL-301 or placebo and at least had 1 assessment in the Double-blind Treatment period. Efficacy analyses were based on the Modified intent-to-treat (mITT) analysis set. All analyses based on mITT were based on each subject's randomized treatment assignment.

Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized subjects who took at least 1 dose of KPL-301 or placebo. Safety analyses were based on the medication that was actually administered to each subject.

Subject analysis set title	Per Protocol Analysis Set
Subject analysis set type	Per protocol

Subject analysis set description:

All mITT subjects without important protocol deviations deemed to impact efficacy or ethical conduct.

Subject analysis set title	PK Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All subjects who received at least 1 dose of KPL-301 and had sufficient KPL-301 concentration data for calculation of KPL-301 PK parameters were included in the PK analysis set.

Primary: Time to Flare by Week 26

End point title	Time to Flare by Week 26[1][2]

End point description:

End point type	Primary

End point timeframe:

By Week 26

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: Placebo hasn't been included in this endpoint as there is no data for Time to Flare - Hazard Ratio. Kaplan-Meier method was used.
P value (Time to Flare) = 0.0263.
[2] - 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 were included for this primary endpoint. Kaplan-Meier method used to estimate the survival functions for each treatment arm.
P value (Time to Flare) = 0.0263.

End point values	KPL-301 150mg			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: weeks/percent				
number (confidence interval 95%)				
Time to Flare - Hazard Ratio (KPL-301 vs Placebo)	0.38 (0.15 to 0.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Sustained Remission at Week 26

End point title	Sustained Remission at Week 26

End point description:

End point type	Secondary

End point timeframe:

At Week 26

End point values	KPL-301 150mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: percent				
number (confidence interval 95%)				
Sustained Remission at Week 26, %	83.2 (67.9 to 91.6)	49.9 (29.6 to 67.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Elevated ESR by Week 26

End point title	Time to Elevated ESR by Week 26

End point description:

End point type	Secondary

End point timeframe:

By Week 26

End point values	KPL-301 150mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: Weeks				
number (not applicable)				
Time to Elevated ESR by Week 26, median	26.1	12.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Elevated CRP by Week 26

End point title	Time to Elevated CRP by Week 26[3]

End point description:

End point type	Secondary

End point timeframe:

By Week 26

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 were included for this secondary endpoint. P value = 0.0378.

End point values	KPL-301 150mg			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: Weeks/percent				
number (confidence interval 95%)				
Hazard Ratio (KPL-301 vs Placebo)	0.43 (0.19 to 0.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Signs/Symptoms of GCA or New/Worsening Vasculitis by Imaging by Week 26

End point title	Time to Signs/Symptoms of GCA or New/Worsening Vasculitis by Imaging by Week 26[4]

End point description:

Time to Symptoms of GCA, New/Worsening Vasculitis

End point type	Secondary

End point timeframe:

By Week 26

Notes:

[4] - 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: Placebo hasn't been included in this endpoint as there is no data for Hazard Ratio (KPL-301 vs Placebo). P value = 0.0651.

End point values	KPL-301 150mg			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: Weeks/percent				
number (confidence interval 95%)				
Hazard Ratio (KPL-301 vs Placebo)	0.49 (0.22 to 1.06)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Steroid Dose at Week 26

End point title	Cumulative Steroid Dose at Week 26

End point description:

End point type	Secondary

End point timeframe:

At Week 26

End point values	KPL-301 150mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: Dose				
least squares mean (standard error)				
Cumulative Steroid Dose	2075.11 (± 109.598)	2401.56 (± 134.691)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Completing Corticosteroid Taper and with Normal ESR by Week 26

End point title	Percentage of Subjects Completing Corticosteroid Taper and with Normal ESR by Week 26

End point description:

End point type	Secondary

End point timeframe:

By Week 26

End point values	KPL-301 150mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: percent				
number (not applicable)				
Subjects Completing Corticosteriod Taper, %	45.2	14.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Completing Corticosteroid Taper and with Normal CRP by Week 26

End point title	Percentage of Subjects Completing Corticosteroid Taper and with Normal CRP by Week 26

End point description:

End point type	Secondary

End point timeframe:

By Week 26

End point values	KPL-301 150mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: percent				
number (not applicable)				
Subjects Completing Corticosteroid Taper, %	23.8	14.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Completing Corticosteroid Taper and with No Signs/Symptoms of GCA by Week 26

End point title	Percentage of Subjects Completing Corticosteroid Taper and

	with No Signs/Symptoms of GCA by Week 26

End point description:

End point type	Secondary

End point timeframe:

By Week 26

End point values	KPL-301 150mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: percent				
number (not applicable)				
Subjects Completing Corticosteroid Taper, %	71.4	32.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative Steroid Dose at the end of the Washout Safety Follow-up Period

End point title	Cumulative Steroid Dose at the end of the Washout Safety Follow-up Period

End point description:

End point type	Secondary

End point timeframe:

At the end of the Washout Safety Follow-up Period

End point values	KPL-301 150mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: Dose				
least squares mean (standard error)				
Cumulative Steroid Dose	2464.81 (± 168.955)	2845.63 (± 207.638)		

Statistical analyses

No statistical analyses for this end point

Secondary: Sustained Remission at week 26 (Independent Adjudication)

End point title	Sustained Remission at week 26 (Independent Adjudication)

End point description:

End point type	Secondary

End point timeframe:

At Week 26

End point values	KPL-301 150mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	28		
Units: percent				
number (confidence interval 95%)				
Sustained Remission at Week 26 (%)	83.2 (67.9 to 91.6)	49.9 (29.6 to 67.3)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were monitored from Day 1 of treatment till Week 26 and during the following 12-week safety follow-up period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	KPL-301 150mg

Reporting group description:

Treatment with KPL-301 150 mg administered subcutaneously (SC) every other week (every 2 weeks). KPL-301 was coadministered with a 26-week corticosteroid taper.

Reporting group title	Placebo

Reporting group description:

Treatment with placebo administered subcutaneously (SC) every other week (every 2 weeks). Placebo was coadministered with a 26-week corticosteroid taper.

Serious adverse events	KPL-301 150mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 42 (4.76%)	3 / 28 (10.71%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	1 / 42 (2.38%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dementia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Oedema peripheral			

subjects affected / exposed	0 / 42 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary fibrosis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	KPL-301 150mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 42 (78.57%)	25 / 28 (89.29%)	
Investigations			
Carbon monoxide diffusing capacity decreased			
subjects affected / exposed	4 / 42 (9.52%)	1 / 28 (3.57%)	
occurrences (all)	4	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 42 (4.76%)	5 / 28 (17.86%)	
occurrences (all)	2	5	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 42 (2.38%)	4 / 28 (14.29%)	
occurrences (all)	1	4	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 42 (14.29%)	7 / 28 (25.00%)	
occurrences (all)	6	7	

Hypoaesthesia			
subjects affected / exposed	0 / 42 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	2 / 42 (4.76%)	2 / 28 (7.14%)	
occurrences (all)	2	2	
Pyrexia			
subjects affected / exposed	0 / 42 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 42 (7.14%)	0 / 28 (0.00%)	
occurrences (all)	3	0	
Vomiting			
subjects affected / exposed	1 / 42 (2.38%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	0 / 42 (0.00%)	3 / 28 (10.71%)	
occurrences (all)	0	3	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 42 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	0 / 42 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	4 / 42 (9.52%)	2 / 28 (7.14%)	
occurrences (all)	4	2	
Back pain			
subjects affected / exposed	3 / 42 (7.14%)	3 / 28 (10.71%)	
occurrences (all)	3	3	
Muscle spasms			

subjects affected / exposed	3 / 42 (7.14%)	3 / 28 (10.71%)	
occurrences (all)	3	3	
Arthralgia			
subjects affected / exposed	2 / 42 (4.76%)	4 / 28 (14.29%)	
occurrences (all)	2	4	
Osteoarthritis			
subjects affected / exposed	1 / 42 (2.38%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
Tendonitis			
subjects affected / exposed	1 / 42 (2.38%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
Musculoskeletal pain			
subjects affected / exposed	0 / 42 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 42 (11.90%)	3 / 28 (10.71%)	
occurrences (all)	5	3	
Upper respiratory tract infection			
subjects affected / exposed	3 / 42 (7.14%)	2 / 28 (7.14%)	
occurrences (all)	3	2	
Rhinitis			
subjects affected / exposed	1 / 42 (2.38%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
Oral herpes			
subjects affected / exposed	0 / 42 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Respiratory tract infection			
subjects affected / exposed	0 / 42 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	2 / 42 (4.76%)	2 / 28 (7.14%)	
occurrences (all)	2	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 October 2018	Rationale for Amendment – Protocol Amendment v2.0 was completed to clarify aspects of protocol version 1.0 as well as to incorporate feedback from global Regulatory and Ethical bodies. Substantial changes to this version include: • Limiting the double-blind period to 26-weeks total, removing the extended exposure for patients who enroll earlier in the study. • Removal of the Open-Label Extension – Per Regulatory feedback, open-label KPL-301 should only be provided to patients after proof of efficacy has been established • Addition of 12-week Washout Safety Follow-up period to ensure patients have continued access to open-label study supplied prednisone and are adequately followed and weaned back to Standard of Care • Updated inclusion criteria regarding pregnancy and contraception methods to ensure highly effective methods of contraception are reflected • Provided clarification on sample size and event calculations • Addition of Serum Pregnancy test during screening, additional urine pregnancy tests, safety labs, and anti-KPL-301 antibody testing during the study. • Addition of Definition of SUSAR and defined Study Termination criteria
30 November 2018	Rationale for Amendment – Protocol Amendment v3.0 was completed to clarify aspects of protocol version 2.0 as well as to incorporate feedback from global Regulatory bodies. Substantial changes to this version include: • Discontinuation of study drug (KPL-301 or placebo) in the event of a GCA Flare • Additional PK samples added to Schedule of Activities • Clarification of individual patient and study stopping criteria • Correction of the US Safety contact number
30 March 2020	Rationale for Amendment – Protocol Amendment v4.0 was completed to clarify aspects of protocol version 3.0 as well as to incorporate feedback from global Regulatory bodies. Substantial changes to this version include: • Updated secondary endpoints and analysis; and inserted study endpoints into the Synopsis Objective section. • The planned number of subjects to be enrolled in the study was updated from approximately 60 to approximately 70 subjects (42 subjects planned to be assigned to the KPL-301 arm and 28 subjects planned to be assigned to the placebo arm) to align with the updated sample size estimation. • Added clarification that SAEs will be recorded in the eCRF within 24 hours of discovery.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported