Clinical trial results:
An Open-Label, Pilot Study to Assess the Efficacy and Safety Of AK002 (Siglec-8) in Subjects with Antihistamine-Resistant Chronic Urticaria

Summary

EudraCT number	2017-002581-51
Trial protocol	DE
Global end of trial date	02 January 2019

Results information

Result version number	v1 (current)
This version publication date	30 April 2021
First version publication date	30 April 2021

Trial information

Trial identification

Sponsor protocol code	AK002-006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03436797
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allakos, Inc.
Sponsor organisation address	975 Island Drive, Suite 201, Redwood City, United States, CA 94065
Public contact	Henrik Rasmussen, MD, PhD Chief Medical Officer, Allakos, Inc., hrasmussen@allakos.com
Scientific contact	Henrik Rasmussen, MD, PhD Chief Medical Officer, Allakos, Inc., hrasmussen@allakos.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	02 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 January 2019
Global end of trial reached?	Yes
Global end of trial date	02 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of AK002 on symptoms in subjects with Chronic Urticaria (CU) (change in urticaria control test [UCT] score)

Protection of trial subjects:

The study was conducted in accordance with regulations governing clinical trials including the Declaration of Helsinki, Protection of Human Volunteers (21 CFR 50), IEC (21 CFR 56 and ICH E6, and Obligations of Clinical Investigators (21 CFR 312 and ICH E6). The Investigator also complied with all applicable privacy regulations (e.g., the Health Insurance Portability and Accountability Act [HIPAA] and European Union Data Protection Directive 95/46/EC).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 February 2018
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	Germany: 30
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	47
EEA total number of subjects	30

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)	39
From 65 to 84 years	8

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

54 subjects were screened, 47 subjects were enrolled and treated in 4 cohorts at 2 centers each in the USA and in Germany: cholinergic urticaria (CholU, 11 subjects), urticaria factitia (UF, 10 subjects), chronic spontaneous urticaria and XOLAIR (omalizumab) naïve (CSU-XN, 14 subjects), and CSU with treatment failure to XOLAIR (CSU-XF, 12 subjects)

Pre-assignment

Screening details:

Subjects who met each of the inclusion and none of the exclusion criteria were eligible to participate in the study.

Period 1

Period 1 title	Treatment and efficacy follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	AK002

Arm description:

Single doses of AK002 were administered by IV infusion every 28 days at Weeks 0, 4, 8, 12, 16, and 20.
The arm included all subjects who were enrolled, did receive at least 1 dose of study drug, and had at least 1 post-baseline assessment of the primary efficacy variable (=modified intent-to-treat population, mITT).

Arm type	Experimental
Investigational medicinal product name	AK002
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

AK002 (15 ± 1.5 mg/mL) was administered as IV infusion starting at 0.3 mg/kg on Day 1. If well tolerated, the dose was increased to 1 mg/kg on Day 29 and Day 57. The dose could be increased further to 3 mg/kg on Days 85, 113, and 141 if the UCT score was <12 and/or the Investigator, in consultation with the Allakos Medical Monitor, deemed it advisable.

Number of subjects in period 1[1]	AK002
Started	45
Completed	37
Not completed	8
Adverse event, serious fatal	1
Consent withdrawn by subject	2
Adverse event, non-fatal	3
Other	1
Lost to follow-up	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 47 subjects were enrolled in this study and received at least one dose of the study drug. 45 of these subjects had at least one post-baseline assessment of the primary efficacy variable, and were reported in the baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	Treatment and efficacy follow-up
Reporting group description: -	

Reporting group values	Treatment and efficacy follow-up	Total	
Number of subjects	45	45	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	42.0		
full range (min-max)	18 to 75	-	
Gender categorical Units: Subjects			
Female	34	34	
Male	11	11	

Subject analysis sets	
Subject analysis set title	CholU
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The CholU cohort included subjects with cholinergic urticaria.	
Subject analysis set title	UF
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The UF cohort included subjects with urticaria factitia.	
Subject analysis set title	CSU-XN
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The CSU-XN cohort included XOLAIR® (omalizumab) naïve subjects with chronic spontaneous urticaria (CSU).	
Subject analysis set title	CSU-XF
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The CSU-XF cohort included subjects with chronic spontaneous urticaria (CSU) who did not achieve an adequate response to XOLAIR® (omalizumab) in the opinion of the Investigator.	

Reporting group values	CholU	UF	CSU-XN
Number of subjects	11	10	13
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
median	33.0	26.5	65
full range (min-max)	18 to 62	19 to 56	30 to 75
Gender categorical			
Units: Subjects			
Female	6	6	13
Male	5	4	0

Reporting group values	CSU-XF		
Number of subjects	11		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
median	29		
full range (min-max)	22 to 60		
Gender categorical			
Units: Subjects			
Female	9		
Male	2		

End points

End points reporting groups

Reporting group title	AK002
Reporting group description:	
Single doses of AK002 were administered by IV infusion every 28 days at Weeks 0, 4, 8, 12, 16, and 20. The arm included all subjects who were enrolled, did receive at least 1 dose of study drug, and had at least 1 post-baseline assessment of the primary efficacy variable (=modified intent-to-treat population, mITT).	
Subject analysis set title	CholU
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The CholU cohort included subjects with cholinergic urticaria.	
Subject analysis set title	UF
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The UF cohort included subjects with urticaria factitia.	
Subject analysis set title	CSU-XN
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The CSU-XN cohort included XOLAIR® (omalizumab) naïve subjects with chronic spontaneous urticaria (CSU).	
Subject analysis set title	CSU-XF
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The CSU-XF cohort included subjects with chronic spontaneous urticaria (CSU) who did not achieve an adequate response to XOLAIR® (omalizumab) in the opinion of the Investigator.	

Primary: Change in UCT from Baseline at Week 22 using LOCF

End point title	Change in UCT from Baseline at Week 22 using LOCF[1]
End point description:	
The primary endpoint was the change in the UCT, a score for symptom control in chronic urticaria (CU). At Baseline, a 4-week recall was to be recorded, prior to first study drug administration. A change of the UCT score of 3 or more points was regarded as clinically relevant (minimal clinically important difference [MCID]).	
End point type	Primary
End point timeframe:	
The change of the UCT was measured from Baseline to Week 22.	

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 statistical tests were performed for this pilot study. Descriptive statistics and confidence intervals were evaluated.

End point values	CholU	UF	CSU-XN	CSU-XF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	10	13	11
Units: UCT score				
arithmetic mean (confidence interval 95%)	6.5 (2.3 to 10.6)	3.4 (0.5 to 6.3)	11.1 (8.6 to 13.5)	4.8 (0.1 to 9.5)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse events were reported from the first dose of AK002 until the end of Follow-up (Week 28).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	CholU cohort
Reporting group description: -	
Reporting group title	UF cohort
Reporting group description: -	
Reporting group title	CSU-XN cohort
Reporting group description: -	
Reporting group title	CSU-XF cohort
Reporting group description: -	
Reporting group title	Total
Reporting group description: All subjects	

Serious adverse events	CholU cohort	UF cohort	CSU-XN cohort
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	2 / 14 (14.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (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
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure acute			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	CSU-XF cohort	Total	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	4 / 47 (8.51%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure acute			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Gastrointestinal disorders			

Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
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: 0 %

Non-serious adverse events	CholU cohort	UF cohort	CSU-XN cohort
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 11 (72.73%)	10 / 10 (100.00%)	10 / 14 (71.43%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Squamous cell carcinoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Thrombophlebitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Wisdom teeth removal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Influenza like illness			
subjects affected / exposed	3 / 11 (27.27%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Chest discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Pharyngeal erythema			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Panic attack			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Body temperature increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram ST segment elevation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	6 / 11 (54.55%)	4 / 10 (40.00%)	5 / 14 (35.71%)
occurrences (all)	7	4	7
Laceration			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Arthropod sting			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0

Foot fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Limb injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Sinus arrhythmia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 11 (18.18%)	2 / 10 (20.00%)	1 / 14 (7.14%)
occurrences (all)	2	2	2
Migraine			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Diabetic neuropathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Dizziness			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hypotonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear canal erythema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	3
Toothache			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	2 / 10 (20.00%)	1 / 14 (7.14%)
occurrences (all)	0	3	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Sensitivity of teeth			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Swollen tongue			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Eczema			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Erythema multiforme			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 11 (9.09%)	2 / 10 (20.00%)	0 / 14 (0.00%)
occurrences (all)	1	2	0
Arthralgia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Bone pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Infections and infestations			

Cystitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Acute sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Appendicitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Folliculitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	4 / 10 (40.00%)	0 / 14 (0.00%)
occurrences (all)	0	7	0
Rhinitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0

Sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	2 / 14 (14.29%)
occurrences (all)	0	1	2
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	CSU-XF cohort	Total	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)	39 / 47 (82.98%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Squamous cell carcinoma			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Thrombophlebitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Wisdom teeth removal			

subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 12 (16.67%)	3 / 47 (6.38%)	
occurrences (all)	2	3	
Fatigue			
subjects affected / exposed	1 / 12 (8.33%)	3 / 47 (6.38%)	
occurrences (all)	2	4	
Influenza like illness			
subjects affected / exposed	0 / 12 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	3 / 47 (6.38%)	
occurrences (all)	1	3	
Chest discomfort			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Chills			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Inflammation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	1 / 12 (8.33%)	2 / 47 (4.26%)	
occurrences (all)	1	2	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 12 (8.33%)	2 / 47 (4.26%)	
occurrences (all)	1	2	

Cough			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Pharyngeal erythema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Panic attack			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Body temperature increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Electrocardiogram ST segment elevation			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	5 / 12 (41.67%)	20 / 47 (42.55%)	
occurrences (all)	10	28	
Laceration			

subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Arthropod sting			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Foot fracture			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Ligament sprain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Muscle strain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Sinus arrhythmia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Tachycardia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 12 (33.33%)	9 / 47 (19.15%)	
occurrences (all)	5	11	
Migraine			

subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Diabetic neuropathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Hypotonia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear canal erythema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 12 (8.33%)	3 / 47 (6.38%)	
occurrences (all)	1	5	
Toothache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	2	
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	4 / 47 (8.51%)	
occurrences (all)	1	5	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Sensitivity of teeth			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Swollen tongue			

subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 12 (8.33%)	2 / 47 (4.26%)	
occurrences (all)	1	2	
Eczema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Erythema multiforme			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Pruritus			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 12 (8.33%)	4 / 47 (8.51%)	
occurrences (all)	1	4	
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	3 / 47 (6.38%)	
occurrences (all)	2	4	
Bone pain			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Pain in jaw			

subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Tendonitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 12 (8.33%)	2 / 47 (4.26%)	
occurrences (all)	1	2	
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Acute sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Appendicitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Folliculitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Gastrointestinal infection			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Gingivitis			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Herpes virus infection			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	

Nasopharyngitis			
subjects affected / exposed	6 / 12 (50.00%)	10 / 47 (21.28%)	
occurrences (all)	13	20	
Rhinitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	
Urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Viral infection			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 12 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Hyperlipidaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 47 (2.13%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 December 2017	Details of the study protocol Amendment 1 included, but were not limited to: - Exclusion Criteria #9 was expanded to include subjects that have been committed to an institution by virtue of an order issued either by the judicial or the administrative authorities to be excluded from the study. - Added Exclusion Criteria#18, "Positive screening for ova and parasite test at baseline." - Added Exclusion Criteria#19, "Treatment of helminthic parasite within 6 months of screening." - Added Exclusion Criteria#20, "Positive HIV serology at screening." - Added Exclusion Criteria#21, "Positive Hepatitis serology at baseline, except for vaccinated patients or patients with past but resolved hepatitis at screening." - Added Exclusion Criteria#22, "Donation or loss of >500 mL of blood within 56 days prior to administration of study drug or donation of plasma within 7 days prior to administration of drug."
23 February 2018	Details of the study protocol Amendment 2 included, but were not limited to: - The EudraCT Number was corrected to 2017-002581-51, and IND number 137491 was added. - The dosing regimen was updated to 0.3 mg/kg for Dose 1 (Day 1) followed by 1 mg/kg for Dose 2 (Day 29) and Dose 3 (Day 57). - The number of study centers was updated to include approximately 4 study centers in the USA and Germany, and the number of subjects to be enrolled was revised for up to 40 subjects among 4 disease groups: up to 10 each of CholU subjects, UF subjects, CSU-XOLAIR (omalizumab) naïve subjects, and CSU subjects that did not have adequate response with XOLAIR (omalizumab).
01 May 2018	Details of the study protocol Amendment 3 included, but were not limited to: - The number of subjects was increased to 48 subjects. Each cohort was increased to approximately 12 subjects. - The number of doses was increased from 3 to 6. For Doses 4, 5, and 6 on Days 85, 113, and 141, respectively, the dose would be increased to 3 mg/kg if the subject had a UCT score of <12 and/or at the discretion of the Investigator in consultation with the Allakos Medical Monitor. If the UCT score was ≥12 and if the Investigator in consultation with the Medical Monitor believed that the subject had achieved adequate symptom improvement, then the subject would stay at a dose of 1 mg/kg. The total study duration was increased to 32 weeks. - The definition of baseline was changed from within 24 hours of first dose to within 48 hours of first dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported