Clinical trial results:
A Phase IIa, Randomised, Double Blind, Placebo Controlled, Parallel Group, Multicentre Study of an Anti OX40L Monoclonal Antibody (KY1005) in Moderate to Severe Atopic Dermatitis

Summary

EudraCT number	2018-002299-41
Trial protocol	GB DE ES
Global end of trial date	08 October 2020

Results information

Result version number	v1 (current)
This version publication date	08 October 2021
First version publication date	08 October 2021

Trial information

Trial identification

Sponsor protocol code	KY1005-CT02

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Kymab Limited
Sponsor organisation address	The Bennet Building (B930), Babraham Research Campus, Cambridge, United Kingdom, CB22 3AT
Public contact	Development Clinical Trial Desk, Kymab Limited, Clinicaltrial@kymab.com
Scientific contact	Development Clinical Trial Desk, Kymab Limited, Clinicaltrial@kymab.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	15 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 October 2020
Global end of trial reached?	Yes
Global end of trial date	08 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the efficacy and safety of KY1005 on the signs of atopic dermatitis (AD) using the Eczema Area and Severity Index (EASI) and the incidence of treatment-emergent adverse events (TEAEs).

Protection of trial subjects:

This study was conducted in accordance with the protocol, all applicable regulatory requirements, the International Council for Harmonisation (ICH) E6 guideline for Good Clinical Practice (GCP) and the general principles of the Declaration of Helsinki.
Written informed consent for the study was obtained from each patient by the Investigator or suitably qualified designee before any protocol-specific procedures were carried out. Written information (including patient information sheets, ICFs, adverts, general practitioner letters) was only discussed with or given to patients once the IEC approved the document in writing.
Patients provided written informed consent on an IEC-approved ICF. Patients were re-consented and ICFs were re-signed before implementation of each protocol amendment, where applicable. Each patient’s ICF was also signed and dated by the person who conducted the informed consent discussion. Informed consent was documented in the patient’s medical records. The patient was given a copy of the information sheet and their signed and dated consent form, and the original ICF was filed in the Investigator site file (ISF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 December 2018
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	Poland: 72
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Germany: 5
Worldwide total number of subjects	89
EEA total number of subjects	86

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	88
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were screened within 29 to 8 days prior to baseline.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Low dose KY1005

Arm description: -

Arm type	Experimental
Investigational medicinal product name	KY1005
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Patients received a low loading dose of KY1005 on Day 1, followed by three maintenance doses at 50% of the loading dose at 28-day intervals on Days 29, 57 and 85.

Arm title	High dose KY1005

Arm description: -

Arm type	Experimental
Investigational medicinal product name	KY1005
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Patients received a high loading dose of KY1005 on Day 1, followed by three maintenance doses at 50% of the loading dose at 28-day intervals on Days 29, 57 and 85.

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Patients received placebo on Day 1, followed by three further doses at 28-day intervals on Days 29, 57 and 85.

Number of subjects in period 1	Low dose KY1005	High dose KY1005	Placebo
Started	29	30	30
Completed	20	22	17
Not completed	9	8	13
Consent withdrawn by subject	6	5	3
Adverse event, non-fatal	-	-	3
Other	2	3	5
Failure to meet randomisation criteria	1	-	-
Protocol deviation	-	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Low dose KY1005
Reporting group description: -	
Reporting group title	High dose KY1005
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Low dose KY1005	High dose KY1005	Placebo
Number of subjects	29	30	30
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)	28	30	30
From 65-84 years	1	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	13	14	11
Male	16	16	19

Reporting group values	Total		
Number of subjects	89		
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)	88		
From 65-84 years	1		
85 years and over	0		
Gender categorical Units: Subjects			
Female	38		
Male	51		

End points

End points reporting groups	
Reporting group title	Low dose KY1005
Reporting group description: -	
Reporting group title	High dose KY1005
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Percentage change in EASI from Baseline to Day 113 (FAS)	
End point title	Percentage change in EASI from Baseline to Day 113 (FAS)
End point description: Full analysis set	
End point type	Primary
End point timeframe: From Baseline to Day 113	

End point values	Low dose KY1005	High dose KY1005	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	27	24	
Units: Percentage				
least squares mean (confidence interval 95%)	-80.12 (-95.55 to -64.68)	-69.97 (-85.04 to -54.90)	-49.37 (-66.02 to -32.72)	

Statistical analyses

Statistical analysis title	Difference in LSM estimate
Comparison groups	Low dose KY1005 v Placebo
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-30.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.43
upper limit	-8.06
Variability estimate	Standard error of the mean
Dispersion value	11.38

Statistical analysis title	Difference in LSM estimate
Comparison groups	Placebo v High dose KY1005
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.072
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-20.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-43.08
upper limit	1.88
Variability estimate	Standard error of the mean
Dispersion value	11.27

Primary: Summary of TEAEs to Day 113

End point title	Summary of TEAEs to Day 113[1]

End point description:

End point type	Primary

End point timeframe:

To Day 113

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: Per protocol no statistical analyses were conducted on this end point.

End point values	Low dose KY1005	High dose KY1005	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	30	29	
Units: Number of patients				
At least one TEAE	18	14	20	
At least one related TEAE	10	6	9	
At least one serious TEAE	1	0	0	
A least one related serious TEAE	1	0	0	
At least one treatment-emergent AESI	0	1	0	
At least one related TEAE of special interest	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first dose to Day 113	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1
Reporting groups	
Reporting group title	Low dose KY1005
Reporting group description: -	
Reporting group title	High dose KY1005
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Low dose KY1005	High dose KY1005	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Infected dermal cyst			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Low dose KY1005	High dose KY1005	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 29 (62.07%)	14 / 30 (46.67%)	20 / 29 (68.97%)
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Hypertension			

subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	1 / 29 (3.45%)
occurrences (all)	0	3	1
Pyrexia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Asthenia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Drug ineffective			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Menometrorrhagia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Menorrhagia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Cough			

subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Mood altered			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	1 / 29 (3.45%)
occurrences (all)	1	2	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Blood potassium increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Blood urine present			

subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Haematocrit increased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Red blood cells urine positive			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Urine analysis abnormal			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Wound			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 29 (0.00%)	3 / 30 (10.00%)	1 / 29 (3.45%)
occurrences (all)	0	12	2
Formication			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Ear pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Eyelid cyst			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Ulcerative keratitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			

Dermatitis atopic			
subjects affected / exposed	3 / 29 (10.34%)	4 / 30 (13.33%)	9 / 29 (31.03%)
occurrences (all)	3	5	16
Hyperhidrosis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	0 / 29 (0.00%)
occurrences (all)	0	2	0
Eczema			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	3
Erythema			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Pain of skin			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Pruritus allergic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Skin erosion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Swelling face			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperprolactinaemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	2 / 29 (6.90%)
occurrences (all)	0	0	2
Musculoskeletal pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Spinal pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 29 (6.90%)	3 / 30 (10.00%)	6 / 29 (20.69%)
occurrences (all)	2	3	9
Folliculitis			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	1 / 29 (3.45%)
occurrences (all)	1	5	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 29 (10.34%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	3	0	1
Skin infection			
subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	1	1	0
Tonsillitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Bacterial infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			

subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Furuncle			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Herpes simplex			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Infected dermal cyst			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Periodontitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Rash pustular			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Skin bacterial infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 29 (0.00%)
occurrences (all)	0	2	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 September 2018	Amendment of exclusion criterion related to recommended washout of systemic immunosuppressive or immunomodulatory drugs Addition of lower weight limit Amendment of exclusion criterion related to anaemia Revision of guidance regarding the adequacy of double barrier contraceptive methods Revision of liver function test criteria in relation to the permanent discontinuation of IMP Establishment of consistent safety follow up for all study participants that covers 4 to 5 half-lives of IMP. Revision of code break process in the event of a medical emergency
19 June 2019	Corrected previous omission in synopsis Clarification that change in immunohistochemistry of K16 would be measured by a qualified pathologist Clarification that Cmax would be determined after all infusions. Reduction of Follow-up Period to Day 253 for all patients Clarification of the personnel who would be blinded Reduction of washout period for systemic Cyclosporin A to within 3 weeks of Baseline Clarification of Total bilirubin >ULN (except in circumstances where Gilbert's Syndrome can be confirmed) Clarification of the duration of birth control measures Clarification of the rules for replacement of patients and dosing Clarification of rules around dosing if a dose needs to be temporarily discontinued Investigator Assessments to be performed by the same Assessor One repeat of safety laboratory tests and vital signs and more flexibility for rescreening Clarification of timing of baseline biopsy Clarification of the type of assay to be used for Inflammatory Proteomic Analysis Reduction in blood volume required during study extension Further clarification of the FAS population Further clarification and detail provided on PK analysis Where previously used incorrectly the term Monitor or Medical Monitor was replaced by Study Monitor Replacement of Amendment 1 by Summary of Protocol Amendments

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was not prospectively powered. Any P values presented are nominal.

Notes: