Clinical trial results:
THE EFFECT OF OC000459 ON EOSINOPHILIC AIRWAY INFLAMMATION AND ASTHMA CONTROL IN SUBJECTS WITH REFRACTORY EOSINOPHILIC ASTHMA: A RANDOMISED, DOUBLE BLIND, PLACEBO CONTROLLED TRIAL

Summary

EudraCT number	2015-001833-26
Trial protocol	GB
Global end of trial date	02 August 2018

Results information

Result version number	v1 (current)
This version publication date	15 August 2019
First version publication date	15 August 2019

Trial information

Trial identification

Sponsor protocol code	OC000459/019/15

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02560610
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Atopix Therapeutics Ltd
Sponsor organisation address	Innovation Centre, 99 Park Drive, Milton Park, Abingdon, United Kingdom, OX14 4RY
Public contact	Clinical Trial Transparency, Chiesi Farmaceutici S.p.A., clinicaltrials_info@chiesi.com
Scientific contact	Clinical Trial Transparency, Chiesi Farmaceutici S.p.A., clinicaltrials_info@chiesi.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	25 February 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of OC000459 on induced sputum eosinophil counts at 12 weeks of treatment compared to placebo.

Protection of trial subjects:

The protocol, together with all required clinical trial documentation, was submitted to the appropriate independent ethics committee (IEC) in all participating sites. A copy of the favourable opinion from the IEC had to be received before the trial could be initiated at an investigational site.This study was conducted in accordance with ICH Good Clinical Practice (GCP) Guideline E6 (1996), the Declaration of Helsinki and the UK Statutory Instrument which incorporates the European Clinical Trial Directives (Directives 2001/20/EC and 2005/28/EC) and subsequent amendments. This study was also performed in compliance with the requirements of the Medicines and Healthcare products Regulatory Agency (MHRA).
The consent document met all applicable local laws and provided the patient with information regarding the purpose, procedures, requirements and restrictions of the study, along with any known risks and potential benefits associated with the investigational product and the established provisions for maintaining the confidentiality of personal information. Subject’s written informed consent obtained prior to any study-related procedures.

Background therapy:

OC000459 is a potent and selective CRTH2 antagonist which blocks the ability of PGD2 to cause chemotaxis and activation of TH2 lymphocytes and eosinophils and is therefore expected to suppress airway inflammation associated with asthma. Studies performed in vitro and in vivo indicate that this mechanism is important in mediating mast cell-dependent accumulation and activation of TH2 lymphocytes and eosinophils as occurs in the airways of subjects with asthma.

Evidence for comparator: -

Actual start date of recruitment	09 September 2016
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: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	25
From 65 to 84 years	14
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

It was planned to screen approximately 70 subjects in the study in order to yield 40 evaluable subjects. A total of 68 subjects were screened and 40 subjects were enrolled and randomised (12 subjects taking OCS at Baseline, 28 subjects not taking OCS at Baseline).

Pre-assignment

Screening details:

Screening was performed including medical history, demographics, height, weight, vital signs, physical examination, spirometry, clinical laboratory investigations, urine pregnancy test for female subjects of child bearing potential, drugs of abuse screen, electrocardiogram, induced sputum eosinophil count, adverse events and concomitant medications

Pre-assignment period milestones

Number of subjects started	68[1]
Number of subjects completed	40

Pre-assignment subject non-completion reasons

Reason: Number of subjects	lack of compliance with elegibilty criteria: 26
Reason: Number of subjects	Consent withdrawn by subject: 1
Reason: Number of subjects	other: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: According with the protocol, it was planned to screen approximately 70 subjects in the study in order to yield 40 evaluable subjects. A total of 68 subjects were screened and 40 subjects were randomised .

Period 1

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

Blinding implementation details:

Randomisation was performed according to the method of minimisation by a designated unblinded statistician. The allocation ratio to OC000459 and placebo was 1:1. Further details of the implementation of the minimisation process were contained in the Randomisation and Blinding Plan. Randomisation code information was sent securely by an unblinded statistician for packaging study drug. Copies of the randomisation codes were stored securely by the unblinded statistician.

Arms

Are arms mutually exclusive?	Yes
Arm title	Study Treatment

Arm description:

Active Treatment Arm with study drug (OC000459 50 mg) tablets administered once daily.
Subjects who were not treated with OCS at Baseline received 12 weeks treatment with OC000459.
Subjects who were receiving OCS at Baseline received OC000459 for 24 weeks; the second 12 weeks of the study were performed in order to evaluate the effects of OCS dose reduction on symptoms and measures of disease activity.

Arm type	Experimental

Investigational medicinal product name	OC000459
Investigational medicinal product code	OC000459
Other name	CP003
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50mg of OC000459 (1 tablet) once daily.
Subjects who were not treated with OCS at Baseline received 12 weeks treatment with OC000459.
Subjects who were receiving OCS at Baseline received OC000459 for 24 weeks; the second 12 weeks of the study were performed in order to evaluate the effects of OCS dose reduction on symptoms and measures of disease activity.

Arm title	Placebo

Arm description:

Arm with all the subjects receiving 1 tablet of placebo once daily.
Subjects who were not treated with OCS at Baseline received 12 weeks treatment with placebo.
Subjects who were receiving OCS at Baseline received placebo for 24 weeks; the second 12 weeks of the study were performed in order to evaluate the effects of OCS dose reduction on symptoms and measures of disease activity.

Arm type	Placebo
Investigational medicinal product name	Placebo for OC000459
Investigational medicinal product code	
Other name	CP004
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet of placebo once daily.
Subjects who were not treated with OCS at Baseline received 12 weeks treatment with placebo.
Subjects who were receiving OCS at Baseline received placebo for 24 weeks; the second 12 weeks of the study were performed in order to evaluate the effects of OCS dose reduction on symptoms and measures of disease activity.

Number of subjects in period 1	Study Treatment	Placebo
Started	20	20
Completed	18	20
Not completed	2	0
Consent withdrawn by subject	1	-
other (missing Visit)	1	-

Baseline characteristics

Reporting groups

Reporting group title	Study Treatment

Reporting group description:

Active Treatment Arm with study drug (OC000459 50 mg) tablets administered once daily.
Subjects who were not treated with OCS at Baseline received 12 weeks treatment with OC000459.
Subjects who were receiving OCS at Baseline received OC000459 for 24 weeks; the second 12 weeks of the study were performed in order to evaluate the effects of OCS dose reduction on symptoms and measures of disease activity.

Reporting group title	Placebo

Reporting group description:

Arm with all the subjects receiving 1 tablet of placebo once daily.
Subjects who were not treated with OCS at Baseline received 12 weeks treatment with placebo.
Subjects who were receiving OCS at Baseline received placebo for 24 weeks; the second 12 weeks of the study were performed in order to evaluate the effects of OCS dose reduction on symptoms and measures of disease activity.

Reporting group values	Study Treatment	Placebo	Total
Number of subjects	20	20	40
Age categorical Units: Subjects			
Adults (18-64 years)	13	12	25
From 65-84 years	6	8	14
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	58.0	59.2	
standard deviation	± 14.94	± 10.97	-
Gender categorical Units: Subjects			
Female	5	7	12
Male	15	13	28
Race Units: Subjects			
white	18	18	36
black	0	2	2
asian	2	0	2

Subject analysis sets

Subject analysis set title	Study Treatment - FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) consisted of all randomised subjects who received at least one dose of double-blind study medication, and had at least one post-baseline primary efficacy assessment , irrespective of compliance with other eligibility and protocol criteria.
For each efficacy endpoint, the analysis was based on the FAS.

Subject analysis set title	Study Treatment - Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis set consisted of all subjects who received at least one dose of double-blind study

medication irrespective of compliance with eligibility and other protocol criteria. All safety analyses were performed on the safety analysis set.

Subject analysis set title	Placebo - FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) consisted of all randomised subjects who received at least one dose of double-blind study medication, and had at least one post-baseline primary efficacy assessment , irrespective of compliance with other eligibility and protocol criteria.
For each efficacy endpoint, the analysis was based on the FAS.

Subject analysis set title	Placebo - Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis set consisted of all subjects who received at least one dose of double-blind study medication irrespective of compliance with eligibility and other protocol criteria. All safety analyses were performed on the safety analysis set.

Reporting group values	Study Treatment - FAS	Study Treatment - Safety	Placebo - FAS
Number of subjects	20	20	19
Age categorical Units: Subjects			
Adults (18-64 years)	13	13	12
From 65-84 years	6	6	7
85 years and over	1	1	0
Age continuous Units: years			
arithmetic mean	58.0	58.0	58.4
standard deviation	± 14.94	± 14.94	± 10.6
Gender categorical Units: Subjects			
Female	5	5	6
Male	15	15	13
Race Units: Subjects			
white	18	18	17
black	0	0	2
asian	2	2	0

Reporting group values	Placebo - Safety		
Number of subjects	20		
Age categorical Units: Subjects			
Adults (18-64 years)	12		
From 65-84 years	8		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	59.2		
standard deviation	± 10.97		
Gender categorical Units: Subjects			
Female	7		
Male	13		

Race Units: Subjects			
white	18		
black	2		
asian	0		

End points

End points reporting groups

Reporting group title	Study Treatment

Reporting group description:

Active Treatment Arm with study drug (OC000459 50 mg) tablets administered once daily.
Subjects who were not treated with OCS at Baseline received 12 weeks treatment with OC000459.
Subjects who were receiving OCS at Baseline received OC000459 for 24 weeks; the second 12 weeks of the study were performed in order to evaluate the effects of OCS dose reduction on symptoms and measures of disease activity.

Reporting group title	Placebo

Reporting group description:

Arm with all the subjects receiving 1 tablet of placebo once daily.
Subjects who were not treated with OCS at Baseline received 12 weeks treatment with placebo.
Subjects who were receiving OCS at Baseline received placebo for 24 weeks; the second 12 weeks of the study were performed in order to evaluate the effects of OCS dose reduction on symptoms and measures of disease activity.

Subject analysis set title	Study Treatment - FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) consisted of all randomised subjects who received at least one dose of double-blind study medication, and had at least one post-baseline primary efficacy assessment , irrespective of compliance with other eligibility and protocol criteria.
For each efficacy endpoint, the analysis was based on the FAS.

Subject analysis set title	Study Treatment - Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis set consisted of all subjects who received at least one dose of double-blind study medication irrespective of compliance with eligibility and other protocol criteria. All safety analyses were performed on the safety analysis set.

Subject analysis set title	Placebo - FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) consisted of all randomised subjects who received at least one dose of double-blind study medication, and had at least one post-baseline primary efficacy assessment , irrespective of compliance with other eligibility and protocol criteria.
For each efficacy endpoint, the analysis was based on the FAS.

Subject analysis set title	Placebo - Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis set consisted of all subjects who received at least one dose of double-blind study medication irrespective of compliance with eligibility and other protocol criteria. All safety analyses were performed on the safety analysis set.

Primary: 1_Ratio of Induced Sputum Eosinophil Count (%) at week 12 to baseline

End point title	1_Ratio of Induced Sputum Eosinophil Count (%) at week 12 to baseline

End point description:

Sputum was induced using nebulised hypertonic saline and processed using standard methods. Sputum was induced using 3%, 4% and 5% saline inhaled in sequence for five minutes via an ultrasonic nebuliser. After each inhalation subjects blew their nose and rinsed their mouth to minimise nasal contamination and expectorated sputum into a sterile pot. Change from baseline at Week 12 of the logarithmic value (log10) of induced sputum eosinophil count data (%) was analysed. Data are presented as adjusted geometric mean ratios with their 95% confidence intervals (CIs).

End point type	Primary

End point timeframe:

from baseline to week 12

End point values	Study Treatment - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[1]	19[2]		
Units: ratio				
geometric mean (confidence interval 95%)	0.237 (0.106 to 0.532)	0.550 (0.240 to 1.260)		

Notes:

[1] - FAS Population

[2] - FAS Population

Statistical analyses

Statistical analysis title	Adjusted geometric mean ratio (week 12/baseline)

Statistical analysis description:

The ratio of induced sputum eosinophil count (%) at Week 12 to baseline was estimated from the analysis of change from baseline at Week 12 of the logarithmic value (log10) of induced sputum eosinophil count data (%). Data are presented as adjusted geometric mean ratio with its 95% CI. Analysis is based on an analysis of covariance model including treatment and use of OCS at screening (yes/no) as factors and baseline induced sputum eosinophils (log10 value) as covariate.

Comparison groups	Study Treatment - FAS v Placebo - FAS
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.151
Method	ANCOVA
Parameter estimate	Adjusted GM Ratio
Point estimate	0.431
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.135
upper limit	1.378

Secondary: 2_ Change from baseline in FEV1 at week 12

End point title	2_ Change from baseline in FEV1 at week 12

End point description:

Spirometry was measured at all visits with a validated and standardised spirometer with the FEV1 and FVC recorded as the best of 3 successive readings within 100 ml. Spirometry was performed before and 20 minutes after the subject received nebulised salbutamol 2.5 mg. Results of change from baseline in FEV1 BEFORE salbutamol only are reported.

End point type	Secondary

End point timeframe:

From baseline to week 12.

End point values	Study Treatment - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[3]	19[4]		
Units: litre(s)				
least squares mean (confidence interval 95%)	0.135 (-0.006 to 0.276)	0.008 (-0.137 to 0.153)		

Notes:

[3] - FAS Population

[4] - FAS Population

Statistical analyses

Statistical analysis title	Adjusted mean difference between treatment groups

Statistical analysis description:

Data are presented as adjusted mean treatment difference (OC000459 vs Placebo) of change from baseline at Week 12 with 95% CI. Analysis is based on an analysis of covariance model including treatment, use of OCS at Screening (yes/no) and screening sputum eosinophil percentage category (>3% and ≤10%,>10% and ≤35%,>35%) as factors, and baseline FEV1 as a covariate.

Comparison groups	Study Treatment - FAS v Placebo - FAS
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.214
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	0.127
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.077
upper limit	0.33

Secondary: 3_ change from baseline in FVC at week 12

End point title	3_ change from baseline in FVC at week 12

End point description:

Spirometry was measured at all visits with a validated and standardised spirometer with the FEV1 and FVC recorded as the best of 3 successive readings within 100 ml. Spirometry was performed before and 20 minutes after the subject received nebulised salbutamol 2.5 mg. Results of change from baseline in FVC BEFORE salbutamol only are reported.

End point type	Secondary

End point timeframe:

From baseline to week 12

End point values	Study Treatment - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[5]	19[6]		
Units: litre(s)				
arithmetic mean (standard deviation)	0.103 (± 0.4116)	0.025 (± 0.3108)		

Notes:

[5] - FAS Population

[6] - FAS Population

Statistical analyses

No statistical analyses for this end point

Secondary: 4_ change from baseline in ACQ-5 average score at week 12

End point title	4_ change from baseline in ACQ-5 average score at week 12

End point description:

The ACQ-5 five-item questionnaire, developed as a measure of subject' asthma control ,was completed at every scheduled visit after Screening. The questions are designed to be self-completed by the subject. The five questions enquire about the frequency and/or severity of symptoms (waking at night, severity of asthma symptoms, activity limitation, shortness of breath and wheeze). The response options for all these questions consist of a zero (no impairment/limitation) to six (total impairment/limitation) scale.

End point type	Secondary

End point timeframe:

from baseline to week 12

End point values	Study Treatment - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[7]	19[8]		
Units: score				
least squares mean (confidence interval 95%)	-0.020 (-0.384 to 0.344)	-0.063 (-0.437 to 0.310)		

Notes:

[7] - FAS Population

[8] - FAS Population

Statistical analyses

Statistical analysis title	Adjusted mean difference between treatment groups

Statistical analysis description:

Data are presented as adjusted mean treatment difference (OC000459 vs Placebo) of change from baseline at Week 12 with 95% CI. Analysis is based on an analysis of covariance model including treatment, use of OCS at Screening (yes/no) and screening sputum eosinophil percentage category (>3% and ≤10%,>10% and ≤35%,>35%) as factors, and baseline ACQ-5 average score as a covariate.

Comparison groups	Study Treatment - FAS v Placebo - FAS

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.868
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	0.043
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.482
upper limit	0.569

Secondary: 5_ACQ-5 Average Score Response at Week 12

End point title	5_ACQ-5 Average Score Response at Week 12

End point description:

The ACQ-5 five-item questionnaire, developed as a measure of subject' asthma control ,was completed at every scheduled visit after Screening. The questions are designed to be self-completed by the subject. The five questions enquire about the frequency and/or severity of symptoms (waking at night, severity of asthma symptoms, activity limitation, shortness of breath and wheeze). The response options for all these questions consist of a zero (no impairment/limitation) to six (total impairment/limitation) scale.
ACQ-5 response is defined as a change from baseline in ACQ-5 Average Score ≤-0.5. If the change from baseline was > -0.5, the subject was classified as a non-responder in terms of ACQ-5. Subjects with missing ACQ-5 average score value at Week 12 were also classified as non-responders.

End point type	Secondary

End point timeframe:

from baseline to week 12

End point values	Study Treatment - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[9]	19[10]		
Units: subjects				
responder	6	8		
non responder (change>-0.5)	12	11		
non responder (missing data)	2	0		

Notes:

[9] - FAS Population

[10] - FAS Population

Statistical analyses

Statistical analysis title	Odds ratio, ACQ-5 Average Score at Week 12

Statistical analysis description:

Analysis is based on a logistic regression model including treatment, use of OCS at Screening (yes/no) and screening sputum eosinophil percentage category (>3% and ≤10%,>10% and ≤35%,>35%) as factors, and baseline ACQ-5 average score as a covariate.
The odds ratio for the treatment with its 95% CI and corresponding p-value were estimated by the

model.

Comparison groups	Study Treatment - FAS v Placebo - FAS
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.212
Method	Regression, Logistic
Parameter estimate	adjusted odds ratio
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	1.88

Secondary: 6_change from baseline in AQLQ(S) overall average score at week 12

End point title	6_change from baseline in AQLQ(S) overall average score at week 12

End point description:

The AQLQ(S) is a standardised version of the Asthma Quality of Life Questionnaire and was given to subjects to complete at every scheduled visit after Screening. Subjects were asked to think about how they had been during the previous two weeks and to respond to each of the 32 questions on a 7-point scale (7 = not impaired at all to 1 = severely impaired). The overall AQLQ(S) score is the mean of all 32 responses and the individual domain scores are the means of the items in those domains (adjusted means with a 95% CI).

End point type	Secondary

End point timeframe:

from baseline to week 12

End point values	Study Treatment - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[11]	19[12]		
Units: score				
least squares mean (confidence interval 95%)	0.061 (-0.283 to 0.405)	0.088 (-0.265 to 0.442)		

Notes:

[11] - FAS Population

[12] - FAS Population

Statistical analyses

Statistical analysis title	Adjusted mean difference between treatment groups

Statistical analysis description:

Data are presented as adjusted mean treatment difference (OC000459 vs Placebo) of change from baseline at Week 12 with 95% CI. Analysis is based on an analysis of covariance model including treatment, use of OCS at Screening (yes/no) and screening sputum eosinophil percentage category (>3% and ≤10%,>10% and ≤35%,>35%) as factors, and baseline AQLQ average score as a covariate.

Comparison groups	Study Treatment - FAS v Placebo - FAS

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.911
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	-0.027
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.524
upper limit	0.469

Secondary: 7_AQLQ Average Score Response at Week 12

End point title	7_AQLQ Average Score Response at Week 12

End point description:

The AQLQ(S) is a standardised version of the Asthma Quality of Life Questionnaire and was given to subjects to complete at every scheduled visit after Screening. Subjects were asked to think about how they had been during the previous two weeks and to respond to each of the 32 questions on a 7-point scale (7 = not impaired at all to 1 = severely impaired). The overall AQLQ(S) score is the mean of all 32 responses and the individual domain scores are the means of the items in those domains.
AQLQ response is defined as a change from baseline in AQLQ Average Score ≥ 0.5. If the change from baseline was < 0.5, the subject was classified as a non-responder in terms of AQLQ. Subjects with missing AQLQ average score value at Week 12 were also classified as non-responders.

End point type	Secondary

End point timeframe:

from baseline to week 12

End point values	Study Treatment - FAS	Placebo - FAS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[13]	19[14]		
Units: subjects				
responder	6	5		
non responder (change <0.5)	12	14		
non responder (missing data)	2	0		

Notes:

[13] - FAS Population

[14] - FAS Population

Statistical analyses

Statistical analysis title	Odds ratio, AQLQ Average Score at Week 12

Statistical analysis description:

Analysis is based on a logistic regression model including treatment, use of OCS at Screening (yes/no) and screening sputum eosinophil percentage category (>3% and ≤10%,>10% and ≤35%,>35%) as factors, and baseline AQLQ average score as a covariate.
The odds ratio for the treatment with its 95% CI and corresponding p-value were estimated by the model.

Comparison groups	Study Treatment - FAS v Placebo - FAS
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.655
Method	Regression, Logistic
Parameter estimate	adjusted odds ratio
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	7.43

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AE, SAE,ADR were collected in first 12 weeks (form Week 0 to week 12)	
Adverse event reporting additional description:	
Adverse events were reported for the Safety Population	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	Study Treatment - Safety
Reporting group description:	
All the subject receiving the study drug (OC000459)	
Reporting group title	Placebo - Safety
Reporting group description:	
all the subjects receiving the placebo	

Serious adverse events	Study Treatment - Safety	Placebo - Safety	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (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			
Pyelonephritis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
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	Study Treatment - Safety	Placebo - Safety	
Total subjects affected by non-serious adverse events subjects affected / exposed	17 / 20 (85.00%)	18 / 20 (90.00%)	
Injury, poisoning and procedural complications Ankle fracture subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	
Vascular disorders Peripheral artery occlusion subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	1 / 20 (5.00%) 1	
Migraine subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2	0 / 20 (0.00%) 0	
Tremor subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	
Immune system disorders Allergy to animal subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	
Seasonal allergy			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Flatulence			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	7 / 20 (35.00%)	10 / 20 (50.00%)	
occurrences (all)	10	11	
Cough			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Hyperventilation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Nasal polyps			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Oropharyngeal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Wheezing			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Infections and infestations			
Eye infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Lower respiratory tract infection			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Respiratory tract infection viral			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	0 / 20 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	3	
Sinusitis			

subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	3	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 20 (10.00%)	5 / 20 (25.00%)	
occurrences (all)	2	5	
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 December 2016	The clinical protocol was amended for modifying the inclusion criteria to facilitate recruitment and for including additional concomitant medications.
19 July 2017	The clinical protocol was amended for clarifying an exclusion criterion and for deleting the list of permitted medications, replaced with the list of non-permitted medications.
25 September 2017	The clinical protocol was amended for giving greater clarity on criteria for the per-protocol set of subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported