Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Phase 2b Dose-Ranging Study to Evaluate the Efficacy and Safety of Orismilast in Adults With Moderate to Severe Atopic Dermatitis

Summary

EudraCT number	2021-006707-15
Trial protocol	DE HU
Global end of trial date	15 February 2024

Results information

Result version number	v1 (current)
This version publication date	31 January 2025
First version publication date	31 January 2025

Trial information

Trial identification

Sponsor protocol code	UNI50001-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 129386

Notes:

Sponsors

Sponsor organisation name	UNION therapeutics A/S
Sponsor organisation address	Tuborg Havnevej 18, Hellerup, Denmark, DK-2900
Public contact	Charlotte Oersted Pedersen, UNION therapeutics A/S, +45 53843044, charlotte.oersted.pedersen@uniontherapeutics.com
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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	18 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the efficacy and safety of a modified-release orismilast tablet versus placebo in patients aged at least 18 years with moderate to severe Atopic Dermatitis (AD).

Protection of trial subjects:

This clinical trial was conducted in compliance with the Declaration of Helsinki and International Council for Harmonisation Good Clinical Practice (GCP) guidelines. Tiral subjects were monitored throughout the study and safety assessments were performed during each visit.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2022
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	Poland: 34
Country: Number of subjects enrolled	Germany: 38
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	United States: 155
Worldwide total number of subjects	235
EEA total number of subjects	80

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)	220
From 65 to 84 years	15

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 235 patients were randomized to treatment. A total of 233 randomized patients were treated and included in the Intent-to-Treat and Safety Populations.

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	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Orismilast Modified Release Tablets 20 mg BID

Arm description:

Oral, twice daily morning and evening
Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.

Arm type	Experimental
Investigational medicinal product name	Orismilast 20 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Modified-release tablet
Routes of administration	Oral use

Dosage and administration details:

Oral, 20mg twice daily morning and evening

Arm title	Orismilast Modified Release Tablets 30 mg BID

Arm description:

Oral, twice daily morning and evening
Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.

Arm type	Experimental
Investigational medicinal product name	Orismilast 30 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Modified-release tablet
Routes of administration	Oral use

Dosage and administration details:

Oral, 30mg twice daily morning and evening

Arm title	Orismilast Modified Release Tablets 40 mg BID

Arm description:

Oral, twice daily morning and evening
Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.

Arm type	Experimental

Investigational medicinal product name	Orismilast 40 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Modified-release tablet
Routes of administration	Oral use

Dosage and administration details:

Oral, 40mg twice daily morning and evening

Arm title	Placebo Tablets BID

Arm description:

Placebo matching tablets. Oral, twice daily morning and evening.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Modified-release tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matching tablets, oral, twice daily morning and evening

Number of subjects in period 1[1]	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Started	58	61	59
Completed	37	35	37
Not completed	21	26	22
Consent withdrawn by subject	7	6	4
Physician decision	-	-	-
Adverse event, non-fatal	8	14	13
Lost to follow-up	2	5	3
Lack of efficacy	4	1	2

Number of subjects in period 1[1]	Placebo Tablets BID
Started	55
Completed	42
Not completed	13
Consent withdrawn by subject	5
Physician decision	1
Adverse event, non-fatal	2
Lost to follow-up	3
Lack of efficacy	2

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: While all 235 participants attended a randomization visit, two of them were not exposed to study medication, left the study, and did not attend another visit.

Baseline characteristics

Reporting groups

Reporting group title	Orismilast Modified Release Tablets 20 mg BID

Reporting group description:

Oral, twice daily morning and evening
Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.

Reporting group title	Orismilast Modified Release Tablets 30 mg BID

Reporting group description:

Oral, twice daily morning and evening
Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.

Reporting group title	Orismilast Modified Release Tablets 40 mg BID

Reporting group description:

Oral, twice daily morning and evening
Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.

Reporting group title	Placebo Tablets BID

Reporting group description:

Placebo matching tablets. Oral, twice daily morning and evening.

Reporting group values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Number of subjects	58	61	59
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			
arithmetic mean	40.2	39.1	42.5
standard deviation	± 14.34	± 13.30	± 15.69
Gender categorical Units: Subjects			
Female	37	27	28
Male	21	34	31
Child-bearing potential Units: Subjects			
Yes	26	19	18

No	31	42	41
Missing	1	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	5	4
Native Hawaiian or Other Pacific Islander	2	1	0
Black or African American	9	11	15
White	43	42	37
More than one race	0	0	0
Unknown or Not Reported	2	2	3
Ethnicity Units: Subjects			
Hispanic or Latino	20	19	16
Not Hispanic or Latino	38	42	42
Unknown or Not Reported	0	0	1
Asthma Diagnosis Units: Subjects			
Yes	13	15	10
No	45	46	49
Disease Duration >2 years Units: Subjects			
Yes	55	59	54
No	3	2	5
Disease Duration Units: year			
arithmetic mean	19.6	19.9	20.4
standard deviation	± 12.83	± 14.91	± 14.40
Height Units: centimetre			
arithmetic mean	168.02	170.45	172.13
standard deviation	± 10.955	± 10.236	± 11.659
Weight Units: kilogram(s)			
arithmetic mean	80.52	80.73	86.57
standard deviation	± 17.123	± 19.469	± 23.368
Body Mass Index (BMI) Units: kilogram(s)/square metre			
arithmetic mean	28.550	27.632	29.485
standard deviation	± 5.7815	± 6.3312	± 8.3062

Reporting group values	Placebo Tablets BID	Total	
Number of subjects	55	233	
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			
arithmetic mean	40.9		
standard deviation	± 16.87	-	
Gender categorical			
Units: Subjects			
Female	27	119	
Male	28	114	
Child-bearing potential			
Units: Subjects			
Yes	17	80	
No	37	151	
Missing	1	2	
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	2	13	
Native Hawaiian or Other Pacific Islander	2	5	
Black or African American	9	44	
White	41	163	
More than one race	0	0	
Unknown or Not Reported	1	8	
Ethnicity			
Units: Subjects			
Hispanic or Latino	23	78	
Not Hispanic or Latino	32	154	
Unknown or Not Reported	0	1	
Asthma Diagnosis			
Units: Subjects			
Yes	10	48	
No	45	185	
Disease Duration >2 years			
Units: Subjects			
Yes	50	218	
No	5	15	
Disease Duration			
Units: year			
arithmetic mean	17.6		
standard deviation	± 14.16	-	
Height			
Units: centimetre			
arithmetic mean	169.25		
standard deviation	± 10.422	-	
Weight			
Units: kilogram(s)			
arithmetic mean	80.89		

standard deviation	± 21.250	-	
Body Mass Index (BMI)			
Units: kilogram(s)/square metre			
arithmetic mean	28.178		
standard deviation	± 6.7782	-	

End points

End points reporting groups

Reporting group title	Orismilast Modified Release Tablets 20 mg BID
Reporting group description:	
Oral, twice daily morning and evening Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.	

Reporting group title	Orismilast Modified Release Tablets 30 mg BID
Reporting group description:	
Oral, twice daily morning and evening Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.	

Reporting group title	Orismilast Modified Release Tablets 40 mg BID
Reporting group description:	
Oral, twice daily morning and evening Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.	

Reporting group title	Placebo Tablets BID
Reporting group description:	
Placebo matching tablets. Oral, twice daily morning and evening.	

Primary: Percent Change From Baseline in Eczema Area and Severity Index (EASI) Score Week 16

End point title	Percent Change From Baseline in Eczema Area and Severity Index (EASI) Score Week 16
End point description:	
The EASI is a tool to measure the severity of clinical signs and the percentage of affected body surface area (BSA) in patients with atopic dermatitis (AD). The EASI is a composite scoring system to evaluate the degree of erythema, induration/papulation, excoriation, and lichenification (each scored separately) for each of 4 body regions, with adjustment for the percentage of BSA involved for each body region and for the proportion of the body region to the whole body. EASI scores range from 0 to 72, with higher scores reflecting greater disease severity. Erythema, induration/papulation, excoriation, and lichenification are scored on a scale of 0 (absent) to 3 (severe) for each body region: head and neck, upper limbs (including the external axillae and hands), trunk (including the internal axillae and groin), and lower limbs (including the buttocks and feet). The extent of affected skin in each body region is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement).	
End point type	Primary
End point timeframe:	
Baseline and Week 16	

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	61	59	55
Units: percent				
least squares mean (standard error)	-55.1 (± 4.89)	-52.2 (± 5.39)	-61.4 (± 5.02)	-50.4 (± 4.98)

Statistical analyses

Statistical analysis title	Orismilast 20 mg vs Placebo
Comparison groups	Orismilast Modified Release Tablets 20 mg BID v Placebo Tablets BID
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.2
upper limit	9
Variability estimate	Standard error of the mean
Dispersion value	6.93

Statistical analysis title	Orismilast 30 mg vs Placebo
Comparison groups	Orismilast Modified Release Tablets 30 mg BID v Placebo Tablets BID
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.8
upper limit	12.3
Variability estimate	Standard error of the mean
Dispersion value	7.15

Statistical analysis title	Orismilast 40 mg vs Placebo
Comparison groups	Placebo Tablets BID v Orismilast Modified Release Tablets 40 mg BID

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-10.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.6
upper limit	2.8
Variability estimate	Standard error of the mean
Dispersion value	6.99

Secondary: Percentage of Participants Achieving 75% Reduction in Eczema Area and Severity Index EASI (EASI75) Response at Week 16

End point title	Percentage of Participants Achieving 75% Reduction in Eczema Area and Severity Index EASI (EASI75) Response at Week 16

End point description:

The EASI is a tool to measure the severity of clinical signs and the percentage of affected body surface area (BSA) in patients with atopic dermatitis (AD). The EASI is a composite scoring system to evaluate the degree of erythema, induration/papulation, excoriation, and lichenification (each scored separately) for each of 4 body regions, with adjustment for the percentage of BSA involved for each body region and for the proportion of the body region to the whole body. EASI scores range from 0 to 72, with higher scores reflecting greater disease severity. Erythema, induration/papulation, excoriation, and lichenification are scored on a scale of 0 (absent) to 3 (severe) for each body region: head and neck, upper limbs (including the external axillae and hands), trunk (including the internal axillae and groin), and lower limbs (including the buttocks and feet). The extent of affected skin in each body region is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement).

End point type	Secondary

End point timeframe:

At Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	61	59	55
Units: percent				
number (not applicable)				
Yes	30.4	25.9	36.4	36.1
No	69.6	74.1	63.6	63.9

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving a Score of Clear (0) or Almost Clear (1) and At Least a 2-point Improvement in Investigator Global Assessment for AD (IGA-AD) at Week 16

End point title	Percentage of Participants Achieving a Score of Clear (0) or Almost Clear (1) and At Least a 2-point Improvement in Investigator Global Assessment for AD (IGA-AD) at Week 16

End point description:

At Week 16

End point type	Secondary

End point timeframe:

The IGA-AD is a measure used by physicians to determine a patient's overall severity of disease. The static version was used for measurement at a single point in time. The Investigator rated the severity of the patient's AD on a 5-point scale ranging from

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	61	59	55
Units: percent				
number (not applicable)				
Yes	26.3	24.3	30.9	9.5
No	73.7	75.7	69.1	90.5

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving At Least a 4-point Improvement in the Peak Pruritus Numerical Rating Scale (NRS) From Baseline at Weeks 1, 2, 4, 8, 12, 16, and 20

End point title	Percentage of Participants Achieving At Least a 4-point Improvement in the Peak Pruritus Numerical Rating Scale (NRS) From Baseline at Weeks 1, 2, 4, 8, 12, 16, and 20

End point description:

The severity of itch (pruritus) due to AD was assessed using a horizontal 11-point NRS. Patients were asked to assess their "worst itching due to AD over the past 24 hours" on an NRS anchored by the terms "no itching" (0) and "worst possible itching" (10).

End point type	Secondary

End point timeframe:

At Weeks 1, 2, 4, 8, 12, 16 and 20

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	60	56	53
Units: percent				
number (not applicable)				
Week 1, Yes	21.4	24.7	31.5	8.0
Week 1, No	78.6	75.3	68.5	92.0
Week 2, Yes	30.4	32.5	34.1	10.3
Week 2, No	69.6	67.5	65.9	89.7
Week 4, Yes	33.6	35.9	30.2	28.4
Week 4, No	66.4	64.1	69.8	71.6
Week 8, Yes	39.5	39.3	46.1	37.2
Week 8, No	60.5	60.7	53.9	62.8
Week 12, Yes	49.5	49.7	52.2	45.2
Week 12, No	50.5	50.3	47.8	54.8
Week 16, Yes	57.0	50.4	59.6	41.7
Week 16, No	43.0	49.6	40.4	58.3
Week 20, Yes	51.2	45.0	47.4	52.1
Week 20, No	48.8	55.0	52.6	47.9

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Peak Pruritus Numerical Rating Scale (NRS) Score at Week 16

End point title	Change From Baseline in the Peak Pruritus Numerical Rating Scale (NRS) Score at Week 16

End point description:

The severity of itch (pruritus) due to AD was assessed using a horizontal 11-point NRS. Patients were asked to assess their "worst itching due to AD over the past 24 hours" on an NRS anchored by the terms "no itching" (0) and "worst possible itching" (10).

End point type	Secondary

End point timeframe:

Baseline to Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	38	42
Units: Units on a scale				
least squares mean (standard error)	-3.8 (± 0.38)	-4.2 (± 0.39)	-4.2 (± 0.38)	-0.32 (± 0.37)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving a Score of Clear (0) or Almost Clear (1) and At Least a 2-point Improvement in Investigator Global Assessment for Atopic Dermatitis (IGA-AD) at Weeks 2, 4, 8, 12, and 20

End point title	Percentage of Participants Achieving a Score of Clear (0) or Almost Clear (1) and At Least a 2-point Improvement in Investigator Global Assessment for Atopic Dermatitis (IGA-AD) at Weeks 2, 4, 8, 12, and 20

End point description:

The IGA-AD is a measure used by physicians to determine a patient's overall severity of disease. The static version was used for measurement at a single point in time. The Investigator rated the severity of the patient's AD on a 5-point scale ranging from 0 (clear) to 4 (severe).

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12, and 20

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	61	59	55
Units: percent				
number (not applicable)				
Week 2, Yes	1.8	3.3	3.4	0.0
Week 2, No	98.2	96.7	96.6	100
Week 4, Yes	4.7	5.3	5.6	1.9
Week 4, No	95.3	94.7	94.4	98.1
Week 8, Yes	19.2	13.0	11.6	6.2
Week 8, No	80.8	87.0	88.4	93.8
Week 12, Yes	20.9	17.5	18.7	7.2
Week 12, No	79.1	82.5	81.3	92.8
Week 20, Yes	28.0	28.2	26.4	16.6
Week 20, No	72.0	71.8	73.6	83.4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Achieving 50% Reduction in Eczema Area and Severity Index (EASI 50) at Week 16

End point title	Number of Participants Achieving 50% Reduction in Eczema Area and Severity Index (EASI 50) at Week 16

End point description:

The EASI is an investigator-assessed instrument measuring the severity of clinical signs and the percentage of affected BSA in patients with AD. EASI scores range from 0 to 72, with higher scores reflecting greater disease severity. The extent of affected skin in each body region is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement).

End point type	Secondary

End point timeframe:

At Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	35	38	43
Units: Number of participants				
Yes	25	21	30	27
No	14	14	8	16

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Achieving 90% Reduction in Eczema Area and Severity Index (EASI 90) at Week16

End point title	Number of Participants Achieving 90% Reduction in Eczema Area and Severity Index (EASI 90) at Week16

End point description:

The EASI is an investigator-assessed instrument measuring the severity of clinical signs and the percentage of affected BSA in patients with AD. EASI scores range from 0 to 72, with higher scores reflecting greater disease severity. The extent of affected skin in each body region is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement).

End point type	Secondary

End point timeframe:

At Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	35	38	43
Units: Number of participants				
Yes	7	7	10	7

No	32	28	28	36

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Affected Body Surface Area (BSA) at Week 16

End point title	Change From Baseline in Affected Body Surface Area (BSA) at Week 16

End point description:

The BSA assessment estimated the extent of disease or skin affected by AD and was expressed as a percentage of total BSA. BSA was determined by the Investigator or designee using the participant's hand (palm + fingers) = 1% BSA rule.

End point type	Secondary

End point timeframe:

Baseline and Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	35	38	42
Units: units on a scale				
least squares mean (standard error)	-13.9 (± 1.57)	-12.4 (± 1.61)	-17.4 (± 1.57)	-13.8 (± 1.53)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dermatology Life Quality Index (DLQI) Score at Week 16

End point title	Change From Baseline in Dermatology Life Quality Index (DLQI) Score at Week 16

End point description:

The DLQI is a 10-item validated questionnaire completed by the patient and used to assess the effect of skin disease on the patient's quality of life during the previous week. The 10 questions cover the following topics: symptoms; embarrassment; interference with shopping and home care, clothing choices, social and leisure activities, sports participation, work or study, close relationships, and sex; and treatment. Each question is scored from 0 to 3 ("not at all," "a little," "a lot," and "very much," respectively), giving a total score ranging from 0 to 30. A high score is indicative of a poor quality of life.

End point type	Secondary

End point timeframe:

Baseline and Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	38	42
Units: score on a scale				
least squares mean (standard error)	-7.5 (± 0.87)	-8.2 (± 0.89)	-9.0 (± 0.86)	-7.5 (± 0.83)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient Oriented Eczema Measure (POEM) Score at Week 16

End point title	Change From Baseline in Patient Oriented Eczema Measure (POEM) Score at Week 16

End point description:

The POEM is a 7-item, validated questionnaire completed by the patient to assess disease symptoms. Patients were asked to respond to questions on frequency of sleep loss and skin dryness, itching, flaking, cracking, bleeding, and weeping over the past week. All answers carry equal weight, with a total possible score ranging from 0 to 28. A high score is indicative of a poor quality of life.

End point type	Secondary

End point timeframe:

Baseline and Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	38	42
Units: score on a scale				
least squares mean (standard error)	-9.8 (± 0.97)	-9.1 (± 0.98)	-10.1 (± 0.95)	-7.5 (± 0.93)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient Global Impression of Severity Scale (PGIS) Score at Week 16

End point title	Change From Baseline in Patient Global Impression of Severity Scale (PGIS) Score at Week 16

End point description:

The PGIS scale is a single question asking the patient how he or she would rate his or her overall AD symptoms over the past 24 hours. The 5 categories of responses are (0) "no symptoms", (1) "very mild", (2) "mild", (3) "moderate", and (4) "severe."

End point type	Secondary

End point timeframe:

Baseline and Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	38	38
Units: score on a scale				
least squares mean (standard error)	-1.5 (± 0.17)	-1.4 (± 0.17)	-1.5 (± 0.16)	-1.1 (± 0.16)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient Global Impression of Change (PGIC) Score at Week 16

End point title	Change From Baseline in Patient Global Impression of Change (PGIC) Score at Week 16

End point description:

The PGIC scale measures change in clinical status of AD. The PGIC is based on a 7-point scale, and the patient will rate the change from the start of treatment as 1 "very much improved," 2 "much improved," 3 "minimally improved," 4 "no change," 5 "minimally worse," 6 "much worse," and 7 "very much worse."

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	35	38	43
Units: score on a scale				
least squares mean (standard error)	2.2 (± 0.20)	2.3 (± 0.21)	2.3 (± 0.20)	2.9 (± 0.19)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Sleep Disturbance Numerical Rating Scale (NRS) Score at Week 16

End point title	Change From Baseline in Sleep Disturbance Numerical Rating Scale (NRS) Score at Week 16

End point description:

The sleep disturbance NRS is a scale used by the patients to report their degree of sleep loss related to AD. Patients were asked the following question in their local language: how would you rate your sleep last night? On a scale of 0 to 10, with 0 being "no sleep loss related to signs/symptoms of AD" and 10 being "I cannot sleep at all because of the signs/symptoms of AD". Higher scores indicate worse outcomes.

End point type	Secondary

End point timeframe:

Baseline and Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	38	42
Units: score on a scale				
least squares mean (standard error)	-3.4 (± 0.41)	-3.7 (± 0.42)	-2.9 (± 0.40)	-2.5 (± 0.39)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Skin Pain Numerical Rating Scale (NRS) Score at Week 16

End point title	Change From Baseline in Skin Pain Numerical Rating Scale (NRS) Score at Week 16

End point description:

The skin pain NRS is a patient-administered, 11-point horizontal scale anchored at 0 and 10, with 0 representing "no pain" and 10 representing "worst pain imaginable." Overall severity of a participant's skin pain is indicated by selecting the number that best describes the worst level of skin pain in the past 24 hours.

End point type	Secondary

End point timeframe:

Baseline and Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	35	38	42
Units: score on a scale				
least squares mean (standard error)	-3.5 (± 0.39)	-3.7 (± 0.39)	-3.6 (± 0.38)	-2.9 (± 0.38)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAE)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAE)

End point description:

An adverse event (AE) is any symptom, physical sign, syndrome, or disease that either emerges during the study or, if present at screening, worsens during the study, regardless of the suspected cause of the event.

End point type	Secondary

End point timeframe:

From Baseline through Weeks 16 and 20.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	61	59	55
Units: Number of participants				
Any TEAEs	44	48	51	35
Any related TEAEs	37	39	42	14
Any Treatment Emergent Serious Adverse Events	1	0	1	0
Death	0	0	0	0
Treatment Emergent Adverse Event of Special Intere	3	10	9	1
TEAEs leading to study drug discontinuation	8	16	14	2
TESAEs leading to study drug discontinuation	0	0	1	0
TEAEs by relationship, unrelated	18	17	22	21
TEAEs by relationship, unlikely	6	7	8	5
TEAEs by relationship, possibly	16	19	22	8
TEAEs by relationship, probably	17	20	15	4
TEAEs by relationship, definitely	18	17	15	3
TEAEs by toxicity grade, Grade 1	37	41	44	30
TEAEs by toxicity grade, Grade 2	19	26	20	9

TEAEs by toxicity grade, Grade 3	4	6	2	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Temperature at Week 16

End point title	Change From Baseline in Body Temperature at Week 16

End point description:

A complete physical examination that included body temperature measurement was performed at screening (Visit 1) and Week 16.

End point type	Secondary

End point timeframe:

Baseline and Weeks 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	35	38	43
Units: degree				
arithmetic mean (standard deviation)	-0.07 (± 0.300)	0.05 (± 0.239)	-0.01 (± 0.350)	0.00 (± 0.324)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Respiration Rate at Week 16

End point title	Change From Baseline in Respiration Rate at Week 16

End point description:

A complete physical examination that included respiration rate measurement was performed at screening (Visit 1) and Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	35	38	43
Units: breathes per minute				
arithmetic mean (standard deviation)	0.1 (± 1.51)	0.2 (± 1.37)	0.1 (± 1.26)	0.3 (± 1.72)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Heart Rate at Week 16

End point title	Change From Baseline in Heart Rate at Week 16

End point description:

A complete physical examination that included heart rate measurement was performed at screening (Visit 1) and Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	35	38	43
Units: Beats per minute				
arithmetic mean (standard error)	3.3 (± 9.59)	1.1 (± 9.99)	4.4 (± 9.01)	-2.5 (± 11.07)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Systolic and Diastolic Blood Pressure at Week 16

End point title	Change From Baseline in Systolic and Diastolic Blood Pressure at Week 16

End point description:

A complete physical examination that included systolic and diastolic blood pressure measurements was performed at screening (Visit 1) and Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	35	38	43
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic Blood Pressure	0.3 (± 11.62)	1.0 (± 12.04)	-1.4 (± 12.66)	-0.1 (± 9.76)
Diastolic Blood Pressure	-0.5 (± 8.46)	-0.6 (± 8.33)	-2.1 (± 6.93)	-1.8 (± 8.23)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Mass Index at Week 16

End point title	Change From Baseline in Body Mass Index at Week 16

End point description:

A complete physical examination that included body mass index measurements was performed at screening (Visit 1) and Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	35	37	43
Units: kilogram(s)/square metre				
arithmetic mean (standard deviation)	-0.28 (± 1.081)	-0.13 (± 0.758)	-0.34 (± 1.252)	0.16 (± 0.773)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes in Electrocardiogram (ECF) at Week 16

End point title	Number of Participants With Clinically Significant Changes in Electrocardiogram (ECF) at Week 16

End point description:
Electrocardiograms were assessed by the investigators based on automatically generated parameters.

End point type	Secondary

End point timeframe:
At Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	61	59	55
Units: Number of participants				
QT interval > 450 msec	0	1	1	2
QT interval > 480 msec	0	0	1	1
QT interval > 500 msec	0	0	1	0
QTc interval > 450 msec	1	4	2	2
QTc interval > 480 msec	0	0	1	1
QTc interval > 500 msec	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Erythrocytes Mean Corpuscular Hemoglobin Concentration at Week 16

End point title	Change From Baseline in Hematology Parameter: Erythrocytes Mean Corpuscular Hemoglobin Concentration at Week 16

End point description:
Laboratory parameters including hematology was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:
Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	37	42
Units: g/L				
arithmetic mean (standard deviation)	5.2 (± 16.82)	5.8 (± 20.08)	2.0 (± 17.65)	4.3 (± 18.07)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Erythrocytes Mean Corpuscular Hemoglobin at Week 16

End point title	Change From Baseline in Hematology Parameter: Erythrocytes Mean Corpuscular Hemoglobin at Week 16

End point description:

Laboratory parameters including hematology was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	37	42
Units: g/L				
arithmetic mean (standard deviation)	-0.24 (± 1.057)	-0.27 (± 0.690)	-0.25 (± 0.816)	-0.14 (± 0.710)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Erythrocytes Mean Corpuscular Volume at Week 16

End point title	Change From Baseline in Hematology Parameter: Erythrocytes Mean Corpuscular Volume at Week 16

End point description:

Laboratory parameters including hematology was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	37	42
Units: g/L				
arithmetic mean (standard deviation)	-2.34 (± 4.833)	-2.80 (± 6.069)	-1.52 (± 6.262)	-1.52 (± 6.535)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Hematocrit at Week 16

End point title	Change From Baseline in Hematology Parameter: Hematocrit at Week 16

End point description:

Laboratory parameters including hematology was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	37	42
Units: L/L				
arithmetic mean (standard deviation)	-0.0125 (± 0.03242)	-0.0100 (± 0.03359)	-0.0061 (± 0.03420)	-0.0045 (± 0.03509)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Hemoglobin at Week 16

End point title	Change From Baseline in Hematology Parameter: Hemoglobin at Week 16

End point description:

Laboratory parameters including hematology was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	37	42
Units: g/L				
arithmetic mean (standard deviation)	-1.5 (± 6.70)	-0.2 (± 6.89)	-1.0 (± 8.12)	0.2 (± 8.33)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Basophils, Eosinophils, Leukocytes, Lymphocytes, Monocytes, and Neutrophils at Week 16

End point title	Change From Baseline in Hematology Parameter: Basophils, Eosinophils, Leukocytes, Lymphocytes, Monocytes, and Neutrophils at Week 16
End point description:	
Laboratory parameters including hematology was evaluated at baseline and at Week 16.	
End point type	Secondary
End point timeframe:	
Baseline and Week 16	

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	37	42
Units: 10^9/L				
arithmetic mean (standard deviation)				
Leukocytes	0.357 (± 2.5643)	-0.061 (± 1.8343)	-0.372 (± 1.6455)	-0.153 (± 1.3115)
Basophils	0.002 (± 0.0131)	0.007 (± 0.0187)	-0.002 (± 0.0133)	-0.002 (± 0.0206)
Eosinophils	-0.048 (± 0.2048)	-0.131 (± 0.6653)	-0.055 (± 0.3146)	-0.020 (± 0.1309)
Lymphocytes	0.031 (± 0.5119)	0.009 (± 0.4377)	-0.065 (± 0.3665)	0.020 (± 0.4073)
Monocytes	0.031 (± 0.1884)	0.017 (± 0.1336)	-0.008 (± 0.1070)	0.021 (± 0.1205)
Neutrophils	0.339 (± 2.2070)	0.040 (± 1.3733)	-0.233 (± 1.5109)	-0.170 (± 1.3980)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Platelets at Week 16	
End point title	Change From Baseline in Hematology Parameter: Platelets at Week 16
End point description: Laboratory parameters including hematology was evaluated at baseline and at Week 16.	
End point type	Secondary
End point timeframe: Baseline and Week 16	

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	36	42
Units: 10^9/L				
arithmetic mean (standard deviation)	22.5 (± 51.03)	11.7 (± 55.24)	-1.8 (± 61.72)	-3.0 (± 37.53)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Reticulocytes at Week 16	
End point title	Change From Baseline in Hematology Parameter: Reticulocytes at Week 16
End point description: Laboratory parameters including hematology was evaluated at baseline and at Week 16.	
End point type	Secondary
End point timeframe: Baseline and Week 16	

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	36	42
Units: percent				
arithmetic mean (standard deviation)	0.008 (± 0.4376)	0.025 (± 0.3758)	-0.137 (± 0.4313)	-0.024 (± 0.3411)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Chemistry Parameter: Alkaline Phosphatase, Gamma Glutamyl Transferase, Lactate Dehydrogenase at Week 16

End point title	Change From Baseline in Chemistry Parameter: Alkaline Phosphatase, Gamma Glutamyl Transferase, Lactate Dehydrogenase at Week 16

End point description:

Laboratory parameters including chemistry was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	34	38	43
Units: U/L				
arithmetic mean (standard deviation)				
Alkaline Phosphatase	-4.8 (± 25.88)	2.1 (± 11.55)	1.5 (± 11.32)	-1.7 (± 11.11)
Gamma Glutamyl Transferase	-6.8 (± 62.55)	-0.8 (± 9.11)	3.3 (± 23.98)	-1.7 (± 6.75)
Lactate Dehydrogenase	-15.8 (± 41.47)	-12.9 (± 58.24)	-12.9 (± 50.15)	-7.9 (± 36.44)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Chemistry Parameter: Alanine Aminotransferase and Aspartate Aminotransferase at Week 16

End point title	Change From Baseline in Chemistry Parameter: Alanine Aminotransferase and Aspartate Aminotransferase at Week 16

End point description:

Laboratory parameters including chemistry was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	34	37	43
Units: U/L				
arithmetic mean (standard deviation)				
Alanine Aminotransferase	-1.5 (± 17.16)	-0.7 (± 10.06)	1.0 (± 10.87)	-0.6 (± 13.13)
Aspartate Aminotransferase	-1.6 (± 13.08)	0.6 (± 9.75)	-0.4 (± 11.35)	-1.4 (± 11.50)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Chemistry Parameter: Albumin at Week 16

End point title	Change From Baseline in Chemistry Parameter: Albumin at Week 16
End point description:	
Laboratory parameters including chemistry was evaluated at baseline and at Week 16.	
End point type	Secondary
End point timeframe:	
Baseline and Week 16	

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	34	38	43
Units: g/L				
arithmetic mean (standard deviation)	-0.4 (± 2.67)	0.0 (± 2.80)	0.0 (± 2.57)	0.1 (± 2.36)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Chemistry Parameter: Bilirubin and Direct Bilirubin at Week 16

End point title	Change From Baseline in Chemistry Parameter: Bilirubin and Direct Bilirubin at Week 16
End point description:	
Laboratory parameters including chemistry was evaluated at baseline and at Week 16.	
End point type	Secondary
End point timeframe:	
Baseline and Week 16	

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	34	37	43
Units: umol/L				
arithmetic mean (standard deviation)				
Bilirubin	0.29 (± 2.487)	0.13 (± 2.948)	0.32 (± 2.361)	0.68 (± 3.234)
Direct Bilirubin	0.03 (± 0.205)	-0.13 (± 0.552)	0.01 (± 0.084)	0.17 (± 0.739)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Chemistry Parameter: Creatinine at Week 16

End point title	Change From Baseline in Chemistry Parameter: Creatinine at Week 16

End point description:

Laboratory parameters including chemistry was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	34	38	43
Units: umol/L				
arithmetic mean (standard deviation)	2.9 (± 13.41)	2.3 (± 12.07)	2.3 (± 12.59)	-1.0 (± 7.58)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Basophils/Leukocytes at Week 16

End point title	Change From Baseline in Hematology Parameter: Basophils/Leukocytes at Week 16

End point description:

Laboratory parameters including hematology was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	37	42
Units: percent				
arithmetic mean (standard deviation)	0.02 (± 0.216)	0.10 (± 0.269)	0.01 (± 0.225)	-0.03 (± 0.359)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Eosinophils/Leukocytes at Week 16

End point title	Change From Baseline in Hematology Parameter: Eosinophils/Leukocytes at Week 16

End point description:

Laboratory parameters including hematology was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	37	42
Units: percent				
arithmetic mean (standard deviation)	-0.42 (± 2.353)	-0.96 (± 4.705)	-0.35 (± 3.323)	-0.28 (± 2.268)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Lymphocytes/Leukocytes at Week 16

End point title	Change From Baseline in Hematology Parameter: Lymphocytes/Leukocytes at Week 16

End point description:

Laboratory parameters including hematology was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	37	42
Units: percent				
arithmetic mean (standard deviation)	-0.48 (± 7.737)	0.46 (± 6.139)	1.05 (± 7.232)	0.94 (± 6.922)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Monocytes/Leukocytes at Week 16

End point title	Change From Baseline in Hematology Parameter: Monocytes/Leukocytes at Week 16

End point description:

Laboratory parameters including hematology was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	37	42
Units: percent				
arithmetic mean (standard deviation)	0.18 (± 2.468)	0.31 (± 1.487)	0.09 (± 1.679)	0.29 (± 2.130)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hematology Parameter: Neutrophils/Leukocytes at Week 16

End point title	Change From Baseline in Hematology Parameter: Neutrophils/Leukocytes at Week 16

End point description:

Laboratory parameters including hematology was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	32	37	42
Units: percent				
arithmetic mean (standard deviation)	0.72 (± 9.487)	0.13 (± 8.508)	-0.67 (± 9.060)	-0.90 (± 9.247)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Chemistry Parameter: Calcium, Chloride, Potassium, Sodium, and Urea Nitrogen at Week 16

End point title	Change From Baseline in Chemistry Parameter: Calcium, Chloride, Potassium, Sodium, and Urea Nitrogen at Week 16

End point description:

Laboratory parameters including chemistry was evaluated at baseline and at Week 16.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	34	38	43
Units: mmol/L				
arithmetic mean (standard deviation)				

Calcium	-0.021 (± 0.1430)	0.013 (± 0.1085)	0.006 (± 0.1260)	-0.015 (± 0.1300)
Chloride	-0.2 (± 3.29)	0.0 (± 3.08)	0.2 (± 3.05)	0.1 (± 3.07)
Potassium	-0.01 (± 0.498)	-0.01 (± 0.393)	-0.18 (± 0.449)	-0.06 (± 0.372)
Sodium	-0.1 (± 2.89)	0.6 (± 3.47)	1.4 (± 2.75)	0.5 (± 2.66)
Urea Nitrogen	-0.207 (± 1.1653)	-0.315 (± 1.2731)	0.104 (± 1.3782)	-0.041 (± 1.5732)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Chemistry Parameter: Phosphate at Week 16

End point title	Change From Baseline in Chemistry Parameter: Phosphate at Week 16
End point description: Laboratory parameters including chemistry was evaluated at baseline and at Week 16.	
End point type	Secondary
End point timeframe: Baseline and Week 16	

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	34	37	43
Units: mmol/L				
arithmetic mean (standard deviation)	0.003 (± 0.1986)	0.045 (± 0.2010)	0.043 (± 0.2661)	-0.009 (± 0.1579)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Worst Case Post-Baseline Urinalysis at Week 16

End point title	Number of Participants With Worst Case Post-Baseline Urinalysis at Week 16
End point description: Laboratory parameters including chemistry was evaluated at baseline and at Week 16.	
End point type	Secondary
End point timeframe: At Week 16	

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	61	59	55
Units: Number of participants				
Amorphous Crystals, Present	1	0	0	0
Bacteria, Increase to 1+	0	0	2	4
Bacteria, Increase to 2+	2	1	1	0
Bacteria, Increase to 3+	0	0	1	0
Bacteria, Increase to 4+	0	0	0	1
Calcium Oxalate Crystals, 1-5	2	1	0	0
Calcium Oxalate Crystals, 6-9	1	0	0	0
Calcium Oxalate Crystals, 10-15	0	0	0	1
Calcium Oxalate Crystals, 16-29	0	0	1	0
Calcium Oxalate Crystals, 30-49	1	0	0	0
Calcium Oxalate Crystals, None	16	11	20	22
Erythrocytes, 1-2	9	2	6	11
Erythrocytes, 3-5	1	1	4	3
Erythrocytes, 6-9	0	1	0	0
Erythrocytes, >75	0	0	0	1
Erythrocytes, None	6	4	7	4
Erythrocytes, Occasional	4	4	4	4
Hyaline Casts, 1-5	0	0	0	1
Hyaline Casts, None	20	12	21	22
Leukocytes, 1-5	8	6	8	9
Leukocytes, 6-9	0	2	1	0
Leukocytes, 16-29	0	0	1	1
Leukocytes, 30-49	1	0	1	0
Leukocytes, 50-75	0	0	1	0
Leukocytes, None	5	1	2	5
Leukocytes, Occasional	6	3	7	8
Mucous Threads, Present	4	4	5	5
Squamous Epithelial Cells, 1-5	10	2	8	6
Squamous Epithelial Cells, 6-9	1	1	1	2
Squamous Epithelial Cells, 10-15	2	1	2	1
Squamous Epithelial Cells, 16-29	0	1	1	1
Squamous Epithelial Cells, None	5	5	5	9
Squamous Epithelial Cells, Occasional	2	2	4	4
Transitional Epithelial Cells, Occasional	2	1	0	1
Uric Acid Crystals, >75	0	0	1	0
Uric Acid Crystals, None	20	11	21	23
Yeast Cells, Present	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hospital Anxiety and Depression Scale (HADS) Score at Week 16

End point title	Change From Baseline in Hospital Anxiety and Depression Scale (HADS) Score at Week 16

End point description:

The HADS is a patient reported outcome, comprises of 7 questions for anxiety and 7 questions for depression, with each answer graded from 0 to 3 with a higher score indicating a worse condition. For each group of questions, scores of 7 or less indicate cases without anxiety or depression, whereas scores of 8 to 10, 11 to 14, and 15 to 21 indicate mild, moderate, and severe cases, respectively.

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	35	38	43
Units: Score on a scale				
arithmetic mean (standard deviation)	-2.2 (± 3.11)	-1.7 (± 3.22)	-1.5 (± 4.25)	-1.4 (± 3.21)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Suicidal Ideation, Suicidal Behavior, and Self-Injurious Behavior Without Suicidal Intent Based on the Columbia-Suicide Severity Rating Scale (C-SSRS)

End point title	Number of Participants With Suicidal Ideation, Suicidal Behavior, and Self-Injurious Behavior Without Suicidal Intent Based on the Columbia-Suicide Severity Rating Scale (C-SSRS)

End point description:

The C-SSRS, Investigator-administered version, was designed to provide a prospective, standardized measure of suicidality. C-SSRS is administered in the form of a clinical interview. The C-SSRS categories have been re-ordered from the actual scale to facilitate the definitions of the endpoints, and to enable clarity in the presentation of the results: Category 1 – Wish to be Dead, Category 2 – Non-specific Active Suicidal Thoughts, Category 3 – Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act, Category 4 – Active Suicidal Ideation with Some Intent to Act, without Specific Plan, Category 5 – Active Suicidal Ideation with Specific Plan and Intent, Category 6 – Preparatory Acts or Behavior, Category 7 – Aborted Attempt, Category 8 – Interrupted Attempt, Category 9 – Actual Attempt (non-fatal), Category 10 – Completed Suicide.

End point type	Secondary

End point timeframe:

At Week 16.

End point values	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID	Placebo Tablets BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	61	59	55
Units: number of subjetcs				
Suicidal Ideation	0	0	0	0
Suicidal Behavior	0	0	0	0
Self-injurious behavior without suicidal intent	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 16 weeks.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Orismilast Modified Release Tablets 20 mg BID
Reporting group description: Oral, twice daily morning and evening Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.	
Reporting group title	Orismilast Modified Release Tablets 30 mg BID
Reporting group description: Oral, twice daily morning and evening Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.	
Reporting group title	Orismilast Modified Release Tablets 40 mg BID
Reporting group description: Oral, twice daily morning and evening Orismilast modified release tablets: Orismilast modified release is a next generation PDE4 inhibitor with high selectivity for the PD4 subtypes linked to inflammation.	
Reporting group title	Placebo Tablets BID
Reporting group description: Placebo matching tablets. Oral, twice daily morning and evening.	

Serious adverse events	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	1 / 59 (1.69%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			

subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
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	Placebo Tablets BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 55 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 58 (75.86%)	48 / 61 (78.69%)	51 / 59 (86.44%)

Vascular disorders			
Flushing			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 58 (1.72%)	2 / 61 (3.28%)	1 / 59 (1.69%)
occurrences (all)	1	2	1
Chest pain			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Drug tolerance decreased			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 58 (1.72%)	4 / 61 (6.56%)	0 / 59 (0.00%)
occurrences (all)	1	4	0
Hunger			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Influenza			

subjects affected / exposed	2 / 58 (3.45%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	2	1	0
Immune system disorders			
Allergy to metals			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Food allergy			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Paranasal sinus discomfort			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Adjustment disorder with depressed mood			

subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	2 / 58 (3.45%)	5 / 61 (8.20%)	5 / 59 (8.47%)
occurrences (all)	2	5	6
Anxiety disorder			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 58 (1.72%)	4 / 61 (6.56%)	3 / 59 (5.08%)
occurrences (all)	1	5	4
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 58 (0.00%)	2 / 61 (3.28%)	1 / 59 (1.69%)
occurrences (all)	0	2	1
Blood pressure systolic increased			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram ST segment depression			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 58 (0.00%)	3 / 61 (4.92%)	0 / 59 (0.00%)
occurrences (all)	0	5	0
Mean cell haemoglobin concentration decreased			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Mean cell volume increased			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Weight decreased			

subjects affected / exposed	2 / 58 (3.45%)	0 / 61 (0.00%)	5 / 59 (8.47%)
occurrences (all)	2	0	5
Injury, poisoning and procedural complications			
Accident at work			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	2
Ligament rupture			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Sunburn			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Wrist fracture			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Bundle branch block right			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Myocardial infarction			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	6 / 58 (10.34%)	8 / 61 (13.11%)	5 / 59 (8.47%)
occurrences (all)	7	10	5
Headache			
subjects affected / exposed	12 / 58 (20.69%)	11 / 61 (18.03%)	17 / 59 (28.81%)
occurrences (all)	15	13	20
Nerve compression			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Sinus headache			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	2 / 58 (3.45%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0
Syncope			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 58 (0.00%)	2 / 61 (3.28%)	2 / 59 (3.39%)
occurrences (all)	0	2	2
Sleep disorder			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Leukocytosis			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Lymphadenitis			

subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 58 (3.45%)	1 / 61 (1.64%)	1 / 59 (1.69%)
occurrences (all)	2	1	1
Eye disorders			
Cataract			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Eye swelling			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Abdominal distension			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	3 / 59 (5.08%)
occurrences (all)	0	0	3
Abdominal pain			
subjects affected / exposed	1 / 58 (1.72%)	5 / 61 (8.20%)	5 / 59 (8.47%)
occurrences (all)	1	6	6
Abdominal pain upper			
subjects affected / exposed	3 / 58 (5.17%)	2 / 61 (3.28%)	2 / 59 (3.39%)
occurrences (all)	3	2	3
Chronic gastritis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			

subjects affected / exposed	19 / 58 (32.76%)	24 / 61 (39.34%)	20 / 59 (33.90%)
occurrences (all)	22	32	24
Dry mouth			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	4 / 58 (6.90%)	2 / 61 (3.28%)	2 / 59 (3.39%)
occurrences (all)	4	2	24
Epigastric discomfort			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Faeces soft			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	3 / 59 (5.08%)
occurrences (all)	1	0	3
Flatulence			
subjects affected / exposed	2 / 58 (3.45%)	0 / 61 (0.00%)	2 / 59 (3.39%)
occurrences (all)	2	0	24
Frequent bowel movements			
subjects affected / exposed	2 / 58 (3.45%)	1 / 61 (1.64%)	2 / 59 (3.39%)
occurrences (all)	2	1	2
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	17 / 58 (29.31%)	23 / 61 (37.70%)	27 / 59 (45.76%)
occurrences (all)	24	29	31
Toothache			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	2 / 58 (3.45%)	9 / 61 (14.75%)	9 / 59 (15.25%)
occurrences (all)	3	13	10
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	3 / 58 (5.17%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	3	1	0

Dermatitis contact			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 58 (1.72%)	1 / 61 (1.64%)	1 / 59 (1.69%)
occurrences (all)	1	1	1
Pruritus			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Rosacea			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Skin disorder			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Bone pain			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	4
Myalgia			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Infections and infestations			
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Diverticulitis			

subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Ear infection			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Febrile infection			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Gastrointestinal infection			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Herpes simplex			
subjects affected / exposed	0 / 58 (0.00%)	2 / 61 (3.28%)	0 / 59 (0.00%)
occurrences (all)	0	2	0
Herpes simplex reactivation			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 58 (1.72%)	2 / 61 (3.28%)	4 / 59 (6.78%)
occurrences (all)	1	4	4
Ophthalmic herpes simplex			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Paronychia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Pyelonephritis			

subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Rhinolaryngitis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 58 (0.00%)	1 / 61 (1.64%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Urinary tract infection fungal			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	2
Decreased appetite			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	2 / 59 (3.39%)
occurrences (all)	1	0	2
Glucose tolerance impaired			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Hypercalcaemia			
subjects affected / exposed	0 / 58 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	1 / 58 (1.72%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	2 / 58 (3.45%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Placebo Tablets BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 55 (63.64%)		
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Drug tolerance decreased			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Hunger			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Oedema peripheral			

subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0 0 / 55 (0.00%) 0		
Immune system disorders Allergy to metals subjects affected / exposed occurrences (all) Food allergy subjects affected / exposed occurrences (all)	 1 / 55 (1.82%) 1 0 / 55 (0.00%) 0		
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all)	 0 / 55 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Paranasal sinus discomfort subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Wheezing subjects affected / exposed occurrences (all)	 0 / 55 (0.00%) 0 0 / 55 (0.00%) 0 1 / 55 (1.82%) 1 0 / 55 (0.00%) 0 0 / 55 (0.00%) 0 0 / 55 (0.00%) 0		
Psychiatric disorders			

Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	7 / 55 (12.73%)		
occurrences (all)	7		
Anxiety disorder			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Blood pressure systolic increased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Electrocardiogram ST segment depression			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Mean cell haemoglobin concentration decreased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Mean cell volume increased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		

Weight decreased			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Accident at work			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Ligament rupture			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Sunburn			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Wrist fracture			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Bundle branch block right			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Myocardial infarction			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	5 / 55 (9.09%)		
occurrences (all)	5		
Nerve compression			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Sinus headache			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	3		
Syncope			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Sleep disorder			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Leukocytosis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Lymphadenitis			

subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Eye swelling			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Chronic gastritis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Diarrhoea			

subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		
Dry mouth			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Epigastric discomfort			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Faeces soft			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Frequent bowel movements			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	5 / 55 (9.09%)		
occurrences (all)	7		
Toothache			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	3 / 55 (5.45%)		
occurrences (all)	3		

Dermatitis contact subjects affected / exposed occurrences (all) Hyperhidrosis subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rosacea subjects affected / exposed occurrences (all) Skin disorder subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1 0 / 55 (0.00%) 0 1 / 55 (1.82%) 1 0 / 55 (0.00%) 0 0 / 55 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 0 / 55 (0.00%) 0 0 / 55 (0.00%) 0 0 / 55 (0.00%) 0 1 / 55 (1.82%) 1		
Infections and infestations Asymptomatic bacteriuria subjects affected / exposed occurrences (all) Conjunctivitis subjects affected / exposed occurrences (all) Diverticulitis	 1 / 55 (1.82%) 1 0 / 55 (0.00%) 0		

subjects affected / exposed	0 / 55 (0.00%)			
occurrences (all)	0			
Ear infection				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences (all)	0			
Febrile infection				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences (all)	0			
Folliculitis				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences (all)	0			
Gastrointestinal infection				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences (all)	0			
Herpes simplex				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences (all)	0			
Herpes simplex reactivation				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences (all)	1			
Herpes zoster				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	4 / 55 (7.27%)			
occurrences (all)	5			
Ophthalmic herpes simplex				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences (all)	0			
Oral herpes				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences (all)	0			
Paronychia				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences (all)	0			
Pyelonephritis				

subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Rhinolaryngitis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		
Urinary tract infection fungal			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Glucose tolerance impaired			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Hypercalcaemia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	2 / 55 (3.64%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 May 2022	The purpose of this amendment was to update the protocol per FDA recommendations related to subject inclusion/exclusion criteria, AESIs, and the Investigator Global Assessment for Atopic Dermatitis scale. Additional updates were made to the statistical analyses per the Sponsor's statistician.
13 April 2023	The purpose of this amendment was to update the protocol per notification letter dated 09-FEB2023 for adjustment of laboratory ranges in exclusion criterion No. 14, the update of the Investigators Brochure for orismilast version 15, dated 05. April 2023 and learnings from the recently completed clinical phase 2b trial, UNI50001-203, with orismilast in patients with moderate to severe psoriasis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported