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 Plaque-Type Psoriasis

Summary

EudraCT number	2021-003209-22
Trial protocol	DE
Global end of trial date	20 December 2022

Results information

Result version number	v1 (current)
This version publication date	31 December 2023
First version publication date	31 December 2023

Trial information

Trial identification

Sponsor protocol code	UNI50001-203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05190419
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UNION therapeutics A/S
Sponsor organisation address	Tuborg Havnevej 18, Hellerup, Denmark, DK-2900
Public contact	Morten Lind Jensen, UNION therapeutics A/S, +45 5357 30 44, clinicaltrials@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	13 February 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 November 2022
Global end of trial reached?	Yes
Global end of trial date	20 December 2022
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 adults with moderate-to-severe plaque-type psoriasis.

Protection of trial subjects:

The study was conducted according to the ethical principles in line with the International Conference on Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements, ensuring welfare of the study subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 December 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 126
Country: Number of subjects enrolled	Germany: 46
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 26
Worldwide total number of subjects	202
EEA total number of subjects	172

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)	178
From 65 to 84 years	24

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 202 participants were randomized at 26 sites in Germany (8 sites), Poland (12 sites), the United Kingdom (1 site), and the US (5 sites).

Pre-assignment

Screening details:

The screening visit took place up to 28 days prior to Day 1. Subjects were screened for eligibility and signed the informed consent form.

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

Blinding implementation details:

At the investigational site, each screened subject was assigned a subject identifier number during screening that was be used on all subject documentation. The subject identifier number contains the site number and the subject number and was assigned in numerical order at the screening visit based on chronological order of screening dates.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Tablets BID

Arm description:

Subjects took placebo tablets twice a day during 16 weeks.

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

Dosage and administration details:

Placebo.
Oral, twice daily morning and evening.

Arm title	Orismilast Modified Release Tablets 20 mg BID

Arm description:

Subjects took Orismilast Modified Release Tablets 20 mg BID twice a day during 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Orismilast Modified Release Tablets 20 mg BID
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg BID
Oral, twice daily morning and evening.

Arm title	Orismilast Modified Release Tablets 30 mg BID

Arm description:

Subjects took Orismilast Modified Release Tablets 30 mg BID twice a day during 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Orismilast Modified Release Tablets 30 mg BID
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

40 mg BID.
Oral, twice daily morning and evening.

Arm title	Orismilast Modified Release Tablets 40 mg BID

Arm description:

Subjects took Orismilast Modified Release Tablets 40 mg BID twice a day during 16 weeks.

Arm type	Experimental
Investigational medicinal product name	Orismilast Modified Release Tablets 40 mg BID
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

40 mg BID.
Oral, twice daily morning and evening.

Number of subjects in period 1	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID
Started	51	48	50
Completed	32	34	33
Not completed	19	14	17
Consent withdrawn by subject	7	1	2
Adverse event, non-fatal	2	10	11
Other	1	1	-
Lost to follow-up	1	2	3
Lack of efficacy	8	-	1

Number of subjects in period 1	Orismilast Modified Release Tablets 40 mg BID
Started	53
Completed	26
Not completed	27
Consent withdrawn by subject	2
Adverse event, non-fatal	21
Other	3
Lost to follow-up	1
Lack of efficacy	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo Tablets BID
Reporting group description:	
Subjects took placebo tablets twice a day during 16 weeks.	
Reporting group title	Orismilast Modified Release Tablets 20 mg BID
Reporting group description:	
Subjects took Orismilast Modified Release Tablets 20 mg BID twice a day during 16 weeks.	
Reporting group title	Orismilast Modified Release Tablets 30 mg BID
Reporting group description:	
Subjects took Orismilast Modified Release Tablets 30 mg BID twice a day during 16 weeks.	
Reporting group title	Orismilast Modified Release Tablets 40 mg BID
Reporting group description:	
Subjects took Orismilast Modified Release Tablets 40 mg BID twice a day during 16 weeks.	

Reporting group values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID
Number of subjects	51	48	50
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	45.10	45.40	48.20
standard deviation	± 11.98	± 13.87	± 13.40
Gender categorical Units: Subjects			
Female	12	17	11
Male	39	31	39
Psoriatic Arthritis Units: Subjects			
Yes	1	2	5
No	50	46	45
Disease duration > 2 years Units: Subjects			
Yes	49	47	47
No	2	1	3
Child-bearing potential			

Units: Subjects			
Yes	10	13	5
No	41	35	45
Disease duration			
Units: year			
arithmetic mean	19.3	22.0	18.1
standard deviation	± 11.33	± 14.21	± 11.99
Height			
Units: centimetre			
arithmetic mean	176.26	174.14	173.87
standard deviation	± 8.67	± 8.78	± 9.30
Weight			
Units: kilogram(s)			
arithmetic mean	91.48	94.85	91.65
standard deviation	± 20.33	± 29.96	± 16.17
BMI			
Units: kilogram(s)/square metre			
arithmetic mean	29.420	31.019	30.464
standard deviation	± 6.271	± 8.548	± 5.963

Reporting group values	Orismilast Modified Release Tablets 40 mg BID	Total	
Number of subjects	53	202	
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	44.30		
standard deviation	± 14.60	-	
Gender categorical			
Units: Subjects			
Female	15	55	
Male	38	147	
Psoriatic Arthritis			
Units: Subjects			
Yes	6	14	
No	47	188	
Disease duration > 2 years			
Units: Subjects			
Yes	49	192	
No	4	10	

Child-bearing potential Units: Subjects			
Yes	10	38	
No	43	164	
Disease duration Units: year			
arithmetic mean	19.8		
standard deviation	± 13.69	-	
Height Units: centimetre			
arithmetic mean	176.90		
standard deviation	± 8.57	-	
Weight Units: kilogram(s)			
arithmetic mean	91.08		
standard deviation	± 21.17	-	
BMI Units: kilogram(s)/square metre			
arithmetic mean	29.000		
standard deviation	± 5.921	-	

End points

End points reporting groups

Reporting group title	Placebo Tablets BID
Reporting group description: Subjects took placebo tablets twice a day during 16 weeks.	
Reporting group title	Orismilast Modified Release Tablets 20 mg BID
Reporting group description: Subjects took Orismilast Modified Release Tablets 20 mg BID twice a day during 16 weeks.	
Reporting group title	Orismilast Modified Release Tablets 30 mg BID
Reporting group description: Subjects took Orismilast Modified Release Tablets 30 mg BID twice a day during 16 weeks.	
Reporting group title	Orismilast Modified Release Tablets 40 mg BID
Reporting group description: Subjects took Orismilast Modified Release Tablets 40 mg BID twice a day during 16 weeks.	

Primary: Percentage change in Psoriasis Activity and Severity Index (PASI) score from baseline at Week 16

End point title	Percentage change in Psoriasis Activity and Severity Index (PASI) score from baseline at Week 16
End point description: The Psoriasis Activity and Severity Index (PASI) is a measure of psoriatic disease severity, taking into account qualitative lesion characteristics (erythema, induration, and desquamation) and percentage of affected skin surface area on defined anatomical regions. PASI score ranges from 0 to 72, with higher scores reflecting greater disease severity. Erythema, induration/thickness, and scaling are scored on a scale of 0 (none) to 4 (very severe) on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. Degree of involvement on each of the 4 anatomic regions is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement). The total qualitative score (sum of erythema, thickness, and scaling scores) is multiplied by the degree of involvement for each anatomic region and then multiplied by a constant. The scores for each anatomic region are combined to yield the final PASI.	
End point type	Primary
End point timeframe: From baseline to Week 16.	

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	48	50	53
Units: percent				
least squares mean (standard error)	-17.30 (± 7.07)	-52.60 (± 6.80)	-61.20 (± 6.67)	-63.70 (± 6.96)

Statistical analyses

Statistical analysis title	Comparison between placebo and Orismilast 20mg
Comparison groups	Placebo Tablets BID v Orismilast Modified Release Tablets 20 mg BID
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-35.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.7
upper limit	-16
Variability estimate	Standard error of the mean
Dispersion value	9.38

Statistical analysis title	Comparison between placebo and Orismilast 30mg
Comparison groups	Placebo Tablets BID v Orismilast Modified Release Tablets 30 mg BID
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-43.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-63.1
upper limit	-24.8
Variability estimate	Standard error of the mean
Dispersion value	9.75

Statistical analysis title	Comparison between placebo and Orismilast 40mg
Comparison groups	Orismilast Modified Release Tablets 40 mg BID v Placebo Tablets BID
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-46.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-65.6
upper limit	-27.3
Variability estimate	Standard error of the mean
Dispersion value	9.75

Secondary: Patients achieving 75% reduction in PASI (PASI75) response at Week 16

End point title	Patients achieving 75% reduction in PASI (PASI75) response at Week 16

End point description:

The PASI is a measure of psoriatic disease severity, taking into account qualitative lesion characteristics (erythema, induration, and desquamation) and percentage of affected skin surface area on defined anatomical regions. PASI score ranges from 0 to 72, with higher scores reflecting greater disease severity. Erythema, induration/thickness, and scaling are scored on a scale of 0 (none) to 4 (very severe) on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. Degree of involvement on each of the 4 anatomic regions is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement). The total qualitative score (sum of erythema, thickness, and scaling scores) is multiplied by the degree of involvement for each anatomic region and then multiplied by a constant. The scores for each anatomic region are combined to yield the final PASI. PASI75 is 75% reduction from Baseline in PASI score.

End point type	Secondary

End point timeframe:

From Baseline to Week 16.

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	48	50	53
Units: Number of patients				
Yes	8	17	22	17
No	26	18	13	11

Statistical analyses

No statistical analyses for this end point

Secondary: Patients achieving a score of clear (0) or almost clear (1) and an ≥2-point improvement in Investigator Global Assessment (IGA) at Week 16

End point title	Patients achieving a score of clear (0) or almost clear (1) and an ≥2-point improvement in Investigator Global Assessment (IGA) at Week 16

End point description:

The IGA is a measure used by physicians to determine the patient's overall severity of disease. The static version is used in this trial for measurement at a single point in time as indicated in the schedule

of assessments. The investigator will rate the severity of patient's psoriasis on a 5-point scale ranging from 0 (clear) to 4 (severe).

End point type	Secondary

End point timeframe:

From Baseline to Week 16

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	48	50	53
Units: percent				
number (not applicable)				
Yes	6.9	26.2	24.5	20.6
No	93.1	73.8	75.5	79.4

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved a Score of Clear (0) or Almost Clear (1) and an at Least 2-point Improvement in Investigator Global Assessment (IGA) at Weeks 4, 8, 12, and 20

End point title	Percentage of Participants Who Achieved a Score of Clear (0) or Almost Clear (1) and an at Least 2-point Improvement in Investigator Global Assessment (IGA) at Weeks 4, 8, 12, and 20

End point description:

The IGA is a measure used by physicians to determine the patient's overall severity of disease. The static version is used in this trial for measurement at a single point in time as indicated in the schedule of assessments. The investigator will rate the severity of patient's psoriasis on a 5-point scale ranging from 0 (clear) to 4 (severe).

End point type	Secondary

End point timeframe:

From Baseline to Week 4, 8, 12 and 20.

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	48	50	53
Units: percent				
number (not applicable)				
Week 4, Yes	2.1	4.2	4.3	4.1
Week 4, No	97.9	95.8	95.7	95.9
Week 8, Yes	0	10.9	17.0	8.4

Week 8, No	100	89.1	83	91.6
Week 12, Yes	4.6	25.4	23.4	17.6
Week 12, No	95.4	74.6	76.6	82.4
Week 20, Yes	11.3	20.8	11.1	10.8
Week 20, No	88.7	79.3	88.9	89.2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved 75% Reduction in PASI (PASI75) Response at Weeks 4, 8, 12, and 20

End point title	Percentage of Participants Who Achieved 75% Reduction in PASI (PASI75) Response at Weeks 4, 8, 12, and 20

End point description:

The PASI is a measure of psoriatic disease severity, taking into account qualitative lesion characteristics (erythema, induration, and desquamation) and percentage of affected skin surface area on defined anatomical regions. PASI score ranges from 0 to 72, with higher scores reflecting greater disease severity. Erythema, induration/thickness, and scaling are scored on a scale of 0 (none) to 4 (very severe) on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. Degree of involvement on each of the 4 anatomic regions is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement). The total qualitative score (sum of erythema, thickness, and scaling scores) is multiplied by the degree of involvement for each anatomic region and then multiplied by a constant. The scores for each anatomic region are combined to yield the final PASI. PASI75 is 75% reduction from Baseline in PASI score.

End point type	Secondary

End point timeframe:

Baseline to Weeks 4, 8, 12, and 20.

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	48	50	53
Units: percent				
number (not applicable)				
Week 4, Yes	6.0	8.4	10.8	9.6
Week 4, No	94.0	91.6	89.2	90.4
Week 8, Yes	11.8	32.5	37.0	31.2
Week 8, No	88.2	67.5	63.0	68.8
Week 12, Yes	12.3	42.5	49.5	38.5
Week 12, No	87.7	57.5	50.5	61.5
Week 20, Yes	18.7	31.6	22.0	29.7
Week 20, No	81.3	68.4	78.0	70.3

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved 50%, 90%, and 100% Reduction in PASI Response at Weeks 4, 8, 12, 16, and 20

End point title	Percentage of Participants Who Achieved 50%, 90%, and 100% Reduction in PASI Response at Weeks 4, 8, 12, 16, and 20

End point description:

The PASI is a measure of psoriatic disease severity, taking into account qualitative lesion characteristics (erythema, induration, and desquamation) and percentage of affected skin surface area on defined anatomical regions. PASI score ranges from 0 to 72, with higher scores reflecting greater disease severity. Erythema, induration/thickness, and scaling are scored on a scale of 0 (none) to 4 (very severe) on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. Degree of involvement on each of the 4 anatomic regions is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement). The total qualitative score (sum of erythema, thickness, and scaling scores) is multiplied by the degree of involvement for each anatomic region and then multiplied by a constant. The scores for each anatomic region are combined to yield the final PASI. PASI 50, 90, and 100 is 50%, 90%, and 100% reduction from Baseline in PASI score, respectively.

End point type	Secondary

End point timeframe:

From Baseline to Weeks 4, 8, 12, 16, and 20.

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	48	50	53
Units: percent				
number (not applicable)				
Week 4, PASI 50	15.69	33.33	36	39.62
Week 4, PASI 90	0	2.08	4	5.66
Week 4, PASI 100	0	0	0	0
Week 8, PASI 50	21.57	58.33	56	50.94
Week 8, PASI 90	1.96	8.33	12	9.43
Week 8, PASI 100	0	0	6	1.89
Week 12, PASI 50	29.41	56.25	64	41.51
Week 12, PASI 90	5.88	20.83	18	15.09
Week 12, PASI 100	0	10.42	8	0
Week 16, PASI 50	25.49	47.92	60	47.17
Week 16, PASI 90	7.84	22.92	20	22.64
Week 16, PASI 100	1.96	8.33	8	1.89
Week 20, PASI 50	23.53	39.58	38	32.08
Week 20, PASI 90	5.88	18.75	12	7.55
Week 20, PASI 100	3.92	4.17	2	1.89

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Psoriasis Activity and Severity Index (PASI) Score at Weeks 4, 8, 12, and 20

End point title	Percent Change From Baseline in Psoriasis Activity and Severity Index (PASI) Score at Weeks 4, 8, 12, and 20

End point description:

The Psoriasis Activity and Severity Index (PASI) is a measure of psoriatic disease severity, taking into account qualitative lesion characteristics (erythema, induration, and desquamation) and percentage of affected skin surface area on defined anatomical regions. PASI score ranges from 0 to 72, with higher scores reflecting greater disease severity. Erythema, induration/thickness, and scaling are scored on a scale of 0 (none) to 4 (very severe) on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. Degree of involvement on each of the 4 anatomic regions is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement). The total qualitative score (sum of erythema, thickness, and scaling scores) is multiplied by the degree of involvement for each anatomic region and then multiplied by a constant. The scores for each anatomic region are combined to yield the final PASI.

End point type	Secondary

End point timeframe:

From Baseline to Weeks 4, 8, 12, and 20.

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	48	50	53
Units: percent				
least squares mean (standard error)				
Week 4	-14.40 (± 4.33)	-35.40 (± 4.40)	-38.40 (± 4.43)	-38.70 (± 4.24)
Week 8	-16.10 (± 5.79)	-48.30 (± 5.76)	-54.20 (± 5.94)	-53.60 (± 5.87)
Week 12	-18.10 (± 6.61)	-56.10 (± 6.30)	-61.70 (± 6.40)	-57.50 (± 6.59)
Week 20	-13.70 (± 9.69)	-35.00 (± 9.11)	-30.50 (± 9.11)	-36.20 (± 10.57)

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The DLQI is a 10-item validated questionnaire completed by the patient used to assess the impact of skin disease on the patient's quality of life (QoL) during the previous week. The 10 questions cover the following topics: symptoms, embarrassment, shopping and home care, clothes, social and leisure, sport, work or study, close relationships, 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 QoL.

End point type	Secondary

End point timeframe:

From Baseline to Weeks 16.

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	34	35	27
Units: percent				
least squares mean (standard error)	-4.9 (± 1.02)	-8.8 (± 1.01)	-7.7 (± 1.00)	-7.3 (± 1.14)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Dermatology Life Quality Index (DLQI) Score at Weeks 20

End point title	Percent Change From Baseline in Dermatology Life Quality Index (DLQI) Score at Weeks 20

End point description:

The DLQI is a 10-item validated questionnaire completed by the patient used to assess the impact of skin disease on the patient's quality of life (QoL) during the previous week. The 10 questions cover the following topics: symptoms, embarrassment, shopping and home care, clothes, social and leisure, sport, work or study, close relationships, 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 QoL.

End point type	Secondary

End point timeframe:

From Baseline to Week 20.

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	33	33	25
Units: percent				
least squares mean (standard error)	-5.1 (± 1.06)	-5.0 (± 1.02)	-4.0 (± 1.02)	-4.9 (± 1.17)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experienced Psoriasis Rebound by Week 20

End point title	Percentage of Participants Who Experienced Psoriasis Rebound

	by Week 20

End point description:

The Psoriasis Activity and Severity Index (PASI) is a measure of psoriatic disease severity, taking into account qualitative lesion characteristics (erythema, induration, and desquamation) and percentage of affected skin surface area on defined anatomical regions. PASI score ranges from 0 to 72, with higher scores reflecting greater disease severity. Erythema, induration/thickness, and scaling are scored on a scale of 0 (none) to 4 (very severe) on 4 anatomic regions of the body: head, trunk, upper limbs, and lower limbs. Degree of involvement on each of the 4 anatomic regions is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement). The total qualitative score (sum of erythema, thickness, and scaling scores) is multiplied by the degree of involvement for each anatomic region and then multiplied by a constant. The scores for each anatomic region are combined to yield the final PASI.

End point type	Secondary

End point timeframe:

From baseline to Week 20.

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	48	50	53
Units: percent				
number (not applicable)	11.76	4.17	10	3.77

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The BSA assessment estimates the extent of disease or skin affected by psoriasis and is expressed as a percentage of total body surface. BSA was determined by the Investigator or designee using the patient palm = 1% BSA rule. The patient’s palm is measured from the wrist to the proximal interphalangeal and thumb.

End point type	Secondary

End point timeframe:

From Baseline to Week 16.

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	35	28
Units: percent				
least squares mean (standard error)	-6.90 (± 1.87)	-13.50 (±	-14.40 (±	-18.10 (±

1.86)	1.85)	2.08)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Total Score of Psoriasis Symptom Scale (PSS) at Week 16

End point title	Percent Change From Baseline in Total Score of Psoriasis Symptom Scale (PSS) at Week 16

End point description:

The PSS is a 4-item patient-completed questionnaire (Rentz 2017). It is patient relevant, its domains are reliable and valid, and it takes few minutes to complete. The PSS assesses severity of pain, itching, redness, and burning during the past 24 hours using a 5-point severity scale from 0 = none to 4 = very severe.

End point type	Secondary

End point timeframe:

From Baseline to Week 16.

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	35	27
Units: percent				
arithmetic mean (standard deviation)	-1.8 (± 3.27)	-5.7 (± 4.25)	-4.8 (± 4.32)	-5.1 (± 3.48)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Each Individual Item of Psoriasis Symptom Scale (PSS) at Week 16

End point title	Percent Change From Baseline in Each Individual Item of Psoriasis Symptom Scale (PSS) at Week 16

End point description:

The PSS is a 4-item patient-completed questionnaire (Rentz 2017). It is patient relevant, its domains are reliable and valid, and it takes few minutes to complete. The PSS assesses severity of pain, itching, redness, and burning during the past 24 hours using a 5-point severity scale from 0 = none to 4 = very severe.

End point type	Secondary

End point timeframe:

From Baseline to Week 16.

End point values	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID	Orismilast Modified Release Tablets 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	35	27
Units: percent				
least squares mean (standard error)				
Pain	-0.4 (± 0.15)	-1.0 (± 0.15)	-0.8 (± 0.15)	-0.7 (± 0.17)
Redness	-0.6 (± 0.15)	-1.4 (± 0.15)	-0.4 (± 0.16)	-1.3 (± 0.16)
Itching	-0.4 (± 0.16)	-1.3 (± 0.16)	-1.2 (± 0.16)	-0.9 (± 0.17)
Burning	-0.5 (± 0.16)	-1.3 (± 0.16)	-1.1 (± 0.16)	-0.9 (± 0.18)

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	Placebo Tablets BID
Reporting group description: -	
Reporting group title	Orismilast Modified Release Tablets 20 mg BID
Reporting group description: -	
Reporting group title	Orismilast Modified Release Tablets 30 mg BID
Reporting group description: -	
Reporting group title	Orismilast Modified Release Tablets 40 mg BID
Reporting group description: -	

Serious adverse events	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 50 (2.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythrodermic psoriasis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 50 (2.00%)
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	Orismilast Modified Release Tablets 40 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 53 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythrodermic psoriasis			
subjects affected / exposed	0 / 53 (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: 1 %

Non-serious adverse events	Placebo Tablets BID	Orismilast Modified Release Tablets 20 mg BID	Orismilast Modified Release Tablets 30 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 51 (45.10%)	37 / 48 (77.08%)	42 / 50 (84.00%)
Investigations			
Electrocardiogram			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	1 / 50 (2.00%)
occurrences (all)	1	2	2
Weight increased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			

subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Crystal urine present			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
Haematocrit increased			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	0 / 50 (0.00%)
occurrences (all)	1	1	0
Mean cell haemoglobin concentration increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Mean cell volume increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 51 (0.00%)	2 / 48 (4.17%)	1 / 50 (2.00%)
occurrences (all)	0	2	1
Hypertension			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 51 (1.96%)	2 / 48 (4.17%)	1 / 50 (2.00%)
occurrences (all)	1	3	1
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 51 (5.88%)	6 / 48 (12.50%)	13 / 50 (26.00%)
occurrences (all)	6	9	16
Dizziness			
subjects affected / exposed	0 / 51 (0.00%)	3 / 48 (6.25%)	7 / 50 (14.00%)
occurrences (all)	0	3	8
Paraesthesia			

subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	2 / 50 (4.00%)
occurrences (all)	3	1	2
Asthenia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	3 / 50 (6.00%)
occurrences (all)	0	0	5
Discomfort			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Back pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	2 / 50 (4.00%)
occurrences (all)	0	1	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 51 (3.92%)	18 / 48 (37.50%)	24 / 50 (48.00%)
occurrences (all)	2	24	35
Nausea			
subjects affected / exposed	2 / 51 (3.92%)	11 / 48 (22.92%)	19 / 50 (38.00%)
occurrences (all)	2	12	23
Vomiting			
subjects affected / exposed	1 / 51 (1.96%)	3 / 48 (6.25%)	4 / 50 (8.00%)
occurrences (all)	1	3	6
Abdominal pain upper			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	3 / 50 (6.00%)
occurrences (all)	0	2	3
Abdominal pain			

subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	1 / 50 (2.00%)
occurrences (all)	1	0	2
Abdominal discomfort			
subjects affected / exposed	1 / 51 (1.96%)	4 / 48 (8.33%)	0 / 50 (0.00%)
occurrences (all)	1	4	0
Dyspepsia			
subjects affected / exposed	0 / 51 (0.00%)	2 / 48 (4.17%)	1 / 50 (2.00%)
occurrences (all)	0	2	1
Frequent bowel movements			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	3 / 50 (6.00%)
occurrences (all)	0	1	3
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Gastritis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Gastrointestinal disorder			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	3 / 51 (5.88%)	3 / 48 (6.25%)	1 / 50 (2.00%)
occurrences (all)	4	3	1
Rash			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	1 / 50 (2.00%)
occurrences (all)	1	1	2
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 51 (5.88%)	1 / 48 (2.08%)	2 / 50 (4.00%)
occurrences (all)	3	1	2
Nasopharyngitis			

subjects affected / exposed	3 / 51 (5.88%)	1 / 48 (2.08%)	4 / 50 (8.00%)
occurrences (all)	3	1	4
Upper respiratory tract infection			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	2 / 50 (4.00%)
occurrences (all)	1	1	2
Bronchitis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Conjunctivitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	2 / 50 (4.00%)
occurrences (all)	1	0	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	1 / 50 (2.00%)
occurrences (all)	1	1	1

Non-serious adverse events	Orismilast Modified Release Tablets 40 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 53 (94.34%)		
Investigations			
Electrocardiogram			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Crystal urine present			

subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Haematocrit increased			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Mean cell haemoglobin concentration increased			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Mean cell volume increased			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 53 (20.75%)		
occurrences (all)	14		
Dizziness			
subjects affected / exposed	8 / 53 (15.09%)		
occurrences (all)	10		
Paraesthesia			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Sciatica			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 4		
Asthenia subjects affected / exposed occurrences (all)	2 / 53 (3.77%) 2		
Discomfort subjects affected / exposed occurrences (all)	1 / 53 (1.89%) 1		
Malaise subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0		
Blood and lymphatic system disorders Back pain subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	24 / 53 (45.28%) 43		
Nausea subjects affected / exposed occurrences (all)	22 / 53 (41.51%) 24		
Vomiting subjects affected / exposed occurrences (all)	7 / 53 (13.21%) 19		
Abdominal pain upper subjects affected / exposed occurrences (all)	6 / 53 (11.32%) 9		
Abdominal pain subjects affected / exposed occurrences (all)	6 / 53 (11.32%) 8		
Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 53 (1.89%) 1		
Dyspepsia			

subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Frequent bowel movements			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	2		
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	3		
Gastritis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorder			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences (all)	2		
Infections and infestations			
COVID-19			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Nasopharyngitis			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
Bronchitis			

subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	0 / 53 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 July 2021	The purpose of this amendment was to update the protocol to provide further details about the study design, study objectives and endpoints, subject selection criteria, as well as data collection and analyses.
20 May 2022	The main purpose of this amendment is to add PK sampling to enable meaningful PK data from the trial. Updates to the study design, study endpoint, subject selection criteria, as well as data collection and analyses were also made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported