Clinical trial results:
A 24 week, randomised, assessor blinded, active-controlled, parallel group, phase 3, 2 arm trial to compare the efficacy and safety of delgocitinib cream 20 mg/g twice-daily with alitretinoin capsules once-daily in adult participants with severe chronic hand eczema

Summary

EudraCT number	2021-003543-16
Trial protocol	DE IT ES FR AT PL NO SK
Global end of trial date	05 December 2023

Results information

Result version number	v2
This version publication date	21 December 2024
First version publication date	25 October 2024
Version creation reason	• Correction of full data set correction

Trial information

Trial identification

Sponsor protocol code	LP0133-1528

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05259722
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LEO Pharma A/S
Sponsor organisation address	Industriparken 55, Ballerup, Denmark, 2750
Public contact	Clinical Disclosure, LEO Pharma A/S, disclosure@leo-pharma.com
Scientific contact	Clinical Disclosure, LEO Pharma A/S, disclosure@leo-pharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 November 2023
Global end of trial reached?	Yes
Global end of trial date	05 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy and health-related quality of life of twice-daily topical application of delgocitinib cream with once-daily oral administration of alitretinoin capsules in the treatment of patients with severe CHE.

Protection of trial subjects:

This trial was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, CIOMS International Ethical Guidelines, applicable ICH GCP guidelines, and other applicable laws and regulations.

Background therapy: -

Evidence for comparator:

N/A

Actual start date of recruitment	15 June 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	United Kingdom: 6
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Germany: 136
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Poland: 180
Country: Number of subjects enrolled	Slovakia: 14
Country: Number of subjects enrolled	Spain: 64
Country: Number of subjects enrolled	Canada: 54
Worldwide total number of subjects	513
EEA total number of subjects	453

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)	471
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial enrolled adult participants with severe CHE and with a documented inadequate response to treatment with TCS or for whom TCS were documented to be otherwise medically inadvisable.

Pre-assignment

Screening details:

Randomization was stratified by subtype (hyperkeratotic/non-hyperkeratotic) and region (North America/Europe).

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Due to the different administration routes for the 2 IMPs, participants were not blinded to treatment assignment. To ensure unbiased clinical assessments, efficacy (IGA-CHE and HECSI) was evaluated by a blinded assessor.

Arms

Are arms mutually exclusive?	Yes
Arm title	Delgocitinib Cream 20 mg/g

Arm description:

Twice-daily topical application for up to 24 weeks.

Delgocitinib: Cream for topical application 20 mg/g.

There was a possibility to stop treatment after 16 weeks if IGA 0/1 was obtained.

Arm type	Experimental
Investigational medicinal product name	Delgocitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

20 mg/g milligram(s)/gram twice daily for up to 24 weeks

Arm title	Alitretinoin Capsules 30 mg Per Capsule

Arm description:

1 capsule per day for up to 24 weeks

Toctino: 1 capsule Toctino 30 mg per day; optional reduction to 10 mg per day in case unacceptable adverse reactions to the higher dose occur.

There was a possibility to stop treatment after 12 weeks if IGA 0/1 was obtained.

Arm type	Active comparator
Investigational medicinal product name	Alitretinoin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

1 capsule per day for up to 24 weeks.
Toctino: 1 capsule toctino 30 mg per day; optional reduction to 10 mg per day in case unacceptable

adverse reactions to the higher dose occur

Number of subjects in period 1	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule
Started	254	259
Completed	219	154
Not completed	35	105
Consent withdrawn by subject	15	33
Discontinuation of IMP, related to COVID-19	1	-
Adverse event, non-fatal	2	24
Various reasons	3	9
Not exposed to IMP	1	12
Lost to follow-up	5	1
Lack of efficacy	8	26

Baseline characteristics

Reporting groups	
Reporting group title	Delgocitinib Cream 20 mg/g

Reporting group description:

Twice-daily topical application for up to 24 weeks.

Delgocitinib: Cream for topical application 20 mg/g.

There was a possibility to stop treatment after 16 weeks if IGA 0/1 was obtained.

Reporting group title	Alitretinoin Capsules 30 mg Per Capsule

Reporting group description:

1 capsule per day for up to 24 weeks

Toctino: 1 capsule Toctino 30 mg per day; optional reduction to 10 mg per day in case unacceptable adverse reactions to the higher dose occur.

There was a possibility to stop treatment after 12 weeks if IGA 0/1 was obtained.

Reporting group values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule	Total
Number of subjects	254	259	513
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	45.4	44.0	
standard deviation	± 13.78	± 14.56	-
Gender categorical Units: Subjects			
Female	167	167	334
Male	87	92	179
Race Units: Subjects			
American Indian or Alaska Native	2	2	4
Asian	9	5	14
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	2	3	5
White	237	240	477
More than one race	1	6	7
Unknown or Not Reported	3	2	5

Ethnicity Units: Subjects			
Hispanic or Latino	22	14	36
Not Hispanic or Latino	226	241	467
Unknown or Not Reported	6	4	10

End points

End points reporting groups

Reporting group title	Delgocitinib Cream 20 mg/g

Reporting group description:

Twice-daily topical application for up to 24 weeks.

Delgocitinib: Cream for topical application 20 mg/g.

There was a possibility to stop treatment after 16 weeks if IGA 0/1 was obtained.

Reporting group title	Alitretinoin Capsules 30 mg Per Capsule

Reporting group description:

1 capsule per day for up to 24 weeks

Toctino: 1 capsule Toctino 30 mg per day; optional reduction to 10 mg per day in case unacceptable adverse reactions to the higher dose occur.

There was a possibility to stop treatment after 12 weeks if IGA 0/1 was obtained.

Primary: Change in HECSI Score From Baseline to Week 12

End point title	Change in HECSI Score From Baseline to Week 12

End point description:

The Hand Eczema Severity Index (HECSI) is an instrument used in clinical trials to rate the severity of 6 clinical signs (erythema, infiltration/papulation, vesicles, fissures, scaling, and oedema) and the extent of the lesions in each of the 5 hand regions (fingertips, fingers [except fingertips], palm of hands, back of hands, and wrists) by use of standard scales. The HECSI score will range from 0 (lowest possible score) to 360 (highest possible score).

End point type	Primary

End point timeframe:

12 weeks

End point values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	249	250		
Units: units on a scale				
arithmetic mean (standard error)	-67.6 (± 3.37)	-51.5 (± 3.36)		

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs alitretinoin

Statistical analysis description:

The change from baseline was analysed using an ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing.

Comparison groups	Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per

	Capsule
Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-16.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.28
upper limit	-8.86

Secondary: HECSI-90 at Week 12

End point title	HECSI-90 at Week 12

End point description:

The Hand Eczema Severity Index (HECSI) is an instrument used in clinical trials to rate the severity of 6 clinical signs (erythema, infiltration/papulation, vesicles, fissures, scaling, and oedema) and the extent of the lesions in each of the 5 hand regions (fingertips, fingers [except fingertips], palm of hands, back of hands, and wrists) by use of standard scales. The HECSI score will range from 0 (lowest possible score) to 360 (highest possible score). HECSI-90 is defined as at least 90% improvement in HECSI score from baseline.

End point type	Secondary

End point timeframe:

12 weeks

End point values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	249	250		
Units: Participants	96	65		

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs alitretinoin

Statistical analysis description:

The difference in response rates was analysed using the Cochran-Mantel-Haenszel test stratified by hyperkeratotic/non-hyperkeratotic subtype. Missing data was imputed as non-response. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing.

Comparison groups	Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule

Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	12.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.34
upper limit	20.78

Secondary: IGA-CHE TS at Week 12

End point title	IGA-CHE TS at Week 12

End point description:

The Investigator's Global Assessment for chronic hand eczema (IGA-CHE) is an instrument used in clinical trials to rate the severity of the participant's global chronic hand eczema (CHE) and is based on a 5-point scale ranging from 0 (clear) to 4 (severe). IGA-CHE treatment success (IGA-CHE TS) is defined as an IGA-CHE score of 0 (clear) or 1 (almost clear) with a ≥2-step improvement from baseline.

End point type	Secondary

End point timeframe:

12 weeks

End point values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	250	253		
Units: Participants	68	42		

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs alitretinoin

Statistical analysis description:

The difference in response rates was analysed using the Cochran-Mantel-Haenszel test stratified by hyperkeratotic/non-hyperkeratotic subtype. Missing data was imputed as non-response. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing.

Comparison groups	Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule

Number of subjects included in analysis	503
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	10.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.31
upper limit	17.87

Secondary: Change in HESD Itch Score (Weekly Average) From Baseline to Week 12

End point title	Change in HESD Itch Score (Weekly Average) From Baseline to Week 12

End point description:

The Hand Eczema Symptom Diary (HESD) is an eDiary in which participants will assess the worst severity of 6 individual signs and symptoms of CHE over the past 24 hours using an 11-point numeric rating scale throughout the trial on a daily basis. This endpoint will only assess the 'itch' component.

End point type	Secondary

End point timeframe:

12 weeks

End point values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	238		
Units: units on a scale				
arithmetic mean (standard error)	-3.0 (± 0.22)	-2.4 (± 0.21)		

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs alitretinoin

Statistical analysis description:

The change from baseline was analysed using an ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing.

Comparison groups	Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule

Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	-0.2

Secondary: Change in HESD Pain Score (Weekly Average) From Baseline to Week 12

End point title	Change in HESD Pain Score (Weekly Average) From Baseline to Week 12

End point description:

The Hand Eczema Symptom Diary (HESD) is an eDiary in which participants will assess the worst severity of 6 individual signs and symptoms of CHE over the past 24 hours using an 11-point numeric rating scale throughout the trial on a daily basis. This endpoint will only assess the 'pain' component.

End point type	Secondary

End point timeframe:

12 weeks

End point values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	238		
Units: units on a scale				
arithmetic mean (standard error)	-2.9 (± 0.23)	-2.3 (± 0.23)		

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs alitretinoin

Statistical analysis description:

The change from baseline was analysed using an ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing.

Comparison groups	Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule

Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	-0.1

Secondary: AUC of HECSI-90 From Baseline up to Week 24

End point title	AUC of HECSI-90 From Baseline up to Week 24

End point description:

The Hand Eczema Severity Index (HECSI) is an instrument used in clinical trials to rate the severity of 6 clinical signs (erythema, infiltration/papulation, vesicles, fissures, scaling, and oedema) and the extent of the lesions in each of the 5 hand regions (fingertips, fingers [except fingertips], palm of hands, back of hands, and wrists) by use of standard scales. The HECSI score will range from 0 (lowest possible score) to 360 (highest possible score). HECSI-90 is defined as at least 90% improvement in HECSI score from baseline. The area under the curve (AUC) at participant level will be determined as follows: 1 will be assigned when response is observed and 0 otherwise. The AUC is interpreted as number of days with 90% reduction in HECSI score until Week 24.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	249	250		
Units: units on a scale				
arithmetic mean (standard error)	51.1 (± 4.11)	43.5 (± 4.22)		

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs alitretinoin

Statistical analysis description:

The AUC was analysed using a robust ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing.

Comparison groups	Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule

Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.81
upper limit	22.86

Secondary: AUC of Change From Baseline in DLQI Score up to Week 24

End point title	AUC of Change From Baseline in DLQI Score up to Week 24

End point description:

The Dermatology Life Quality Index (DLQI) is a validated questionnaire consisting of 10 items addressing the participant's perception of the impact of their skin disease on different aspects of their quality of life over the last week. The DLQI score is the sum of the 10 items (score ranging from 0 to 30). The area under the curve (AUC) at patient level will be determined from the change from baseline in DLQI score estimated piecewise from Week 0 to Week 24. Differences will be analysed with opposite sign to interpret positive area as improvement in scores and negative area as worsening.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	236		
Units: units on a scale				
arithmetic mean (standard error)	1124.7 (± 61.37)	790.7 (± 62.67)		

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs alitretinoin

Statistical analysis description:

The AUC was analysed using a robust ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing.

Comparison groups	Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule

Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	334
Confidence interval	
level	95 %
sides	2-sided
lower limit	195.69
upper limit	472.26

Secondary: Change in HECSI Score From Baseline to Week 24

End point title	Change in HECSI Score From Baseline to Week 24

End point description:

The Hand Eczema Severity Index (HECSI) is an instrument used in clinical trials to rate the severity of 6 clinical signs (erythema, infiltration/papulation, vesicles, fissures, scaling, and oedema) and the extent of the lesions in each of the 5 hand regions (fingertips, fingers [except fingertips], palm of hands, back of hands, and wrists) by use of standard scales. The HECSI score will range from 0 (lowest possible score) to 360 (highest possible score).

End point type	Secondary

End point timeframe:

24 weeks

End point values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	249	250		
Units: units on a scale				
arithmetic mean (standard error)	-69.6 (± 3.78)	-45.1 (± 3.77)		

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs alitretinoin

Statistical analysis description:

The change from baseline was analysed using an ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing.

Comparison groups	Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule

Number of subjects included in analysis	499
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.001 [2]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-24.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.55
upper limit	-16.36

Notes:

[1] - Non-inferiority (margin=10) was tested before superiority.

[2] - Non-inferiority (margin=10) p-value <0.001, superiority p-value <0.001

Secondary: Number of Treatment-emergent AEs From Baseline up to Week 26

End point title	Number of Treatment-emergent AEs From Baseline up to Week 26

End point description:

An adverse event (AE) will be considered treatment emergent if started after the first application of investigational medicinal product (IMP), or if started before the first application of IMP and worsened in severity after first dose of IMP.

End point type	Secondary

End point timeframe:

26 weeks

End point values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253	247		
Units: events	280	620		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Treatment-emergent SAEs From Baseline up to Week 26

End point title	Number of Treatment-emergent SAEs From Baseline up to Week 26

End point description:

A serious adverse event (SAE) will be considered treatment emergent if started after the first application of investigational medicinal product (IMP), or if started before the first application of IMP and worsened in severity after first dose of IMP.

End point type	Secondary

End point timeframe:

26 weeks

End point values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253	247		
Units: events	5	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of AEs Leading to IMP Discontinuation up to Week 24

End point title	Number of AEs Leading to IMP Discontinuation up to Week 24

End point description:

The investigational medicinal product (IMP) will be discontinued permanently in case of an AE that, in the opinion of the investigator or sponsor's medical expert, contraindicates further dosing. The investigator will assess the relationship between investigational medicinal product (IMP) and the adverse event (AE).

End point type	Secondary

End point timeframe:

24 weeks

End point values	Delgocitinib Cream 20 mg/g	Alitretinoin Capsules 30 mg Per Capsule		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253	247		
Units: events	4	44		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to Week 24

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Alitretinoin Capsules 30 mg Per Capsule

Reporting group description:

1 capsule per day for up to 24 weeks

Toctino: 1 capsule Toctino 30 mg per day; optional reduction to 10 mg per day in case unacceptable adverse reactions to the higher dose occur

Reporting group title	Delgocitinib Cream 20 mg/g

Reporting group description:

Twice-daily topical application for up to 24 weeks.

Delgocitinib: Cream for topical application 20 mg/g.

There was a possibility to stop treatment after 12 or 16 weeks if IGA 0/1 was obtained.

Serious adverse events	Alitretinoin Capsules 30 mg Per Capsule	Delgocitinib Cream 20 mg/g	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 247 (4.86%)	5 / 253 (1.98%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood potassium increased			
subjects affected / exposed	0 / 247 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	1 / 247 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	1 / 247 (0.40%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign salivary gland neoplasm			
subjects affected / exposed	1 / 247 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Deep vein thrombosis postoperative			
subjects affected / exposed	1 / 247 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 247 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 247 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal inflammation			
subjects affected / exposed	1 / 247 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 247 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Mediastinal cyst			

subjects affected / exposed	1 / 247 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Hand dermatitis			
subjects affected / exposed	1 / 247 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 247 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 247 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	0 / 247 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis norovirus			
subjects affected / exposed	0 / 247 (0.00%)	1 / 253 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 247 (0.40%)	0 / 253 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Alitretinoin Capsules 30 mg Per Capsule	Delgocitinib Cream 20 mg/g	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	143 / 247 (57.89%)	58 / 253 (22.92%)	
Investigations			
Blood triglycerides increased			
subjects affected / exposed	7 / 247 (2.83%)	2 / 253 (0.79%)	
occurrences (all)	8	2	
Vascular disorders			
Flushing			
subjects affected / exposed	5 / 247 (2.02%)	0 / 253 (0.00%)	
occurrences (all)	6	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 247 (2.43%)	1 / 253 (0.40%)	
occurrences (all)	6	1	
Headache			
subjects affected / exposed	79 / 247 (31.98%)	10 / 253 (3.95%)	
occurrences (all)	113	19	
Migraine			
subjects affected / exposed	6 / 247 (2.43%)	2 / 253 (0.79%)	
occurrences (all)	7	2	
Eye disorders			
Dry eye			
subjects affected / exposed	7 / 247 (2.83%)	0 / 253 (0.00%)	
occurrences (all)	7	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 247 (2.02%)	0 / 253 (0.00%)	
occurrences (all)	5	0	
Lip dry			
subjects affected / exposed	8 / 247 (3.24%)	0 / 253 (0.00%)	
occurrences (all)	8	0	
Nausea			
subjects affected / exposed	14 / 247 (5.67%)	1 / 253 (0.40%)	
occurrences (all)	15	1	
Respiratory, thoracic and mediastinal disorders			

Epistaxis			
subjects affected / exposed	5 / 247 (2.02%)	1 / 253 (0.40%)	
occurrences (all)	6	1	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	5 / 247 (2.02%)	1 / 253 (0.40%)	
occurrences (all)	5	1	
Eczema			
subjects affected / exposed	5 / 247 (2.02%)	2 / 253 (0.79%)	
occurrences (all)	6	2	
Erythema			
subjects affected / exposed	9 / 247 (3.64%)	1 / 253 (0.40%)	
occurrences (all)	10	1	
Dry skin			
subjects affected / exposed	9 / 247 (3.64%)	3 / 253 (1.19%)	
occurrences (all)	9	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 247 (2.43%)	2 / 253 (0.79%)	
occurrences (all)	6	2	
Infections and infestations			
COVID-19			
subjects affected / exposed	9 / 247 (3.64%)	5 / 253 (1.98%)	
occurrences (all)	9	5	
Nasopharyngitis			
subjects affected / exposed	34 / 247 (13.77%)	30 / 253 (11.86%)	
occurrences (all)	46	38	
Upper respiratory tract infection			
subjects affected / exposed	8 / 247 (3.24%)	6 / 253 (2.37%)	
occurrences (all)	8	8	
Urinary tract infection			
subjects affected / exposed	10 / 247 (4.05%)	1 / 253 (0.40%)	
occurrences (all)	11	1	
Metabolism and nutrition disorders			
Hypercholesterolaemia			

subjects affected / exposed	9 / 247 (3.64%)	0 / 253 (0.00%)	
occurrences (all)	10	0	
Hypertriglyceridaemia			
subjects affected / exposed	6 / 247 (2.43%)	3 / 253 (1.19%)	
occurrences (all)	7	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2022	The protocol was amended in order to implement changes from local amendments (UK and Canada).
24 June 2022	The protocol was amended in order to add the patient reported outcomes PGI-S and PGI-C.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported