Clinical trial results:
A phase 3 clinical trial to confirm efficacy and evaluate safety of twice-daily delgocitinib cream 20 mg/g compared with cream vehicle for a 16-week treatment period in adult subjects with moderate to severe chronic hand eczema (DELTA 2)

Summary

EudraCT number	2020-002961-32
Trial protocol	NL DK BE PL ES
Global end of trial date	06 January 2023

Results information

Result version number	v2 (current)
This version publication date	29 September 2024
First version publication date	18 January 2024
Version creation reason	• Correction of full data set Correction of data

Trial information

Trial identification

Sponsor protocol code	LP0133-1402

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	25 January 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 December 2022
Global end of trial reached?	Yes
Global end of trial date	06 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm the efficacy of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle in the treatment of adult subjects with moderate to severe chronic hand eczema (CHE).

Protection of trial subjects:

This clinical trial was conducted to conform to the principles of the Declaration of Helsinki, the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, in compliance with the approved protocol, and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 May 2021
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	Canada: 97
Country: Number of subjects enrolled	Netherlands: 24
Country: Number of subjects enrolled	Poland: 96
Country: Number of subjects enrolled	Spain: 65
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	Denmark: 22
Country: Number of subjects enrolled	Germany: 147
Worldwide total number of subjects	473
EEA total number of subjects	376

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)	436
From 65 to 84 years	36
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

473 participants from 49 sites in 7 countries (Belgium, Canada, Denmark, Germany, the Netherlands, Poland, and Spain) were randomised in this trial. The first participant was screened on 25-May-2021 and the last participant completed the trial on 06-Jan-2023.

Pre-assignment

Screening details:

557 participants were screened in this trial. Of these, 84 participants (15.1%) were excluded prior to randomisation. The main reason for exclusion prior to randomisation was screening failure (12.4%).

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, Assessor

Blinding implementation details:

This was a double-blind trial. The packaging and labelling of the IMPs contained no evidence of their identity. It was not considered possible to differentiate between the IMPs solely by sensory evaluation.

Arms

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

Arm description: -

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

Dosage and administration details:

A thin layer covering the affected areas twice daily for 16 weeks. The applications were to be performed approximately 12 hours apart to clean and dry skin of the affected areas of the hands and wrists.

Arm title	Cream vehicle

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Cream vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

A thin layer covering the affected areas twice daily for 16 weeks. The applications were to be performed approximately 12 hours apart to clean and dry skin of the affected areas of the hands and wrists.

Number of subjects in period 1	Delgocitinib cream 20 mg/g	Cream vehicle
Started	314	159
Completed	291	122
Not completed	23	37
Consent withdrawn by subject	10	16
Adverse event, non-fatal	1	6
Other	1	-
Pregnancy	2	-
Lost to follow-up	2	1
Not dosed	1	-
Lack of efficacy	6	14

Baseline characteristics

Reporting groups	
Reporting group title	Delgocitinib cream 20 mg/g
Reporting group description: -	
Reporting group title	Cream vehicle
Reporting group description: -	

Reporting group values	Delgocitinib cream 20 mg/g	Cream vehicle	Total
Number of subjects	314	159	473
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	286	150	436
From 65-84 years	28	8	36
85 years and over	0	1	1
Age continuous Units: years			
arithmetic mean	45.3	42.6	
standard deviation	± 14.6	± 14.3	-
Gender categorical Units: Subjects			
Female	204	108	312
Male	110	51	161
Baseline IGA-CHE score			
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).			
Units: Subjects			
0 - Clear	0	0	0
1 - Almost clear	0	0	0
2 - Mild	0	0	0
3 - Moderate	239	121	360
4 - Severe	75	38	113
Ethnicity Units: Subjects			
Hispanic or Latino	2	5	7
Not Hispanic or Latino	310	152	462
Unknown or Not Reported	2	2	4
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	8	7	15

Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	2	1	3
White	295	146	441
More than one race	1	3	4
Unknown or Not Reported	7	2	9

Baseline HECSI score			

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), with a higher score indicating greater severity.

Data not available for 1 participant in the delgocitinib cream 20 mg/g group.

Units: Units on a scale			
arithmetic mean	64.3	67.7	
standard deviation	± 37.9	± 39.5	-

Baseline HESD pain score (weekly average)			

The Hand Eczema Symptom Diary (HESD) pain score is one component of the HESD eDiary. In the HESD eDiary, 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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis.

Data not available for 2 participants each in the delgocitinib cream 20 mg/g group and in the cream vehicle group.

Units: units on a scale			
arithmetic mean	6.62	6.46	
standard deviation	± 1.81	± 1.96	-

Baseline HESD score (weekly average)			

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. The HESD score is derived as the average of the 6 signs and symptoms.

Data not available for 2 participants each in the delgocitinib cream 20 mg/g group and in the cream vehicle group.

Units: units on a scale			
arithmetic mean	6.97	6.91	
standard deviation	± 1.46	± 1.51	-

Baseline DLQI score			

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); a high score is indicative of a poor quality of life.

Data not available for 4 participants in the delgocitinib cream 20 mg/g group.

Units: units on a scale			
arithmetic mean	12.1	12.2	
standard deviation	± 6.2	± 6.6	-

Baseline HEIS score			

The Hand Eczema Impact Scale (HEIS) addresses 9 items within the following domains: Proximal Daily Activity Limitations (PDAL), embarrassment with the appearance of the hands, frustration with CHE, sleep, work, and physical functioning. Each item is scored on a 5-point scale ranging from 0 (not at all) to 4 (extremely). The HEIS score is the average of the 9 items.

Data not available for 4 participants in the delgocitinib cream 20 mg/g group.

Units: units on a scale			
arithmetic mean	2.42	2.46	
standard deviation	± 0.79	± 0.84	-

Baseline HEIS PDAL score			
Proximal Daily Activity Limitations (PDAL) is one of the domain scores in Hand Eczema Impact Scale (HEIS) assessing the participant's perceived impact on their daily activities. Each item is scored on a 5-point scale ranging from 0 (not at all) to 4 (extremely). HEIS PDAL score is the average of the 3 items. Data not available for 4 participants in the delgocitinib cream 20 mg/g group.			
Units: units on a scale			
arithmetic mean	2.54	2.56	
standard deviation	± 0.90	± 0.94	-
Baseline HESD itch score (weekly average)			
The Hand Eczema Symptom Diary (HESD) itch score is one component of the HESD eDiary. In the HESD eDiary, 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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. Data not available for 2 participants each in the delgocitinib cream 20 mg/g group and in the cream vehicle group.			
Units: units on a scale			
arithmetic mean	6.99	6.98	
standard deviation	± 1.55	± 1.51	-

End points

End points reporting groups

Reporting group title	Delgocitinib cream 20 mg/g
Reporting group description: -	
Reporting group title	Cream vehicle
Reporting group description: -	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All participants randomized and exposed to IMP.	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All participants exposed to IMP.	

Primary: Investigator’s Global Assessment for chronic hand eczema (IGA-CHE) score of 0 (clear) or 1 (almost clear) with at least a 2-step improvement from baseline (IGA-CHE treatment success [IGA-CHE TS]) at Week 16

End point title	Investigator’s Global Assessment for chronic hand eczema (IGA-CHE) score of 0 (clear) or 1 (almost clear) with at least a 2-step improvement from baseline (IGA-CHE treatment success [IGA-CHE TS]) at Week 16
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	Primary
End point timeframe:	
Week 0 to Week 16	

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313[1]	159		
Units: Participants with IGA-CHE TS	91	11		

Notes:

[1] - Data is not available for 1 participant in the Delgocitinib cream 20 mg/g group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle
Statistical analysis description:	
Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.	
Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle

Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	22.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.8
upper limit	28.5

Notes:

[2] - 5% significance level (two-sided).

Secondary: IGA-CHE TS at Week 8

End point title	IGA-CHE TS at Week 8

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 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:

Week 0 to Week 8

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313[3]	159		
Units: Participants with IGA-CHE TS	101	15		

Notes:

[3] - Data is not available for 1 participant in the Delgocitinib cream 20 mg/g group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	22.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	16
upper limit	29.8

Notes:

[4] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: IGA-CHE TS at Week 4

End point title	IGA-CHE TS at Week 4

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 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:

Week 0 to Week 4

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313[5]	159		
Units: Participants with IGA-CHE TS	46	13		

Notes:

[5] - Data is not available for 1 participant in the Delgocitinib cream 20 mg/g group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.043 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	12.3

Notes:

[6] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: At least 75% improvement in Hand Eczema Severity Index (HECSI) score from baseline (HECSI-75) at Week 16.

End point title	At least 75% improvement in Hand Eczema Severity Index (HECSI) score from baseline (HECSI-75) at Week 16.

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), with a higher score indicating greater severity. HECSI-75 is defined as at least 75% improvement in HECSI score from baseline.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313[7]	159		
Units: Participants with HECSI-75	155	29		

Notes:

[7] - Data is not available for 1 participant in the Delgocitinib cream 20 mg/g group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	31.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.1
upper limit	39.5

Notes:

[8] - Evaluated at 1% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: HECSI-75 at Week 8.

End point title	HECSI-75 at Week 8.

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), with a higher score indicating greater severity. HECSI-75 is defined as at least 75% improvement in HECSI score from baseline.

End point type	Secondary

End point timeframe:

Week 0 to Week 8

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313[9]	159		
Units: Participants with HECSI-75	158	31		

Notes:

[9] - Data is not available for 1 participant in the Delgocitinib cream 20 mg/g group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	31
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.7
upper limit	39.3

Notes:

[10] - Evaluated at 1% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: At least 90% improvement in HECSI score from baseline (HECSI-90) at Week 16.

End point title	At least 90% improvement in HECSI score from baseline (HECSI-90) at Week 16.

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), with a higher score indicating greater severity. HECSI-90 is defined as at least 90% improvement in HECSI score from baseline.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313[11]	159		
Units: Participants with HECSI-90	97	14		

Notes:

[11] - Data is not available for 1 participant in the Delgocitinib cream 20 mg/g group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	22.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.4
upper limit	29

Notes:

[12] - Evaluated at 1% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Percentage change in HECSI score from baseline to Week 16.

End point title	Percentage change in HECSI score from baseline to Week 16.

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), with a higher score indicating greater severity.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313[13]	159		
Units: Percentage change in HECSI score				
least squares mean (standard error)	-58.9 (± 3.2)	-13.4 (± 4.5)		

Notes:

[13] - Data is not available for 1 participant in the Delgocitinib cream 20 mg/g group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Primary analysis of primary estimand 'composite'. Missing data for subjects who did not attend the visit was imputed as WOCF (including baseline value). For subjects who received rescue treatment or subjects who have permanently discontinued the IMP, observed data was considered non-response by using WOCF (including baseline value).

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [14]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-45.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-56.4
upper limit	-34.6

Notes:

[14] - Evaluated at 1% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Reduction of Hand Eczema Symptom Diary (HESD) itch score (weekly average) of ≥4 points from baseline at Week 16.

End point title	Reduction of Hand Eczema Symptom Diary (HESD) itch score (weekly average) of ≥4 points from baseline at Week 16.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. This endpoint will only assess the 'itch' component and will be evaluated among participants with a baseline HESD itch score (weekly average) ≥4 points.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309[15]	156[16]		
Units: Participants with ≥4 points reduction	146	31		

Notes:

[15] - Data is not available for 5 participants in the Delgocitinib cream 20 mg/g group

[16] - Data is not available for 3 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Cream vehicle v Delgocitinib cream 20 mg/g
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [17]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	27.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	19
upper limit	35.8

Notes:

[17] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Reduction of HESD itch score (weekly average) of ≥4 points from baseline at Week 8.

End point title	Reduction of HESD itch score (weekly average) of ≥4 points from baseline at Week 8.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. This endpoint will only assess the 'itch' component and will be evaluated among participants with a baseline HESD itch score (weekly average) ≥4 points.

End point type	Secondary

End point timeframe:

Week 0 to Week 8

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309[18]	156[19]		
Units: Participants with ≥4 points reduction	131	21		

Notes:

[18] - Data is not available for 5 participants in the Delgocitinib cream 20 mg/g group

[19] - Data is not available for 3 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [20]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.3
upper limit	36.7

Notes:

[20] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Reduction of HESD itch score (weekly average) of ≥4 points from baseline at Week 4.

End point title	Reduction of HESD itch score (weekly average) of ≥4 points from baseline at Week 4.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. This endpoint will only assess the 'itch' component and will be evaluated among participants with a baseline HESD itch score (weekly average) ≥4 points.

End point type	Secondary

End point timeframe:

Week 0 to Week 4

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309[21]	156[22]		
Units: Participants with ≥4 points reduction	94	19		

Notes:

[21] - Data is not available for 5 participants in the Delgocitinib cream 20 mg/g group

[22] - Data is not available for 3 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [23]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	18.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	11
upper limit	25.6

Notes:

[23] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Reduction of HESD itch score (weekly average) of ≥4 points from baseline at Week 2.

End point title	Reduction of HESD itch score (weekly average) of ≥4 points from baseline at Week 2.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. This endpoint will only assess the 'itch' component and will be evaluated among participants with a baseline HESD itch score (weekly average) ≥4 points.

End point type	Secondary

End point timeframe:

Week 0 to Week 2

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309[24]	156[25]		
Units: Participants with ≥4 points reduction	40	10		

Notes:

[24] - Data is not available for 5 participants in the Delgocitinib cream 20 mg/g group

[25] - Data is not available for 3 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031 [26]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	12

Notes:

[26] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Change in HESD itch score (weekly average) from baseline to Week 16.

End point title	Change in HESD itch score (weekly average) from baseline to Week 16.

End point description:

HESD is a 6-item PRO instrument designed to assess severity of CHE signs and symptoms. Participants assess the worst severity of 6 individual signs and symptoms of CHE over the past 24 hours using an 11-point numeric rating scale with anchors of 0 =‘no (symptom)’ and 10 =‘severe (symptom)’. The HESD score is derived as an average of the 6 items.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312	157		
Units: Change in HESD itch score				
least squares mean (standard error)	-3.4 (± 0.2)	-1.4 (± 0.2)		

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Primary analysis of primary estimand 'composite'. The percentage change from baseline was analysed using an ANCOVA model with effects of treatment group, region, baseline IGA-CHE score, and baseline HESD itch value. Missing data for subjects who did not attend the visit was imputed as WOCF (including baseline value). For subjects who received rescue treatment or subjects who have permanently discontinued the IMP, observed data was considered non-response by using WOCF (including baseline value)

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	469
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [27]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-1.4

Notes:

[27] - Evaluated at 1% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Reduction of HESD score (weekly average) of ≥4 points from baseline at Week 16.

End point title	Reduction of HESD score (weekly average) of ≥4 points from baseline at Week 16.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. The HESD score is derived as the average of the 6 signs and symptoms. This endpoint will be evaluated among participants with a baseline HESD score (weekly average) ≥4 points.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	308[28]	153[29]		
Units: Participants with ≥4 points reduction	137	32		

Notes:

[28] - Data is not available for 6 participants in the Delgocitinib cream 20 mg/g group

[29] - Data is not available for 6 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [30]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	23.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.1
upper limit	32.2

Notes:

[30] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Reduction of HESD score (weekly average) of ≥4 points from baseline at Week 8.

End point title	Reduction of HESD score (weekly average) of ≥4 points from baseline at Week 8.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. The HESD score is derived as the average of the 6 signs and symptoms. This endpoint will be evaluated among participants with a baseline HESD score (weekly average) ≥4 points.

End point type	Secondary

End point timeframe:

Week 0 to Week 8

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	308[31]	153[32]		
Units: Participants with ≥4 points reduction	115	19		

Notes:

[31] - Data is not available for 6 participants in the Delgocitinib cream 20 mg/g group

[32] - Data is not available for 6 participants in the cream vehicle group

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [33]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	25
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.5
upper limit	32.5

Notes:

[33] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Reduction of HESD score (weekly average) of ≥4 points from baseline at Week 4.

End point title	Reduction of HESD score (weekly average) of ≥4 points from baseline at Week 4.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. The HESD score is derived as the average of the 6 signs and symptoms. This endpoint will be evaluated among participants with a baseline HESD score (weekly average) ≥4 points.

End point type	Secondary

End point timeframe:

Week 0 to Week 4

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	308[34]	153[35]		
Units: Participants with ≥4 points reduction	80	14		

Notes:

[34] - Data is not available for 6 participants in the Delgocitinib cream 20 mg/g group

[35] - Data is not available for 6 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [36]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	16.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.2
upper limit	23.7

Notes:

[36] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Change in HESD score (weekly average) from baseline to Week 16.

End point title	Change in HESD score (weekly average) from baseline to Week 16.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. The HESD score is derived as the average of the 6 signs and symptoms.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312[37]	157[38]		
Units: Change in HESD score				
least squares mean (standard error)	-3.2 (± 0.1)	-1.4 (± 0.2)		

Notes:

[37] - Data is not available for 2 participants in the Delgocitinib cream 20 mg/g group

[38] - Data is not available for 2 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Primary analysis of primary estimand 'composite'. Missing data for subjects who did not attend the visit was imputed as WOCF (including baseline value). For subjects who received rescue treatment or subjects who have permanently discontinued the IMP, observed data was considered non-response by using WOCF (including baseline value).

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	469
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [39]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-1.4

Notes:

[39] - Evaluated at 1% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Reduction of HESD pain score (weekly average) of ≥4 points from baseline at Week 16.

End point title	Reduction of HESD pain score (weekly average) of ≥4 points from baseline at Week 16.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. This endpoint will only assess the 'pain' component and will be evaluated among participants with a baseline HESD pain score (weekly average) ≥4 points.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[40]	141[41]		
Units: Participants with ≥4 points reduction	143	32		

Notes:

[40] - Data is not available for 20 participants in the Delgocitinib cream 20 mg/g group

[41] - Data is not available for 18 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	435
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [42]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	26
Confidence interval	
level	95 %
sides	2-sided
lower limit	17
upper limit	35.1

Notes:

[42] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Reduction of HESD pain score (weekly average) of ≥4 points from baseline at Week 8.

End point title	Reduction of HESD pain score (weekly average) of ≥4 points from baseline at Week 8.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. This endpoint will only assess the 'pain' component and will be evaluated among participants with a baseline HESD pain score (weekly average) ≥4 points.

End point type	Secondary

End point timeframe:

Week 0 to Week 8

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[43]	141[44]		
Units: Participants with ≥4 points reduction	124	18		

Notes:

[43] - Data is not available for 20 participants in the Delgocitinib cream 20 mg/g group

[44] - Data is not available for 18 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	435
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [45]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.7
upper limit	37.4

Notes:

[45] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Reduction of HESD pain score (weekly average) of ≥4 points from baseline at Week 4.

End point title	Reduction of HESD pain score (weekly average) of ≥4 points from baseline at Week 4.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. This endpoint will only assess the 'pain' component and will be evaluated among participants with a baseline HESD pain score (weekly average) ≥4 points.

End point type	Secondary

End point timeframe:

Week 0 to Week 4

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294[46]	141[47]		
Units: Participants with ≥4 points reduction	91	15		

Notes:

[46] - Data is not available for 20 participants in the Delgocitinib cream 20 mg/g group

[47] - Data is not available for 18 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	435
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [48]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	20.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.1
upper limit	27.8

Notes:

[48] - Evaluated at 5% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Change in HESD pain score (weekly average) from baseline to Week 16.

End point title	Change in HESD pain score (weekly average) from baseline to Week 16.

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 with anchors of 0 ='no (symptom)' and 10 ='severe (symptom)' throughout the trial on a daily basis. This endpoint will only assess the 'pain' component.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312[49]	157[50]		
Units: Change in HESD pain score				
least squares mean (standard error)	-3.3 (± 0.2)	-1.3 (± 0.2)		

Notes:

[49] - Data is not available for 2 participants in the Delgocitinib cream 20 mg/g group

[50] - Data is not available for 2 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Primary analysis of primary estimand 'composite'. Missing data for subjects who did not attend the visit was imputed as WOCF (including baseline value). For subjects who received rescue treatment or subjects who have permanently discontinued the IMP, observed data was considered non-response by using WOCF (including baseline value).

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	469
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [51]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	-1.5

Notes:

[51] - Evaluated at 1% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Reduction of Dermatology Life Quality Index (DLQI) score of ≥4 points from baseline at Week 16.

End point title	Reduction of Dermatology Life Quality Index (DLQI) score of ≥4 points from baseline at Week 16.

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); a high score is indicative of a poor quality of life. This endpoint will be evaluated among participants with a baseline DLQI score ≥4 points..

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299[52]	153[53]		
Units: Participants with ≥4 points reduction	216	70		

Notes:

[52] - Data is not available for 15 participants in the Delgocitinib cream 20 mg/g group

[53] - Data is not available for 6 participants in the cream vehicle group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Based on the primary analysis of the primary estimand 'composite'. Subjects with missing data, subjects who received rescue treatment, or subjects who permanently discontinued IMP were considered non-responders.

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [54]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	26.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	17
upper limit	35.9

Notes:

[54] - Evaluated at 1% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Change in DLQI score from baseline to Week 16.

End point title	Change in DLQI score from baseline to Week 16.

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); a high score is indicative of a poor quality of life.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310[55]	159		
Units: Change in DLQI score				
least squares mean (standard error)	-7.0 (± 0.3)	-3.1 (± 0.5)		

Notes:

[55] - Data is not available for 4 participants in the Delgocitinib cream 20 mg/g group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Primary analysis of primary estimand 'composite'. Missing data for subjects who did not attend the visit was imputed as WOCF (including baseline value). For subjects who received rescue treatment or subjects who have permanently discontinued the IMP, observed data was considered non-response by using WOCF (including baseline value).

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	469
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [56]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	-2.8

Notes:

[56] - Evaluated at 1% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Change in Hand Eczema Impact Scale (HEIS) score from baseline to Week 16.

End point title	Change in Hand Eczema Impact Scale (HEIS) score from baseline to Week 16.

End point description:

The Hand Eczema Impact Scale (HEIS) addresses 9 items within the following domains: Proximal Daily Activity Limitations (PDAL), embarrassment with the appearance of the hands, frustration with CHE, sleep, work, and physical functioning. Each item is scored on a 5-point scale ranging from 0 (not at all) to 4 (extremely). The HEIS score is the average of the 9 items.

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310[57]	159		
Units: Change in HEIS score				
least squares mean (standard error)	-1.45 (± 0.06)	-0.64 (± 0.08)		

Notes:

[57] - Data is not available for 4 participants in the Delgocitinib cream 20 mg/g group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Primary analysis of primary estimand 'composite'. Missing data for subjects who did not attend the visit was imputed as WOCF (including baseline value). For subjects who received rescue treatment or subjects who have permanently discontinued the IMP, observed data was considered non-response by using WOCF (including baseline value).

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	469
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [58]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	-0.62

Notes:

[58] - Evaluated at 1% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Change in HEIS PDAL score from baseline to Week 16.

End point title	Change in HEIS PDAL score from baseline to Week 16.

End point description:

Proximal Daily Activity Limitations (PDAL) is one of the items addressed in the Hand Eczema Impact Scale (HEIS) and is scored on a 5-point scale ranging from 0 (not at all) to 4 (extremely).

End point type	Secondary

End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310[59]	159		
Units: Change in HEIS PDAL score				
least squares mean (standard error)	-1.48 (± 0.06)	-0.66 (± 0.08)		

Notes:

[59] - Data is not available for 4 participants in the Delgocitinib cream 20 mg/g group.

Statistical analyses

Statistical analysis title	Delgocitinib cream 20 mg/g vs. cream vehicle

Statistical analysis description:

Primary analysis of primary estimand 'composite'. Missing data for subjects who did not attend the visit was imputed as WOCF (including baseline value). For subjects who received rescue treatment or subjects who have permanently discontinued the IMP, observed data was considered non-response by using WOCF (including baseline value).

Comparison groups	Delgocitinib cream 20 mg/g v Cream vehicle
Number of subjects included in analysis	469
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [60]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.01
upper limit	-0.62

Notes:

[60] - Evaluated at 1% significance level (two-sided) and significant as per testing hierarchy using hierarchical tests, alpha splitting and alpha recycling controlling overall type 1 error at 5% (two-sided).

Secondary: Number of treatment-emergent AEs from baseline up to Week 16. (Week 18 for subjects not participating in the LTE trial) per subject

End point title	Number of treatment-emergent AEs from baseline up to Week 16. (Week 18 for subjects not participating in the LTE trial) per subject

End point description:

An adverse event (AE) were 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 of trial was defined as Week 16 for participants who rolled over to the long-term extension trial and as Week 18 for participants who did not roll over.

End point type	Secondary

End point timeframe:

16 weeks (18 weeks for participants not participating in the long-term extension trial [LP0133-1403])

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313[61]	159		
Units: Adverse events	269	145		

Notes:

[61] - Data is not available for 1 participant in the Delgocitinib cream 20 mg/g group.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
16 weeks	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0
Reporting groups	
Reporting group title	Delgocitinib cream 20 mg/g
Reporting group description: -	
Reporting group title	Cream vehicle
Reporting group description: -	

Serious adverse events	Delgocitinib cream 20 mg/g	Cream vehicle	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 313 (1.60%)	3 / 159 (1.89%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Cardiac tamponade			
subjects affected / exposed	0 / 313 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 313 (0.32%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 313 (0.32%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Notalgia paraesthetica			

subjects affected / exposed	0 / 313 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	0 / 313 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Hand dermatitis			
subjects affected / exposed	1 / 313 (0.32%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 313 (0.32%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	1 / 313 (0.32%)	0 / 159 (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	Delgocitinib cream 20 mg/g	Cream vehicle	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 313 (22.36%)	43 / 159 (27.04%)	
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 313 (6.07%)	9 / 159 (5.66%)	
occurrences (all)	25	11	
Skin and subcutaneous tissue disorders			
Hand dermatitis			

subjects affected / exposed	2 / 313 (0.64%)	5 / 159 (3.14%)	
occurrences (all)	2	5	
Infections and infestations			
COVID-19			
subjects affected / exposed	36 / 313 (11.50%)	20 / 159 (12.58%)	
occurrences (all)	36	20	
Nasopharyngitis			
subjects affected / exposed	21 / 313 (6.71%)	10 / 159 (6.29%)	
occurrences (all)	24	10	
Pharyngitis			
subjects affected / exposed	3 / 313 (0.96%)	5 / 159 (3.14%)	
occurrences (all)	3	6	
Herpes simplex			
subjects affected / exposed	1 / 313 (0.32%)	4 / 159 (2.52%)	
occurrences (all)	1	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 August 2021	This amendment was written to comply with requests from health authorities and to proceed with administrative and editorial changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported