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 1)

Summary

EudraCT number	2020-002960-30
Trial protocol	FR PL IT
Global end of trial date	31 October 2022

Results information

Result version number	v1 (current)
This version publication date	15 November 2023
First version publication date	15 November 2023

Trial information

Trial identification

Sponsor protocol code	LP0133-1401

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	17 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2022
Global end of trial reached?	Yes
Global end of trial date	31 October 2022
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	10 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	Poland: 105
Country: Number of subjects enrolled	France: 81
Country: Number of subjects enrolled	Germany: 135
Country: Number of subjects enrolled	Italy: 45
Country: Number of subjects enrolled	Canada: 97
Country: Number of subjects enrolled	United Kingdom: 24
Worldwide total number of subjects	487
EEA total number of subjects	366

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)	451
From 65 to 84 years	35
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

487 participants from 51 sites in 6 countries (Canada, France, Germany, Italy, Poland, and United Kingdom) were randomised in this trial. The first participant was screened on 10-May-2021 and the last participant completed the trial on 31-Oct-2022.

Pre-assignment

Screening details:

566 participants were screened in this trial. Of these, 79 participants (14.0%) were excluded prior to randomisation. The main reason for exclusion prior to randomisation was screening failure (11.1%).

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	325	162
Completed	305	141
Not completed	20	21
Consent withdrawn by subject	11	5
Adverse event, non-fatal	2	6
Other	2	1
Lost to follow-up	-	2
Lack of efficacy	5	7

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	325	162	487
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)	297	154	451
From 65-84 years	27	8	35
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	44.3	42.9	
standard deviation	± 14.3	± 14.1	-
Gender categorical Units: Subjects			
Female	202	104	306
Male	123	58	181
Baseline IGA-CHE score Units: Subjects			
0 - Clear	0	0	0
1 - Almost clear	0	0	0
2 - Mild	0	0	0
3 - Moderate	218	109	327
4 - Severe	107	53	160
Baseline HECSI score Units: Units on a scale			
arithmetic mean	77.6	77.3	
standard deviation	± 46.4	± 53.6	-

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: -	

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:

IGA-CHE rates the severity of the participant's global disease and is based on a 5-point scale ranging from 0 (clear) to 4 (severe).

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	325	162		
Units: Participants with IGA-CHE TS	64	16		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	487
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	9.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.6
upper limit	16.1

Notes:

[1] - 5% significance level (two-sided).

Secondary: IGA-CHE TS at Week 8.

End point title	IGA-CHE TS at Week 8.

End point description:

IGA-CHE rates the severity of the participant's global disease and is based on a 5-point scale ranging from 0 (clear) to 4 (severe).

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	325	162		
Units: Participants with IGA-CHE TS	74	17		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	487
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	12.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.7
upper limit	18.9

Notes:

[2] - Evaluated at 4% 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:

IGA-CHE rates the severity of the participant's global disease and is based on a 5-point scale ranging from 0 (clear) to 4 (severe).

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	325	162		
Units: Participants with IGA-CHE TS	50	8		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	487
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	10.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.3
upper limit	15.6

Notes:

[3] - Evaluated at 4% 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:

HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The total HECSI score is based on a 4-point severity scale ranging from 0 (none/absent) to 3 (severe) and a 5-point scale rating the affected area(s) ranging from 0 (0% affected area) to 4 (76% to 100% affected area). The highest possible HECSI score is 360.

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	325	162		
Units: Participants with HECSI-75	160	38		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	487
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	25.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.2
upper limit	34.3

Notes:

[4] - 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:

HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The total HECSI score is based on a 4-point severity scale ranging from 0 (none/absent) to 3 (severe) and a 5-point scale rating the affected area(s) ranging from 0 (0% affected area) to 4 (76% to 100% affected area). The highest possible HECSI score is 360.

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	325	162		
Units: Participants with HECSI-75	163	42		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	487
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	24.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.5
upper limit	33

Notes:

[5] - 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:

HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The total HECSI score is based on a 4-point severity scale ranging from 0 (none/absent) to 3 (severe) and a 5-point scale rating the affected area(s) ranging from 0 (0% affected area) to 4 (76% to 100% affected area). The highest possible HECSI score is 360.

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	325	162		
Units: Participants with HECSI-90	96	20		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	487
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.1
upper limit	24.3

Notes:

[6] - 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:

HECSI is an instrument used in clinical trials to rate the severity of 6 clinical signs of hand eczema and the extent of the lesions on each of 5 hand areas by use of standard scales. The total HECSI score is based on a 4-point severity scale ranging from 0 (none/absent) to 3 (severe) and a 5-point scale rating the affected area(s) ranging from 0 (0% affected area) to 4 (76% to 100% affected area). The highest possible HECSI score is 360.

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	325	162		
Units: Percentage change in HECSI score				
least squares mean (standard error)	-56.5 (± 3.4)	-21.2 (± 4.8)		

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 HESCI 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	487
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [7]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-35.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.7
upper limit	-23.8

Notes:

[7] - 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:

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	323	161		
Units: Participants with ≥4 points reduction	152	37		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	484
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	24.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.5
upper limit	32.6

Notes:

[8] - 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:

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 8

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	323	161		
Units: Participants with ≥4 points reduction	138	35		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	484
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	21
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.6
upper limit	29.4

Notes:

[9] - Evaluated at 4% 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:

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 4

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	323	161		
Units: Participants with ≥4 points reduction	99	18		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	484
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	19.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.5
upper limit	26.5

Notes:

[10] - Evaluated at 4% 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:

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 2

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	323	161		
Units: Participants with ≥4 points reduction	50	10		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	484
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	9.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.8
upper limit	14.7

Notes:

[11] - Evaluated at 4% 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	324	162		
Units: Change in HESD itch score				
least squares mean (standard error)	-3.6 (± 0.2)	-1.9 (± 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	486
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [12]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-1.2

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: 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:

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	309	156		
Units: Participants with ≥4 points reduction	146	38		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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 [13]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	22.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	14
upper limit	31.7

Notes:

[13] - 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:

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 8

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	156		
Units: Participants with ≥4 points reduction	123	27		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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 [14]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	22.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.4
upper limit	30.6

Notes:

[14] - Evaluated at 4% 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:

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 4

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	156		
Units: Participants with ≥4 points reduction	92	16		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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 [15]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	19.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.5
upper limit	26.5

Notes:

[15] - Evaluated at 4% 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:

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	324	162		
Units: Change in HESD score				
least squares mean (standard error)	-3.4 (± 0.1)	-1.7 (± 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 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	486
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [16]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-1.2

Notes:

[16] - 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:

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	291	149		
Units: Participants with ≥4 points reduction	143	41		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	440
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [17]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	21.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.4
upper limit	30.9

Notes:

[17] - Evaluated at 4% 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:

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 8

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	291	149		
Units: Participants with ≥4 points reduction	134	33		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	440
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [18]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	23.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.2
upper limit	32.7

Notes:

[18] - Evaluated at 4% 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:

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 4

End point values	Delgocitinib cream 20 mg/g	Cream vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	291	149		
Units: Participants with ≥4 points reduction	100	22		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	440
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [19]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	19.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.8
upper limit	27.5

Notes:

[19] - Evaluated at 4% 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:

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	324	162		
Units: Change in HESD pain score				
least squares mean (standard error)	-3.4 (± 0.2)	-1.8 (± 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 pain 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	486
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [20]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	-1

Notes:

[20] - 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:

DLQI is a validated questionnaire with content specific to those with dermatologic conditions. It consists 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. Each item is scored on a 4-point Likert scale ranging from 0 = 'not at all /not relevant' to 3 = 'very much'. 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	305	148		
Units: Participants with ≥4 points reduction	227	74		

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'. The difference in response rates between delgocitinib cream 20 mg/g and cream vehicle was analysed using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). 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	453
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [21]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	24.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	15
upper limit	33.9

Notes:

[21] - 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:

DLQI is a validated questionnaire with content specific to those with dermatologic conditions. It consists 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. Each item is scored on a 4-point Likert scale ranging from 0 = ‘not at all /not relevant’ to 3 = ‘very much’. 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	321	158		
Units: Change in DLQI score				
least squares mean (standard error)	-7.6 (± 0.3)	-3.9 (± 0.4)		

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 DLQI 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	479
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [22]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	-2.6

Notes:

[22] - 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:

HEIS includes 9 items addressing the participant’s perception of the impact of hand eczema on their daily activities, embarrassment, frustration, sleep, work, and physical functioning over the past 7 days. 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. The highest possible score is 4, and a high score is indicative of a high impact. 6 domain scores can be calculated for HEIS: Proximal Daily Activity Limitations (PDAL) (average of 3 items), embarrassment with the appearance of the hands (average of 2 items), frustration with CHE (1 item), sleep (1 item), work (1 item), and physical functioning (1 item).

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	321	158		
Units: Change in HEIS score				
least squares mean (standard error)	-1.46 (± 0.05)	-0.82 (± 0.08)		

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 HEIS 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	479
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [23]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.83
upper limit	-0.45

Notes:

[23] - 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:

HEIS includes 9 items addressing the participant’s perception of the impact of hand eczema on their daily activities, embarrassment, frustration, sleep, work, and physical functioning over the past 7 days. 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. The highest possible score is 4, and a high score is indicative of a high impact. 6 domain scores can be calculated for HEIS: Proximal Daily Activity Limitations (PDAL) (average of 3 items), embarrassment with the appearance of the hands (average of 2 items), frustration with CHE (1 item), sleep (1 item), work (1 item), and physical functioning (1 item).

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	321	158		
Units: Change in HEIS PDAL score				
least squares mean (standard error)	-1.46 (± 0.06)	-0.86 (± 0.08)		

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 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	479
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [24]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	-0.4

Notes:

[24] - 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).

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Week 0 to Week 16	
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	6 / 325 (1.85%)	3 / 162 (1.85%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gallbladder adenocarcinoma			
subjects affected / exposed	1 / 325 (0.31%)	0 / 162 (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			
Post procedural haemorrhage			
subjects affected / exposed	1 / 325 (0.31%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 325 (0.00%)	1 / 162 (0.62%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Generalised tonic-clonic seizure			

subjects affected / exposed	1 / 325 (0.31%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	1 / 325 (0.31%)	0 / 162 (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			
Dermatitis atopic			
subjects affected / exposed	0 / 325 (0.00%)	1 / 162 (0.62%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 325 (0.31%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 325 (0.00%)	1 / 162 (0.62%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Keratitis bacterial			
subjects affected / exposed	1 / 325 (0.31%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 325 (0.31%)	0 / 162 (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	69 / 325 (21.23%)	42 / 162 (25.93%)	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	9 / 325 (2.77%) 13	4 / 162 (2.47%) 6	
Immune system disorders Allergy to metals alternative dictionary used: MedDRA 24.0 subjects affected / exposed occurrences (all)	7 / 325 (2.15%) 7	3 / 162 (1.85%) 3	
Skin and subcutaneous tissue disorders Hand dermatitis subjects affected / exposed occurrences (all) Dermatitis contact subjects affected / exposed occurrences (all)	1 / 325 (0.31%) 1 4 / 325 (1.23%) 4	7 / 162 (4.32%) 10 4 / 162 (2.47%) 4	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	35 / 325 (10.77%) 35 23 / 325 (7.08%) 25	14 / 162 (8.64%) 14 14 / 162 (8.64%) 16	

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, to accommodate for the conduct of the trial in Russia, 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