



Clinical trial results:

A phase 2b, double-blind, randomised, 5-arm, vehicle-controlled, dose-ranging trial to evaluate the efficacy and safety of twice daily topical application of delgocitinib cream 1, 3, 8, and 20 mg/g for 16 weeks in adult subjects with mild to severe chronic hand eczema

Summary

EudraCT number	2018-000900-40
Trial protocol	DK
Global end of trial date	20 April 2020

Results information

Result version number	v1 (current)
This version publication date	12 June 2021
First version publication date	12 June 2021

Trial information

Trial identification

Sponsor protocol code	LP0133-1273
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03683719
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, +45 44945888, disclosure@leo-pharma.com
Scientific contact	Clinical Disclosure, LEO Pharma A/S, +45 44945888, 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	14 October 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this research trial was to test different strengths of a new trial medication, delgocitinib cream 1, 3, 8, and 20 mg/g, and to investigate how treatment with delgocitinib cream affects chronic hand eczema. This was judged by a range of assessments that rate the severity and extent of chronic hand eczema and its symptoms, as well as general health status and quality of life.

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	28 November 2018
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	Denmark: 58
Country: Number of subjects enrolled	Germany: 179
Country: Number of subjects enrolled	United States: 21
Worldwide total number of subjects	258
EEA total number of subjects	237

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)	233

From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

258 participants from 26 sites in 3 countries (U.S., Denmark, Germany) were randomised in this trial. The first participant was screened on 28-Nov-2018 and the last participant completed the trial on 20-Apr-2020.

Pre-assignment

Screening details:

305 participants were screened for this trial. Of these, 47 participants (15.4%) were screening failures. The main reason for screening failure was failure to meet eligibility criteria (11.8%). The eligibility criterion most frequently not met was exclusion criterion 21 (positive HBsAg, HBsAb, HBcAb, or antiHCV serology at screening [3.3%]).

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	Investigator, Assessor, Subject

Blinding implementation details:

This was a double-blind study in which it was not possible to differentiate between the IMPs solely by sensory evaluation. Neither the participant nor any of the investigators or LEO Pharma staff involved in the treatment or clinical evaluation and monitoring of the participants were aware of the treatment received. The packaging and labelling of the IMPs contained no evidence of their identity.

Arms

Are arms mutually exclusive?	Yes
Arm title	Delgocitinib cream 1 mg/g

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Delgocitinib cream
Investigational medicinal product code	
Other name	LEO 124249 cream
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Applied twice daily for 16 weeks.

Arm title	Delgocitinib cream 3 mg/g
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Delgocitinib cream
Investigational medicinal product code	
Other name	LEO 124249 cream
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Applied twice daily for 16 weeks.

Arm title	Delgocitinib cream 8 mg/g
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	Delgocitinib cream
Investigational medicinal product code	
Other name	LEO 124249 cream
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Applied twice daily for 16 weeks.

Arm title	Delgocitinib cream 20 mg/g
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Delgocitinib cream
Investigational medicinal product code	
Other name	LEO 124249 cream
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Applied twice daily for 16 weeks.

Arm title	Delgocitinib cream vehicle
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Delgocitinib cream vehicle
Investigational medicinal product code	
Other name	LEO 124249 cream
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Participants applied the investigational medicinal product (delgocitinib cream 1, 3, 8, or 20 mg/g or delgocitinib cream vehicle) as a twice daily cutaneous application for 16 weeks. The applications were performed approximately 12 hours apart.

Number of subjects in period 1	Delgocitinib cream 1 mg/g	Delgocitinib cream 3 mg/g	Delgocitinib cream 8 mg/g
Started	52	51	52
Completed	40	38	44
Not completed	12	13	8
Consent withdrawn by subject	4	4	3
Adverse event, non-fatal	6	6	-
Lost to follow-up	1	-	-
Other personal reasons	-	-	1
Lack of efficacy	1	3	4

Number of subjects in period 1	Delgocitinib cream 20 mg/g	Delgocitinib cream vehicle
Started	53	50
Completed	46	36
Not completed	7	14
Consent withdrawn by subject	5	5

Adverse event, non-fatal	1	3
Lost to follow-up	1	1
Other personal reasons	-	1
Lack of efficacy	-	4

Baseline characteristics

Reporting groups

Reporting group title	Delgocitinib cream 1 mg/g
Reporting group description: -	
Reporting group title	Delgocitinib cream 3 mg/g
Reporting group description: -	
Reporting group title	Delgocitinib cream 8 mg/g
Reporting group description: -	
Reporting group title	Delgocitinib cream 20 mg/g
Reporting group description: -	
Reporting group title	Delgocitinib cream vehicle
Reporting group description: -	

Reporting group values	Delgocitinib cream 1 mg/g	Delgocitinib cream 3 mg/g	Delgocitinib cream 8 mg/g
Number of subjects	52	51	52
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)	48	45	46
From 65-84 years	4	6	6
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	44.3	46.1	47.9
standard deviation	± 13.6	± 14.6	± 12.9
Gender categorical Units: Subjects			
Female	37	28	32
Male	15	23	20
Baseline IGA-CHE score Units: Subjects			
0 - Clear	0	0	0
1 - Almost clear	0	0	0
2 - Mild	13	13	11
3 - Moderate	29	29	29
4 - Severe	10	9	12
Baseline HECSI score Units: Units on a scale			
arithmetic mean	59.0	52.4	49.5
standard deviation	± 48.0	± 35.9	± 29.3

Reporting group values	Delgocitinib cream 20 mg/g	Delgocitinib cream vehicle	Total
Number of subjects	53	50	258
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)	50	44	233
From 65-84 years	3	6	25
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	43.9	47.8	
standard deviation	± 15.1	± 16.2	-
Gender categorical Units: Subjects			
Female	34	27	158
Male	19	23	100
Baseline IGA-CHE score Units: Subjects			
0 - Clear	0	0	0
1 - Almost clear	0	0	0
2 - Mild	12	12	61
3 - Moderate	31	27	145
4 - Severe	10	11	52
Baseline HECSI score Units: Units on a scale			
arithmetic mean	65.7	52.7	
standard deviation	± 58.3	± 34.9	-

End points

End points reporting groups

Reporting group title	Delgocitinib cream 1 mg/g
Reporting group description: -	
Reporting group title	Delgocitinib cream 3 mg/g
Reporting group description: -	
Reporting group title	Delgocitinib cream 8 mg/g
Reporting group description: -	
Reporting group title	Delgocitinib cream 20 mg/g
Reporting group description: -	
Reporting group title	Delgocitinib 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 (IGA-CHE treatment success) from baseline to 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 (IGA-CHE treatment success) from baseline to Week 16.
End point description:	IGA-CHE is an instrument used in clinical trials to rate the severity of participant's global disease stage 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 1 mg/g	Delgocitinib cream 3 mg/g	Delgocitinib cream 8 mg/g	Delgocitinib cream 20 mg/g
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	51	52	53
Units: Participants reaching IGA-CHE success	11	4	19	20

End point values	Delgocitinib cream vehicle			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: Participants reaching IGA-CHE success	4			

Statistical analyses

Statistical analysis title	Delgocitinib cream 1 mg/g vs. vehicle cream
Statistical analysis description:	
The difference in response rates between the active delgocitinib cream doses and delgocitinib cream vehicle was analysed separately for each of the active dose groups using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). The null hypothesis of no difference in response rates between the delgocitinib cream active doses and delgocitinib cream vehicle was tested against the 2-sided alternative that there is a difference.	
Comparison groups	Delgocitinib cream vehicle v Delgocitinib cream 1 mg/g
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05 ^[1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	13.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	26.24

Notes:

[1] - The statistical test was not controlled for multiplicity. Data at visits following premature discontinuation of IMP or initiation of rescue medication before Week 16 were considered missing and imputed as non-responders (as were any other missing data).

Statistical analysis title	Delgocitinib cream 3 mg/g vs. vehicle cream
Statistical analysis description:	
The difference in response rates between the active delgocitinib cream doses and delgocitinib cream vehicle was analysed separately for each of the active dose groups using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). The null hypothesis of no difference in response rates between the delgocitinib cream active doses and delgocitinib cream vehicle was tested against the 2-sided alternative that there is a difference.	
Comparison groups	Delgocitinib cream vehicle v Delgocitinib cream 3 mg/g
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05 ^[2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.44
upper limit	10.39

Notes:

[2] - The statistical test was not controlled for multiplicity. Data at visits following premature discontinuation of IMP or initiation of rescue medication before Week 16 were considered missing and imputed as non-responders (as were any other missing data).

Statistical analysis title	Delgocitinib cream 8 mg/g vs. vehicle cream
Statistical analysis description:	
The difference in response rates between the active delgocitinib cream doses and delgocitinib cream vehicle was analysed separately for each of the active dose groups using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). The null hypothesis of no difference in response rates between the delgocitinib cream active doses and delgocitinib cream vehicle	

was tested against the 2-sided alternative that there is a difference.

Comparison groups	Delgocitinib cream vehicle v Delgocitinib cream 8 mg/g
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	28.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.8
upper limit	42.64

Notes:

[3] - The statistical test was not controlled for multiplicity. Data at visits following premature discontinuation of IMP or initiation of rescue medication before Week 16 were considered missing and imputed as non-responders (as were any other missing data).

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

The difference in response rates between the active delgocitinib cream doses and delgocitinib cream vehicle was analysed separately for each of the active dose groups using the Cochran-Mantel-Haenszel test stratified by region and disease severity (baseline IGA-CHE score). The null hypothesis of no difference in response rates between the delgocitinib cream active doses and delgocitinib cream vehicle was tested against the 2-sided alternative that there is a difference.

Comparison groups	Delgocitinib cream vehicle v Delgocitinib cream 20 mg/g
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	29.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.56
upper limit	44.67

Notes:

[4] - The statistical test was not controlled for multiplicity. Data at visits following premature discontinuation of IMP or initiation of rescue medication before Week 16 were considered missing and imputed as non-responders (as were any other missing data).

Statistical analysis title	Dose-response analysis
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Statistical analysis description:

The primary endpoint was evaluated by determining if there was a dose-response relationship between the IGA-CHE response rate at Week 16 and the dose administered, using the Multiple Comparison Procedure - Modelling (MCP-Mod) methodology. Several candidate parametric models were assumed and multiple comparison techniques were used to choose the model(s) most likely to represent the true underlying dose-response curve.

Comparison groups	Delgocitinib cream 1 mg/g v Delgocitinib cream 3 mg/g v Delgocitinib cream 8 mg/g v Delgocitinib cream 20 mg/g v Delgocitinib cream vehicle
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Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[5]
Method	Multiple contrast test

Notes:

[5] - P-values were adjusted for multiple comparisons. Models with an adjusted p-value <0.025 were statistically sign. different from a flat dose-response model. Model: IGA-CHE TS = Treatment + Region + Baseline IGA-CHE.

Secondary: Change in Hand Eczema Severity Index (HECSI) from baseline to Week 16.

End point title	Change in Hand Eczema Severity Index (HECSI) from baseline to Week 16.
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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
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End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 1 mg/g	Delgocitinib cream 3 mg/g	Delgocitinib cream 8 mg/g	Delgocitinib cream 20 mg/g
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	51	52	53
Units: Change in HECSI from baseline to Week 16				
least squares mean (standard error)	-39.81 (± 3.71)	-35.93 (± 3.77)	-46.69 (± 3.63)	-41.99 (± 3.59)

End point values	Delgocitinib cream vehicle			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: Change in HECSI from baseline to Week 16				
least squares mean (standard error)	-26.40 (± 3.80)			

Statistical analyses

Statistical analysis title	Delgocitinib cream 1 mg/g vs. vehicle cream
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Statistical analysis description:

Least Square (LS) Means were calculated using a mixed model for repeated measurements on the post-baseline responses up to Week 16 with an unstructured covariance matrix, Kenward-Roger approximation to estimate denominator degrees of freedom, and the mean modelled as follows:

Change from baseline in HECSI

= treatment × visit + baseline HECSI × visit + region + baseline IGA-CHE.

The primary comparison between each active delgocitinib dose and vehicle was at Week 16.

Comparison groups	Delgocitinib cream 1 mg/g v Delgocitinib cream vehicle
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.01 ^[6]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-13.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.82
upper limit	-4.01

Notes:

[6] - The statistical test was not controlled for multiplicity.

Statistical analysis title	Delgocitinib cream 3 mg/g vs. vehicle cream
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Statistical analysis description:

Least Square (LS) Means were calculated using a mixed model for repeated measurements on the post-baseline responses up to Week 16 with an unstructured covariance matrix, Kenward-Roger approximation to estimate denominator degrees of freedom, and the mean modelled as follows:

Change from baseline in HECSI

= treatment × visit + baseline HECSI × visit + region + baseline IGA-CHE.

The primary comparison between each active delgocitinib dose and vehicle was at Week 16.

Comparison groups	Delgocitinib cream vehicle v Delgocitinib cream 3 mg/g
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 ^[7]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-9.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.04
upper limit	-0.02

Notes:

[7] - The statistical test was not controlled for multiplicity.

Statistical analysis title	Delgocitinib cream 8 mg/g vs. vehicle cream
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Statistical analysis description:

Least Square (LS) Means were calculated using a mixed model for repeated measurements on the post-baseline responses up to Week 16 with an unstructured covariance matrix, Kenward-Roger approximation to estimate denominator degrees of freedom, and the mean modelled as follows:

Change from baseline in HECSI

= treatment × visit + baseline HECSI × visit + region + baseline IGA-CHE.

The primary comparison between each active delgocitinib dose and vehicle was at Week 16.

Comparison groups	Delgocitinib cream vehicle v Delgocitinib cream 8 mg/g
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[8]
Method	Mixed models analysis
Parameter estimate	Median difference (net)
Point estimate	-20.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.56
upper limit	-11.02

Notes:

[8] - The statistical test was not controlled for multiplicity.

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

Least Square (LS) Means were calculated using a mixed model for repeated measurements on the post-baseline responses up to Week 16 with an unstructured covariance matrix, Kenward-Roger approximation to estimate denominator degrees of freedom, and the mean modelled as follows:

Change from baseline in HECSI

= treatment × visit + baseline HECSI × visit + region + baseline IGA-CHE.

The primary comparison between each active delgocitinib dose and vehicle was at Week 16.

Comparison groups	Delgocitinib cream vehicle v Delgocitinib cream 20 mg/g
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 ^[9]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-15.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.82
upper limit	-6.36

Notes:

[9] - The statistical test was not controlled for multiplicity.

Statistical analysis title	Dose-response analysis
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Statistical analysis description:

The secondary endpoint "Change from baseline to Week 16 in HECSI score" was evaluated by determining if there was a dose-response relationship between the change from baseline in HECSI score at Week 16 and the dose administered, using the Multiple Comparison Procedure - Modelling (MCP-Mod) methodology. Several candidate parametric models were assumed and multiple comparison techniques were used to choose the model(s) most likely to represent the true underlying dose-response curve.

Comparison groups	Delgocitinib cream 1 mg/g v Delgocitinib cream 3 mg/g v Delgocitinib cream 8 mg/g v Delgocitinib cream 20 mg/g v Delgocitinib cream vehicle
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Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[10]
Method	Multiple contrast test

Notes:

[10] - P-values were adj. for multiple comparisons. Models with an adj. p-value <0.025 were statistically sign. different from a flat dose-response model. Model: Change = Treatment + Baseline + Region + Baseline IGA-CHE.

Secondary: Time to IGA-CHE treatment success.

End point title	Time to IGA-CHE treatment success.
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End point description:

Time to IGA-CHE treatment success response is defined as the time from baseline to first assessment of an IGA-CHE score of 0 (clear) or 1 (almost clear) with at least a 2-step improvement. The median time to achieve success in IGA-CHE was not estimable in all groups, as fewer participants (less than 50 percent) reached success in IGA-CHE in delgocitinib cream 1 mg/g, delgocitinib cream 3 mg/g, and delgocitinib cream vehicle. Therefore, values are only reported for delgocitinib cream 8 mg/g and delgocitinib cream 20 mg/g.

End point type	Secondary
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End point timeframe:

Week 0 to Week 16

End point values	Delgocitinib cream 1 mg/g	Delgocitinib cream 3 mg/g	Delgocitinib cream 8 mg/g	Delgocitinib cream 20 mg/g
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52 ^[11]	51 ^[12]	52	53
Units: Median time to achieve treatment success				
number (not applicable)	9999	9999	82	98

Notes:

[11] - 9999=number NA. IGA-CHE TS was reached in <50% of participants, therefore median time not estimable

[12] - 9999=number NA. IGA-CHE TS was reached in <50% of participants, therefore median time not estimable

End point values	Delgocitinib cream vehicle			
Subject group type	Reporting group			
Number of subjects analysed	50 ^[13]			
Units: Median time to achieve treatment success				
number (not applicable)	9999			

Notes:

[13] - 9999=number NA. IGA-CHE TS was reached in <50% of participants, therefore median time not estimable

Statistical analyses

Statistical analysis title	Delgocitinib cream 1 mg/g vs. vehicle cream
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Statistical analysis description:

Time to IGA-CHE TS was defined as the time from the date of the first IMP application to first assessment of IGA-CHE TS. Subjects without baseline observation were censored at the date of the first IMP application. Subjects with baseline observation not achieving IGA-CHE TS during the treatment period were censored at the date of the last visit with a valid post-baseline assessment on or prior to the

date of discontinuation of IMP or initiation of rescue medication, whichever occurred first.

Comparison groups	Delgocitinib cream 1 mg/g v Delgocitinib cream vehicle
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	other ^[14]
P-value	< 0.05 ^[15]
Method	Logrank

Notes:

[14] - Treatment groups were compared using a 2-sided log-rank test stratified by region and baseline IGA-CHE score. An event was defined as the first time achieving IGA-CHE TS.

[15] - IGA-CHE TS was reached in less than 50% of participants, therefore the median time was not estimable.

The statistical test was not controlled for multiplicity.

Statistical analysis title	Delgocitinib cream 3 mg/g vs. vehicle cream
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Statistical analysis description:

Time to IGA-CHE TS was defined as the time from the date of the first IMP application to first assessment of IGA-CHE TS. Subjects without baseline observation were censored at the date of the first IMP application. Subjects with baseline observation not achieving IGA-CHE TS during the treatment period were censored at the date of the last visit with a valid post-baseline assessment on or prior to the date of discontinuation of IMP or initiation of rescue medication, whichever occurred first.

Comparison groups	Delgocitinib cream 3 mg/g v Delgocitinib cream vehicle
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other ^[16]
P-value	> 0.1 ^[17]
Method	Logrank

Notes:

[16] - Treatment groups were compared using a 2-sided log-rank test stratified by region and baseline IGA-CHE score. An event was defined as the first time achieving IGA-CHE TS.

[17] - IGA-CHE TS was reached in less than 50% of participants, therefore the median time was not estimable.

The statistical test was not controlled for multiplicity.

Statistical analysis title	Delgocitinib cream 8 mg/g vs. vehicle cream
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Statistical analysis description:

Time to IGA-CHE TS was defined as the time from the date of the first IMP application to first assessment of IGA-CHE TS. Subjects without baseline observation were censored at the date of the first IMP application. Subjects with baseline observation not achieving IGA-CHE TS during the treatment period were censored at the date of the last visit with a valid post-baseline assessment on or prior to the date of discontinuation of IMP or initiation of rescue medication, whichever occurred first.

Comparison groups	Delgocitinib cream 8 mg/g v Delgocitinib cream vehicle
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	other ^[18]
P-value	< 0.0001 ^[19]
Method	Logrank

Notes:

[18] - Treatment groups were compared using a 2-sided log-rank test stratified by region and baseline IGA-CHE score. An event was defined as the first time achieving IGA-CHE TS.

[19] - The statistical test was not controlled for multiplicity.

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

Time to IGA-CHE TS was defined as the time from the date of the first IMP application to first assessment of IGA-CHE TS. Subjects without baseline observation were censored at the date of the first IMP application. Subjects with baseline observation not achieving IGA-CHE TS during the treatment period were censored at the date of the last visit with a valid post-baseline assessment on or prior to the

date of discontinuation of IMP or initiation of rescue medication, whichever occurred first.

Comparison groups	Delgocitinib cream 20 mg/g v Delgocitinib cream vehicle
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	other ^[20]
P-value	< 0.01 ^[21]
Method	Logrank

Notes:

[20] - Treatment groups were compared using a 2-sided log-rank test stratified by region and baseline IGA-CHE score. An event was defined as the first time achieving IGA-CHE TS.

[21] - The statistical test was not controlled for multiplicity.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

18 weeks (from first application of IMP up until the last visit (safety follow-up visit))

Adverse event reporting additional description:

At all visits/phone call, the participants were asked a non-leading question by the investigator about AEs, for example: "How have you felt since I saw you last?" No specific symptoms were to be asked for.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Delgocitinib cream 1 mg/g
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Reporting group description: -

Reporting group title	Delgocitinib cream 3 mg/g
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Reporting group description: -

Reporting group title	Delgocitinib cream 8 mg/g
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Reporting group description: -

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

Reporting group title	Delgocitinib cream vehicle
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Reporting group description: -

Serious adverse events	Delgocitinib cream 1 mg/g	Delgocitinib cream 3 mg/g	Delgocitinib cream 8 mg/g
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)	2 / 51 (3.92%)	1 / 52 (1.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Dizziness postural			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Pemphigoid			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			

subjects affected / exposed	0 / 52 (0.00%)	0 / 51 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Delgocitinib cream 20 mg/g	Delgocitinib cream vehicle	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 53 (0.00%)	0 / 50 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Dizziness postural			
subjects affected / exposed	0 / 53 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Pemphigoid			
subjects affected / exposed	0 / 53 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 53 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Delgocitinib cream 1 mg/g	Delgocitinib cream 3 mg/g	Delgocitinib cream 8 mg/g
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 52 (38.46%)	25 / 51 (49.02%)	25 / 52 (48.08%)
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 52 (3.85%)	2 / 51 (3.92%)	6 / 52 (11.54%)
occurrences (all)	2	4	7
Gastrointestinal disorders			

Toothache subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 3	1 / 51 (1.96%) 1	0 / 52 (0.00%) 0
Skin and subcutaneous tissue disorders			
Eczema subjects affected / exposed occurrences (all)	5 / 52 (9.62%) 5	4 / 51 (7.84%) 5	3 / 52 (5.77%) 7
Pruritus subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 3	2 / 51 (3.92%) 2	1 / 52 (1.92%) 1
Dermatitis atopic subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	3 / 51 (5.88%) 3	0 / 52 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	0 / 51 (0.00%) 0	2 / 52 (3.85%) 2
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	9 / 52 (17.31%) 11	15 / 51 (29.41%) 22	15 / 52 (28.85%) 16
Influenza subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	1 / 51 (1.96%) 1	0 / 52 (0.00%) 0

Non-serious adverse events	Delgocitinib cream 20 mg/g	Delgocitinib cream vehicle	
Total subjects affected by non-serious adverse events subjects affected / exposed	26 / 53 (49.06%)	24 / 50 (48.00%)	
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 5	2 / 50 (4.00%) 2	
Gastrointestinal disorders			
Toothache subjects affected / exposed occurrences (all)	0 / 53 (0.00%) 0	0 / 50 (0.00%) 0	
Skin and subcutaneous tissue disorders			

<p>Eczema</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>6 / 53 (11.32%)</p> <p>7</p>	<p>8 / 50 (16.00%)</p> <p>9</p>	
<p>Pruritus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 53 (5.66%)</p> <p>3</p>	<p>1 / 50 (2.00%)</p> <p>1</p>	
<p>Dermatitis atopic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 53 (0.00%)</p> <p>0</p>	<p>0 / 50 (0.00%)</p> <p>0</p>	
<p>Musculoskeletal and connective tissue disorders</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 53 (5.66%)</p> <p>3</p>	<p>1 / 50 (2.00%)</p> <p>1</p>	
<p>Infections and infestations</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Influenza</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>14 / 53 (26.42%)</p> <p>20</p> <p>4 / 53 (7.55%)</p> <p>4</p>	<p>20 / 50 (40.00%)</p> <p>20</p> <p>0 / 50 (0.00%)</p> <p>0</p>	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2018	The main reason for the amendment was to add an exclusion criterion to ensure that participants who previously participated in a clinical trial with delgocitinib were not allowed to participate in this trial. The amendment was approved prior to first participant first visit.
07 December 2018	The main reason for the amendment was to address comments to the protocol received from the U.S. Food and Drug Administration (FDA). Exclusion criterion 1 was revised to ensure exclusion of participants with a diagnosis of tinea manuum. The participant's Global Assessment of disease severity (PaGa) scale was updated. The Patient Global Impression of Change (PGI-C) questionnaire was added as a PRO to support the planned psychometric properties analyses. A tuberculosis test was added to further safeguard participants in risk of (re)activation of latent tuberculosis. Participant assessment of local tolerability (stinging/burning) was added as an active safety assessment. Miscellaneous other changes/updates have also been implemented.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported