



Clinical trial results:

A phase 1 open-label, multi-centre, single-arm trial to evaluate the safety and pharmacokinetics (including MUSt) of twice daily topical application of delgocitinib cream for 8 weeks in adults, adolescents, and children with moderate to severe atopic dermatitis (AD).

Summary

EudraCT number	2021-000404-37
Trial protocol	Outside EU/EEA
Global end of trial date	29 October 2021

Results information

Result version number	v1 (current)
This version publication date	27 April 2022
First version publication date	27 April 2022

Trial information

Trial identification

Sponsor protocol code	LP0133-1181
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03826901
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 Specialist, LEO Pharma A/S, 0045 4494 5888, disclosure@leo-pharma.com
Scientific contact	Clinical Disclosure Specialist, LEO Pharma A/S, 0045 4494 5888, 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	29 November 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part 1: adolescents and adults (12 years and above)

- To evaluate safety of twice daily applications of delgocitinib cream in the treatment of adults and adolescents with moderate to severe AD.

Part 2: children (2-11 years)

- To evaluate safety of twice daily applications of delgocitinib cream in the treatment of children with moderate to severe AD under maximal usage conditions.

Protection of trial subjects:

Part 1 and Part 2 of the trial were separated by a safety evaluation. The purpose of the safety evaluation was to minimise the potential risks in children. Exposure of children (age 2 to 11 years) to delgocitinib cream was not initiated before the safety data from Part 1 were evaluated by a safety committee. In Part 2 of the trial, an independent data monitoring committee assessed safety for children (age 2 to 11 years) during conduct.

This clinical trial was conducted in compliance with the Declaration of Helsinki as adopted by the 18th World Medical Association General Assembly (1964) and subsequent amendments. All subjects received written and verbal information concerning the clinical trial. Subjects were asked to consent that their personal data were recorded, collected, processed and could be transferred to EU and non-EU countries in accordance with any national legislation regulating privacy and data protection.

If medically necessary (i.e. to control intolerable AD symptoms), rescue treatment for AD could be provided to subjects at the discretion of the investigator.

Background therapy:

Subjects could use an emollient throughout the trial as needed from screening (Visit 1) and throughout the treatment period (to Visit 8). The emollient was to preferably be an additive-free, basic bland emollient.

Evidence for comparator: -

Actual start date of recruitment	20 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 31
Country: Number of subjects enrolled	Canada: 15
Worldwide total number of subjects	46
EEA total number of subjects	0

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)	20
Adolescents (12-17 years)	12
Adults (18-64 years)	13
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Trial start date: 20-Feb-2019; Trial completion date: 29-Oct-2021. The trial was conducted in 2 countries: the United States and Canada.

Pre-assignment

Screening details:

At screening (Visit 1), the subjects' eligibility to enter the trial was checked. The screening period had a minimum duration of 1 week and a maximal duration of 4 weeks.

Period 1

Period 1 title	Treatment period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Children (2-11 years)

Arm description:

At baseline (Visit 2), subjects were enrolled if eligible. The first application of investigational medicinal product (IMP) occurred at the trial site on Visit 2 after subject eligibility confirmation, baseline assessments, pre-dose PK blood draw, and IMP instructions were carried out. All IMP applications were performed by the subject/ subject's caregiver.

Subjects returned to the trial site for the scheduled visits. However, Visits 3, 4, and 7 could be conducted remotely, if preferred. The last IMP application occurred before the subjects attended Visit 8.

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

Dosage and administration details:

20 mg/g twice daily topical application for 8 weeks. The applications were to be performed preferably 12 hours apart, and minimum 8 hours apart.

Arm title	Adolescents (12-17 years)
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Arm description:

At baseline (Visit 2), subjects were enrolled if eligible. The first application of investigational medicinal product (IMP) occurred at the trial site on Visit 2 after subject eligibility confirmation, baseline assessments, pre-dose PK blood draw, and IMP instructions were carried out. All IMP applications were performed by the subject/ subject's caregiver.

Subjects returned to the trial site for the scheduled visits. However, Visits 3, 4, and 7 could be conducted remotely, if preferred. The last IMP application occurred before the subjects attended Visit 8.

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

Dosage and administration details:

20 mg/g twice daily topical application for 8 weeks. The applications were to be performed preferably 12 hours apart, and minimum 8 hours apart.

Arm title	Adults (>=18 years)
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Arm description:

At baseline (Visit 2), subjects were enrolled if eligible. The first application of investigational medicinal product (IMP) occurred at the trial site on Visit 2 after subject eligibility confirmation, baseline assessments, pre-dose PK blood draw, and IMP instructions were carried out. All IMP applications were performed by the subject/ subject's caregiver.

Subjects returned to the trial site for the scheduled visits. However, Visits 3, 4, and 7 could be conducted remotely, if preferred. The last IMP application occurred before the subjects attended Visit 8.

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

Dosage and administration details:

20 mg/g twice daily topical application for 8 weeks. The applications were to be performed preferably 12 hours apart, and minimum 8 hours apart.

Number of subjects in period 1	Children (2-11 years)	Adolescents (12-17 years)	Adults (>=18 years)
Started	20	12	14
Completed	20	12	12
Not completed	0	0	2
Adverse event, non-fatal	-	-	1
Lack of efficacy	-	-	1

Period 2

Period 2 title	Safety follow-up period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Children (2-11 years)

Arm description:

All subjects attended a safety follow-up visit approximately 2 weeks after the last IMP application. This visit marked the end of trial participation.

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Adolescents (12-17 years)

Arm description:

All subjects attended a safety follow-up visit approximately 2 weeks after the last IMP application. This visit marked the end of trial participation.

Arm type	No intervention
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No investigational medicinal product assigned in this arm	
Arm title	Adults (≥ 18 years)
Arm description: All subjects attended a safety follow-up visit approximately 2 weeks after the last IMP application. This visit marked the end of trial participation.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Children (2-11 years)	Adolescents (12-17 years)	Adults (≥ 18 years)
Started	20	12	12
Completed	20	12	12

Baseline characteristics

Reporting groups

Reporting group title	Children (2-11 years)
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Reporting group description:

At baseline (Visit 2), subjects were enrolled if eligible. The first application of investigational medicinal product (IMP) occurred at the trial site on Visit 2 after subject eligibility confirmation, baseline assessments, pre-dose PK blood draw, and IMP instructions were carried out. All IMP applications were performed by the subject/ subject's caregiver.

Subjects returned to the trial site for the scheduled visits. However, Visits 3, 4, and 7 could be conducted remotely, if preferred. The last IMP application occurred before the subjects attended Visit 8.

Reporting group title	Adolescents (12-17 years)
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Reporting group description:

At baseline (Visit 2), subjects were enrolled if eligible. The first application of investigational medicinal product (IMP) occurred at the trial site on Visit 2 after subject eligibility confirmation, baseline assessments, pre-dose PK blood draw, and IMP instructions were carried out. All IMP applications were performed by the subject/ subject's caregiver.

Subjects returned to the trial site for the scheduled visits. However, Visits 3, 4, and 7 could be conducted remotely, if preferred. The last IMP application occurred before the subjects attended Visit 8.

Reporting group title	Adults (>=18 years)
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Reporting group description:

At baseline (Visit 2), subjects were enrolled if eligible. The first application of investigational medicinal product (IMP) occurred at the trial site on Visit 2 after subject eligibility confirmation, baseline assessments, pre-dose PK blood draw, and IMP instructions were carried out. All IMP applications were performed by the subject/ subject's caregiver.

Subjects returned to the trial site for the scheduled visits. However, Visits 3, 4, and 7 could be conducted remotely, if preferred. The last IMP application occurred before the subjects attended Visit 8.

Reporting group values	Children (2-11 years)	Adolescents (12-17 years)	Adults (>=18 years)
Number of subjects	20	12	14
Age categorical			
Units: Subjects			
Children (2-11 years)	20	0	0
Adolescents (12-17 years)	0	12	0
Adults (18-64 years)	0	0	13
From 65-84 years	0	0	1
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	6.2	14.8	37.7
standard deviation	± 3.3	± 1.9	± 18.0
Gender categorical			
Units: Subjects			
Female	7	8	6
Male	13	4	8
Race			
Units: Subjects			
White	8	7	12
Black or African American	7	2	0
Asian	3	2	2

Native Hawaiian or other Pacific islander	0	0	0
American Indian or Alaska native	0	1	0
Other	2	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	3	0	2
Not Hispanic or Latino	17	12	12
vIGA-AD			
The validated Investigator Global Assessment scale for Atopic Dermatitis (vIGA-AD) is an instrument used in clinical trials to assess the subject's global disease severity and is based on a 5 point scale ranging from 0 (clear) to 4 (severe).			
Units: Subjects			
0- Clear	0	0	0
1 - Almost clear	0	0	0
2 - Mild	0	0	0
3 - Moderate	10	7	12
4- Severe	10	5	2
EASI Total			
The EASI is a validated measure used in clinical practice and clinical trials to assess the severity and extent of AD. The EASI is a composite index with scores ranging from 0 to 72, with higher values indicating more severe or more extensive condition.			
Units: Score			
arithmetic mean	27.2	20.1	19.9
standard deviation	± 9.9	± 7.4	± 7.4
BSA			
Total body surface area (BSA) affected by atopic dermatitis.			
Units: Percentage			
arithmetic mean	46.0	31.8	33.6
standard deviation	± 13.1	± 6.3	± 5.8

Reporting group values	Total		
Number of subjects	46		
Age categorical Units: Subjects			
Children (2-11 years)	20		
Adolescents (12-17 years)	12		
Adults (18-64 years)	13		
From 65-84 years	1		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	21		
Male	25		
Race Units: Subjects			
White	27		
Black or African American	9		
Asian	7		

Native Hawaiian or other Pacific islander	0		
American Indian or Alaska native	1		
Other	2		
Ethnicity			
Units: Subjects			
Hispanic or Latino	5		
Not Hispanic or Latino	41		
vIGA-AD			
The validated Investigator Global Assessment scale for Atopic Dermatitis (vIGA-AD) is an instrument used in clinical trials to assess the subject's global disease severity and is based on a 5 point scale ranging from 0 (clear) to 4 (severe).			
Units: Subjects			
0- Clear	0		
1 - Almost clear	0		
2 - Mild	0		
3 - Moderate	29		
4- Severe	17		
EASI Total			
The EASI is a validated measure used in clinical practice and clinical trials to assess the severity and extent of AD. The EASI is a composite index with scores ranging from 0 to 72, with higher values indicating more severe or more extensive condition.			
Units: Score			
arithmetic mean			
standard deviation	-		
BSA			
Total body surface area (BSA) affected by atopic dermatitis.			
Units: Percentage			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Children (2-11 years)
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Reporting group description:

At baseline (Visit 2), subjects were enrolled if eligible. The first application of investigational medicinal product (IMP) occurred at the trial site on Visit 2 after subject eligibility confirmation, baseline assessments, pre-dose PK blood draw, and IMP instructions were carried out. All IMP applications were performed by the subject/ subject's caregiver.

Subjects returned to the trial site for the scheduled visits. However, Visits 3, 4, and 7 could be conducted remotely, if preferred. The last IMP application occurred before the subjects attended Visit 8.

Reporting group title	Adolescents (12-17 years)
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Reporting group description:

At baseline (Visit 2), subjects were enrolled if eligible. The first application of investigational medicinal product (IMP) occurred at the trial site on Visit 2 after subject eligibility confirmation, baseline assessments, pre-dose PK blood draw, and IMP instructions were carried out. All IMP applications were performed by the subject/ subject's caregiver.

Subjects returned to the trial site for the scheduled visits. However, Visits 3, 4, and 7 could be conducted remotely, if preferred. The last IMP application occurred before the subjects attended Visit 8.

Reporting group title	Adults (≥ 18 years)
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Reporting group description:

At baseline (Visit 2), subjects were enrolled if eligible. The first application of investigational medicinal product (IMP) occurred at the trial site on Visit 2 after subject eligibility confirmation, baseline assessments, pre-dose PK blood draw, and IMP instructions were carried out. All IMP applications were performed by the subject/ subject's caregiver.

Subjects returned to the trial site for the scheduled visits. However, Visits 3, 4, and 7 could be conducted remotely, if preferred. The last IMP application occurred before the subjects attended Visit 8.

Reporting group title	Children (2-11 years)
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Reporting group description:

All subjects attended a safety follow-up visit approximately 2 weeks after the last IMP application. This visit marked the end of trial participation.

Reporting group title	Adolescents (12-17 years)
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Reporting group description:

All subjects attended a safety follow-up visit approximately 2 weeks after the last IMP application. This visit marked the end of trial participation.

Reporting group title	Adults (≥ 18 years)
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Reporting group description:

All subjects attended a safety follow-up visit approximately 2 weeks after the last IMP application. This visit marked the end of trial participation.

Primary: number of AEs

End point title	number of AEs ^[1]
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End point description:

End point type	Primary
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End point timeframe:

from baseline to Week 8

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The data for the primary endpoint were summarised descriptively, and no comparative analyses were made.

End point values	Children (2-11 years)	Adolescents (12-17 years)	Adults (>=18 years)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	12	14	
Units: AEs	23	5	9	

Statistical analyses

No statistical analyses for this end point

Primary: number of subjects with AEs

End point title	number of subjects with AEs ^[2]
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End point description:

End point type	Primary
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End point timeframe:

from baseline to Week 8

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The data for the primary endpoint were summarised descriptively, and no comparative analyses were made.

End point values	Children (2-11 years)	Adolescents (12-17 years)	Adults (>=18 years)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	12	14	
Units: subjects	9	3	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax at Day 8

End point title	Cmax at Day 8
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End point description:

End point type	Secondary
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End point timeframe:

Day 8

End point values	Children (2-11 years)	Adolescents (12-17 years)	Adults (≥ 18 years)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	10	13	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	3.26 (\pm 369.32)	0.70 (\pm 216.42)	1.20 (\pm 188.27)	

Statistical analyses

No statistical analyses for this end point

Secondary: AUC at Day 8

End point title	AUC at Day 8
End point description:	
End point type	Secondary
End point timeframe:	
Day 8	

End point values	Children (2-11 years)	Adolescents (12-17 years)	Adults (≥ 18 years)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	8	13	
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	23.30 (\pm 313.27)	5.93 (\pm 289.39)	8.39 (\pm 231.48)	

Statistical analyses

No statistical analyses for this end point

Secondary: tmax at Day 8

End point title	tmax at Day 8
End point description:	
End point type	Secondary
End point timeframe:	
Day 8	

End point values	Children (2-11 years)	Adolescents (12-17 years)	Adults (>=18 years)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	10	13	
Units: hours				
geometric mean (geometric coefficient of variation)	2.59 (± 126.17)	3.44 (± 137.61)	1.88 (± 103.56)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to Week 8

Adverse event reporting additional description:

The analysis was based on safety analysis set

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	Adults (>=18 years)
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Reporting group description: -

Reporting group title	Adolescents (12-17 years)
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Reporting group description: -

Reporting group title	Children (2-11 years)
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Reporting group description: -

Reporting group title	All subjects
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Reporting group description: -

Serious adverse events	Adults (>=18 years)	Adolescents (12-17 years)	Children (2-11 years)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	0 / 20 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 46 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Adults (>=18 years)	Adolescents (12-17 years)	Children (2-11 years)
Total subjects affected by non-serious adverse events subjects affected / exposed	5 / 14 (35.71%)	3 / 12 (25.00%)	9 / 20 (45.00%)
Vascular disorders Flushing subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 12 (0.00%) 0	1 / 20 (5.00%) 1
Nervous system disorders Headache subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1 1 / 14 (7.14%) 1	1 / 12 (8.33%) 1 1 / 12 (8.33%) 1	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0
General disorders and administration site conditions Application site pain subjects affected / exposed occurrences (all) Face oedema subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0 0 / 14 (0.00%) 0	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 12 (0.00%) 0	1 / 20 (5.00%) 1
Eye disorders Conjunctivitis allergic subjects affected / exposed occurrences (all) Periorbital oedema subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0 0 / 14 (0.00%) 0	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea	0 / 14 (0.00%) 0 0	0 / 12 (0.00%) 0 0	1 / 20 (5.00%) 1 1

subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 12 (0.00%) 0	1 / 20 (5.00%) 2
Vomiting subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 12 (0.00%) 0	1 / 20 (5.00%) 1
Respiratory, thoracic and mediastinal disorders			
Asthma subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 12 (0.00%) 0	1 / 20 (5.00%) 1
Nasal congestion subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 12 (0.00%) 0	1 / 20 (5.00%) 1
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 12 (8.33%) 1	0 / 20 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 12 (8.33%) 1	0 / 20 (0.00%) 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 12 (0.00%) 0	3 / 20 (15.00%) 3
Drug eruption subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 12 (0.00%) 0	0 / 20 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 12 (0.00%) 0	0 / 20 (0.00%) 0
Erythema subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 12 (0.00%) 0	2 / 20 (10.00%) 2
Pruritus subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 12 (0.00%) 0	1 / 20 (5.00%) 1
Rash			

subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Folliculitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 12 (8.33%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 14 (0.00%)	0 / 12 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Periorbital cellulitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 12 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	All subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 46 (36.96%)		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 46 (4.35%)		
occurrences (all)	2		
Presyncope			

subjects affected / exposed occurrences (all)	2 / 46 (4.35%) 2		
General disorders and administration site conditions Application site pain subjects affected / exposed occurrences (all) Face oedema subjects affected / exposed occurrences (all)	1 / 46 (2.17%) 1 1 / 46 (2.17%) 1		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	1 / 46 (2.17%) 1		
Eye disorders Conjunctivitis allergic subjects affected / exposed occurrences (all) Periorbital oedema subjects affected / exposed occurrences (all)	1 / 46 (2.17%) 1 1 / 46 (2.17%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	1 / 46 (2.17%) 1 2 / 46 (4.35%) 3 1 / 46 (2.17%) 1		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) Nasal congestion	1 / 46 (2.17%) 1		

subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	4 / 46 (8.70%)		
occurrences (all)	4		
Drug eruption			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	2 / 46 (4.35%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	2		
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Folliculitis			

subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		
Periorbital cellulitis			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 January 2019	The main reason for the amendment was to address comments to other protocols under this IND received from the US Food and Drug Administration (FDA). Miscellaneous other changes/updates were also implemented.
10 September 2020	The main reason for the amendment was to add an independent data monitoring for Part 2 based on regulatory advice received from Paediatric Committee (PDCO) of the European Medicines Agency (EMA). Furthermore, the dose strength in Part 2 was defined as 20 mg/g based on the results of the LP0133-1275 dose-ranging trial, and the evaluation by the safety committee from Part 1.
25 February 2021	The main reason for the amendment was to address comments to the protocol received from the US Food and Drug Administration. Furthermore, to follow authorities' restrictions related to the COVID-19 pandemic, guidance was provided on how to proceed in case the subjects were not able to come to the site for the visits.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported