Clinical trial results:
A phase 2 trial to evaluate the efficacy and safety of orally administered LEO 152020 tablets compared with placebo tablets for up to 16 weeks of treatment in adults with moderate to severe atopic dermatitis

Summary

EudraCT number	2020-004561-39
Trial protocol	DE CZ PL ES
Global end of trial date	26 July 2023

Results information

Result version number	v1
This version publication date	05 May 2024
First version publication date	05 May 2024

Trial information

Trial identification

Sponsor protocol code	LP0190-1488

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05117060
WHO universal trial number (UTN)	U1111-1281-1895

Notes:

Sponsors

Sponsor organisation name	JW Pharmaceutical
Sponsor organisation address	JW Gwacheon Tower, 38, Gwacheon-daero 7-gil, Gwacheon-si, Gyeonggi-do, Korea, Republic of, 13840
Public contact	Soojin Park, JW Pharmaceutical , +82 -1588-2675, park.soojin@jwhealthcare.com
Scientific contact	Soojin Park, JW Pharmaceutical , +82 -1588-2675, park.soojin@jwhealthcare.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	31 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 July 2023
Global end of trial reached?	Yes
Global end of trial date	26 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the exposure response relationship of LEO 152020 and evaluate efficacy of LEO 152020 compared with placebo for up to 16 weeks of treatment in subjects with moderate to severe AD

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013) and ICH GCP (2016), including archiving of essential documents.

Background therapy: -

Evidence for comparator:

Not applicable.

Actual start date of recruitment	13 December 2021
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	Australia: 14
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	Japan: 36
Country: Number of subjects enrolled	United States: 25
Country: Number of subjects enrolled	Poland: 48
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Czechia: 28
Country: Number of subjects enrolled	Germany: 27
Worldwide total number of subjects	216
EEA total number of subjects	107

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	208
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This trial was conducted at 45 sites that screened subjects in 8 countries (Australia, Canada, Czech Republic (Czechia), Germany, Japan, Poland, Spain and the United States).

Pre-assignment

Screening details:

285 subjects were screened and 216 were randomized in a 4:3:3:4 ratio into the 4 treatment groups.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LEO 152020 - Dosing Regimen 1 (higher dose)

Arm description:

Self-administration of film coated tablets of LEO 152020 (last administration at Week 16).

Arm type	Experimental
Investigational medicinal product name	LEO 152020 film-coated tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Self-administration of tablets daily. Film-coated tablet.

Arm title	LEO 152020 - Dosing Regimen 2 (middle dose)

Arm description:

Self-administration of film coated tablets of LEO 152020 and LEO 152020 placebo (last administration at Week 16).

Arm type	Experimental
Investigational medicinal product name	LEO 152020 film-coated tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Self-administration of tablets daily. Film-coated tablet

Investigational medicinal product name	LEO 152020 placebo film-coated tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Self-administration of tablets daily. Film-coated placebo tablet

Arm title	LEO 152020 - Dosing Regimen 3 (low dose)

Arm description:

Self-administration of film coated tablets of LEO 152020 and LEO 152020 placebo (last administration at Week 16).

Arm type	Experimental
Investigational medicinal product name	LEO 152020 film-coated tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Self-administration of tablets daily. Film-coated tablet

Investigational medicinal product name	LEO 152020 placebo film-coated tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Self-administration of tablets daily. Film-coated placebo tablet

Arm title	LEO 152020 - placebo

Arm description:

Self-administration of LEO 152020 placebo (last administration at Week 16).

Arm type	Placebo
Investigational medicinal product name	LEO 152020 placebo film-coated tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Self-administration of tablets daily. Film-coated placebo tablet

Number of subjects in period 1	LEO 152020 - Dosing Regimen 1 (higher dose)	LEO 152020 - Dosing Regimen 2 (middle dose)	LEO 152020 - Dosing Regimen 3 (low dose)
Started	61	45	49
Completed	44	29	33
Not completed	17	16	16
Consent withdrawn by subject	8	5	5
Adverse event, non-fatal	3	5	6
Other	2	1	3
Lost to follow-up	-	-	-
Lack of efficacy	4	5	2

Number of subjects in period 1	LEO 152020 - placebo
Started	61
Completed	46
Not completed	15

Consent withdrawn by subject	6
Adverse event, non-fatal	1
Other	1
Lost to follow-up	1
Lack of efficacy	6

Baseline characteristics

Reporting groups	
Reporting group title	LEO 152020 - Dosing Regimen 1 (higher dose)
Reporting group description:	
Self-administration of film coated tablets of LEO 152020 (last administration at Week 16).	
Reporting group title	LEO 152020 - Dosing Regimen 2 (middle dose)
Reporting group description:	
Self-administration of film coated tablets of LEO 152020 and LEO 152020 placebo (last administration at Week 16).	
Reporting group title	LEO 152020 - Dosing Regimen 3 (low dose)
Reporting group description:	
Self-administration of film coated tablets of LEO 152020 and LEO 152020 placebo (last administration at Week 16).	
Reporting group title	LEO 152020 - placebo
Reporting group description:	
Self-administration of LEO 152020 placebo (last administration at Week 16).	

Reporting group values	LEO 152020 - Dosing Regimen 1 (higher dose)	LEO 152020 - Dosing Regimen 2 (middle dose)	LEO 152020 - Dosing Regimen 3 (low dose)
Number of subjects	61	45	49
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)	59	42	48
From 65-84 years	2	3	1
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	36.2	35.2	35.2
standard deviation	± 13.3	± 15.0	± 13.5
Gender categorical			
Units: Subjects			
Female	32	21	30
Male	29	24	19

Reporting group values	LEO 152020 - placebo	Total	
Number of subjects	61	216	
Age categorical			
Units: Subjects			
In utero	0	0	

Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	59	208	
From 65-84 years	2	8	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	33.4		
standard deviation	± 12.9	-	
Gender categorical			
Units: Subjects			
Female	35	118	
Male	26	98	

End points

End points reporting groups

Reporting group title	LEO 152020 - Dosing Regimen 1 (higher dose)
Reporting group description:	
Self-administration of film coated tablets of LEO 152020 (last administration at Week 16).	
Reporting group title	LEO 152020 - Dosing Regimen 2 (middle dose)
Reporting group description:	
Self-administration of film coated tablets of LEO 152020 and LEO 152020 placebo (last administration at Week 16).	
Reporting group title	LEO 152020 - Dosing Regimen 3 (low dose)
Reporting group description:	
Self-administration of film coated tablets of LEO 152020 and LEO 152020 placebo (last administration at Week 16).	
Reporting group title	LEO 152020 - placebo
Reporting group description:	
Self-administration of LEO 152020 placebo (last administration at Week 16).	

Primary: Change in EASI From Baseline to Week 16

End point title	Change in EASI From Baseline to Week 16
End point description:	
The Eczema Area and Severity Index (EASI) is a validated measure used in clinical trials to evaluate the extent and severity of atopic dermatitis. EASI is a composite score ranging from 0 to 72 with higher scores indicating a more extensive or severe condition.	
End point type	Primary
End point timeframe:	
Week 16	

End point values	LEO 152020 - Dosing Regimen 1 (higher dose)	LEO 152020 - Dosing Regimen 2 (middle dose)	LEO 152020 - Dosing Regimen 3 (low dose)	LEO 152020 - placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	45	49	61
Units: score on a scale				
arithmetic mean (confidence interval 95%)	-9.99 (-12.85 to -7.13)	-8.83 (-12.63 to -5.04)	-8.87 (-12.47 to -5.28)	-9.11 (-11.88 to -6.35)

Statistical analyses

Statistical analysis title	Change in EASI from baseline to Week 16
Comparison groups	LEO 152020 - Dosing Regimen 1 (higher dose) v LEO 152020 - placebo

Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.663
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.85
upper limit	3.1

Notes:

[1] - The mixed model was fitted to the entire dataset of 216 subjects, but only 122 of the subjects were in the two treatment groups compared.

Statistical analysis title	Change in EASI from baseline to Week 16
Comparison groups	LEO 152020 - Dosing Regimen 2 (middle dose) v LEO 152020 - placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.907
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.42
upper limit	4.97

Notes:

[2] - The mixed model was fitted to the entire dataset of 216 subjects, but only 106 of the subjects were in the two treatment groups compared.

Statistical analysis title	Change in EASI from baseline to Week 16
Comparison groups	LEO 152020 - placebo v LEO 152020 - Dosing Regimen 3 (low dose)
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.917
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.29
upper limit	4.77

Notes:

[3] - The mixed model was fitted to the entire dataset of 216 subjects, but only 110 of the subjects were in the two treatment groups compared.

Secondary: Number of adverse events from baseline to week 16+3 days per subject

End point title	Number of adverse events from baseline to week 16+3 days per subject

End point description:

Only treatment-emergent adverse events will be reported for this outcome measure. An adverse event will be considered treatment emergent if occurring after the first dose of treatment (Week 0) and up until 3 days after the last dose of treatment (Week 16+3 days for a participant completing the 16-week treatment period).

End point type	Secondary

End point timeframe:

Week 0 to week 16-3 days

End point values	LEO 152020 - Dosing Regimen 1 (higher dose)	LEO 152020 - Dosing Regimen 2 (middle dose)	LEO 152020 - Dosing Regimen 3 (low dose)	LEO 152020 - placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	31	33	38
Units: events	109	67	80	75

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 16 weeks	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	LEO 152020 - Dosing Regimen 1 (higher dose)
Reporting group description: Self-administration of film coated tablets of LEO 152020 (last administration at Week 16).	
Reporting group title	LEO 152020 - Dosing Regimen 2 (middle dose)
Reporting group description: Self-administration of film coated tablets of LEO 152020 and LEO 152020 placebo (last administration at Week 16).	
Reporting group title	LEO 152020 - Dosing Regimen 3 (low dose)
Reporting group description: Self-administration of film coated tablets of LEO 152020 and LEO 152020 placebo (last administration at Week 16).	
Reporting group title	LEO 152020 - Placebo
Reporting group description: Self-administration of LEO 152020 placebo (last administration at Week 16).	

Serious adverse events	LEO 152020 - Dosing Regimen 1 (higher dose)	LEO 152020 - Dosing Regimen 2 (middle dose)	LEO 152020 - Dosing Regimen 3 (low dose)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 61 (0.00%)	2 / 45 (4.44%)	1 / 49 (2.04%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma in situ			
subjects affected / exposed	0 / 61 (0.00%)	0 / 45 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Eczema herpeticum			
subjects affected / exposed	0 / 61 (0.00%)	2 / 45 (4.44%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	LEO 152020 - Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 61 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma in situ			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Eczema herpeticum			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	LEO 152020 - Dosing Regimen 1 (higher dose)	LEO 152020 - Dosing Regimen 2 (middle dose)	LEO 152020 - Dosing Regimen 3 (low dose)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 61 (47.54%)	24 / 45 (53.33%)	23 / 49 (46.94%)
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 61 (1.64%)	3 / 45 (6.67%)	6 / 49 (12.24%)
occurrences (all)	2	3	10
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 61 (3.28%)	4 / 45 (8.89%)	2 / 49 (4.08%)
occurrences (all)	2	4	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 61 (6.56%)	1 / 45 (2.22%)	0 / 49 (0.00%)
occurrences (all)	5	1	0
Nausea			

subjects affected / exposed	8 / 61 (13.11%)	2 / 45 (4.44%)	5 / 49 (10.20%)
occurrences (all)	10	2	5
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	10 / 61 (16.39%)	11 / 45 (24.44%)	7 / 49 (14.29%)
occurrences (all)	14	15	8
Infections and infestations			
COVID-19			
subjects affected / exposed	6 / 61 (9.84%)	6 / 45 (13.33%)	2 / 49 (4.08%)
occurrences (all)	6	6	2
Nasopharyngitis			
subjects affected / exposed	6 / 61 (9.84%)	4 / 45 (8.89%)	3 / 49 (6.12%)
occurrences (all)	6	6	3
Upper respiratory tract infection			
subjects affected / exposed	3 / 61 (4.92%)	3 / 45 (6.67%)	2 / 49 (4.08%)
occurrences (all)	3	3	3

Non-serious adverse events	LEO 152020 - Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 61 (39.34%)		
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	6		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 61 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Dermatitis atopic subjects affected / exposed occurrences (all)	13 / 61 (21.31%) 14		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1		
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 61 (4.92%) 3		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	7 / 61 (11.48%) 7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 October 2021	The main purpose of the protocol amendment was to: • Allow data collection after the occurrence of intercurrent events (initiation of rescue treatment and permanent discontinuation of investigational medicinal product [IMP]) and incorporate the data when applying the treatment policy strategy to handle these events. The collection of data described is in line with ICH E9 (R1) addendum. Consequently, sections related to rescue treatment, permanent discontinuation of IMP / withdrawal from trial, estimand strategy, and statistical analysis methods were revised. • Include subjects with mild and moderate renal impairment in the trial. • Increase monitoring to safeguard subject safety and well-being. • Update of the contraception requirements for men and women.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported