# 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<br>subjects affected / exposed<br>occurrences (all) | 13 / 61 (21.31%)<br>14 | | |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all) | 1 / 61 (1.64%)<br>1 | | |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 3 / 61 (4.92%)<br>3 | | |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 7 / 61 (11.48%)<br>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:<br>• 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.<br>• Include subjects with mild and moderate renal impairment in the trial.<br>• Increase monitoring to safeguard subject safety and well-being.<br>• 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