



Clinical trial results:

A 24 week, randomised, assessor blinded, active-controlled, parallel group, phase 3, 2 arm trial to compare the efficacy and safety of delgocitinib cream 20 mg/g twice-daily with alitretinoin capsules once-daily in adult participants with severe chronic hand eczema

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2021-003543-16 |
| Trial protocol | DE IT ES FR AT PL NO SK |
| Global end of trial date | 05 December 2023 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 |
| This version publication date | 25 October 2024 |
| First version publication date | 25 October 2024 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | LP0133-1528 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05259722 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | LEO Pharma A/S |
| Sponsor organisation address | Industriparken 55, Ballerup, Denmark, 2750 |
| Public contact | Clinical Disclosure, LEO Pharma A/S, disclosure@leo-pharma.com |
| Scientific contact | Clinical Disclosure, LEO Pharma A/S, disclosure@leo-pharma.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 19 February 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 November 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 05 December 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy and health-related quality of life of twice-daily topical application of delgocitinib cream with once-daily oral administration of alitretinoin capsules in the treatment of patients with severe CHE.

Protection of trial subjects:

This trial was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, CIOMS International Ethical Guidelines, applicable ICH GCP guidelines, and other applicable laws and regulations.

Background therapy: -

Evidence for comparator:

N/A

| | |
|---|--------------|
| Actual start date of recruitment | 15 June 2022 |
| 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 | Norway: 2 |
| Country: Number of subjects enrolled | Poland: 180 |
| Country: Number of subjects enrolled | Slovakia: 14 |
| Country: Number of subjects enrolled | Spain: 64 |
| Country: Number of subjects enrolled | Austria: 5 |
| Country: Number of subjects enrolled | France: 30 |
| Country: Number of subjects enrolled | Germany: 136 |
| Country: Number of subjects enrolled | Italy: 22 |
| Country: Number of subjects enrolled | Canada: 54 |
| Country: Number of subjects enrolled | United Kingdom: 6 |
| Worldwide total number of subjects | 513 |
| EEA total number of subjects | 453 |

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) | 471 |
| From 65 to 84 years | 42 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The trial enrolled adult participants with severe CHE and with a documented inadequate response to treatment with TCS or for whom TCS were documented to be otherwise medically inadvisable.

Pre-assignment

Screening details:

Randomization was stratified by subtype (hyperkeratotic/non-hyperkeratotic) and region (North America/Europe).

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

Due to the different administration routes for the 2 IMPs, participants were not blinded to treatment assignment. To ensure unbiased clinical assessments, efficacy (IGA-CHE and HECSI) was evaluated by a blinded assessor.

Arms

| | |
|------------------------------|----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Delgocitinib Cream 20 mg/g |

Arm description:

Twice-daily topical application for up to 24 weeks.

Delgocitinib: Cream for topical application 20 mg/g.

There was a possibility to stop treatment after 16 weeks if IGA 0/1 was obtained.

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

Dosage and administration details:

20 mg/g milligram(s)/gram twice daily for up to 24 weeks

| | |
|------------------|---|
| Arm title | Alitretinoin Capsules 30 mg Per Capsule |
|------------------|---|

Arm description:

1 capsule per day for up to 24 weeks

Toctino: 1 capsule Toctino 30 mg per day; optional reduction to 10 mg per day in case unacceptable adverse reactions to the higher dose occur.

There was a possibility to stop treatment after 12 weeks if IGA 0/1 was obtained.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Alitretinoin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, soft |
| Routes of administration | Oral use |

Dosage and administration details:

1 capsule per day for up to 24 weeks.

Toctino: 1 capsule toctino 30 mg per day; optional reduction to 10 mg per day in case unacceptable

adverse reactions to the higher dose occur

| Number of subjects in period 1 | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule |
|---|---------------------------------------|--|
| Started | 254 | 259 |
| Completed | 219 | 154 |
| Not completed | 35 | 105 |
| Consent withdrawn by subject | 15 | 33 |
| Discontinuation of IMP, related to COVID-19 | 1 | - |
| Adverse event, non-fatal | 2 | 24 |
| Various reasons | 3 | 9 |
| Not exposed to IMP | 1 | 12 |
| Lost to follow-up | 5 | 1 |
| Lack of efficacy | 8 | 26 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------------------|
| Reporting group title | Delgocitinib Cream 20 mg/g |
|-----------------------|----------------------------|

Reporting group description:

Twice-daily topical application for up to 24 weeks.

Delgocitinib: Cream for topical application 20 mg/g.

There was a possibility to stop treatment after 16 weeks if IGA 0/1 was obtained.

| | |
|-----------------------|---|
| Reporting group title | Alitretinoin Capsules 30 mg Per Capsule |
|-----------------------|---|

Reporting group description:

1 capsule per day for up to 24 weeks

Toctino: 1 capsule Toctino 30 mg per day; optional reduction to 10 mg per day in case unacceptable adverse reactions to the higher dose occur.

There was a possibility to stop treatment after 12 weeks if IGA 0/1 was obtained.

| Reporting group values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | Total |
|---|-------------------------------|--|-------|
| Number of subjects | 254 | 259 | 513 |
| Age categorical Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 45.4 | 44.0 | |
| standard deviation | ± 13.78 | ± 14.56 | - |
| Gender categorical Units: Subjects | | | |
| Female | 167 | 167 | 334 |
| Male | 87 | 92 | 179 |
| Race Units: Subjects | | | |
| American Indian or Alaska Native | 2 | 2 | 4 |
| Asian | 9 | 5 | 14 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 1 |
| Black or African American | 2 | 3 | 5 |
| White | 237 | 240 | 477 |
| More than one race | 1 | 6 | 7 |
| Unknown or Not Reported | 3 | 2 | 5 |

| | | | |
|-------------------------|-----|-----|-----|
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 22 | 14 | 36 |
| Not Hispanic or Latino | 226 | 241 | 467 |
| Unknown or Not Reported | 6 | 4 | 10 |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Delgocitinib Cream 20 mg/g |
| Reporting group description: Twice-daily topical application for up to 24 weeks. Delgocitinib: Cream for topical application 20 mg/g. There was a possibility to stop treatment after 16 weeks if IGA 0/1 was obtained. | |
| Reporting group title | Alitretinoin Capsules 30 mg Per Capsule |
| Reporting group description: 1 capsule per day for up to 24 weeks Toctino: 1 capsule Toctino 30 mg per day; optional reduction to 10 mg per day in case unacceptable adverse reactions to the higher dose occur. There was a possibility to stop treatment after 12 weeks if IGA 0/1 was obtained. | |

Primary: Change in HECSI Score From Baseline to Week 12

| | |
|---|--|
| End point title | Change in HECSI Score From Baseline to Week 12 |
| End point description: The Hand Eczema Severity Index (HECSI) is an instrument used in clinical trials to rate the severity of 6 clinical signs (erythema, infiltration/papulation, vesicles, fissures, scaling, and oedema) and the extent of the lesions in each of the 5 hand regions (fingertips, fingers [except fingertips], palm of hands, back of hands, and wrists) by use of standard scales. The HECSI score will range from 0 (lowest possible score) to 360 (highest possible score). | |
| End point type | Primary |
| End point timeframe: 12 weeks | |

| End point values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | | |
|----------------------------------|----------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 250 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | -67.6 (± 3.37) | -51.5 (± 3.36) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Delgocitinib cream 20 mg/g vs alitretinoin |
| Statistical analysis description: The change from baseline was analysed using an ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing. | |
| Comparison groups | Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per |

| | |
|---|-----------------------|
| | Capsule |
| Number of subjects included in analysis | 499 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | -16.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -23.28 |
| upper limit | -8.86 |

Secondary: HECSI-90 at Week 12

| | |
|--|---------------------|
| End point title | HECSI-90 at Week 12 |
| End point description: | |
| <p>The Hand Eczema Severity Index (HECSI) is an instrument used in clinical trials to rate the severity of 6 clinical signs (erythema, infiltration/papulation, vesicles, fissures, scaling, and oedema) and the extent of the lesions in each of the 5 hand regions (fingertips, fingers [except fingertips], palm of hands, back of hands, and wrists) by use of standard scales. The HECSI score will range from 0 (lowest possible score) to 360 (highest possible score). HECSI-90 is defined as at least 90% improvement in HECSI score from baseline.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| 12 weeks | |

| End point values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | | |
|-----------------------------|----------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 250 | | |
| Units: Participants | 96 | 65 | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Delgocitinib cream 20 mg/g vs alitretinoin |
| Statistical analysis description: | |
| <p>The difference in response rates was analysed using the Cochran-Mantel-Haenszel test stratified by hyperkeratotic/non-hyperkeratotic subtype. Missing data was imputed as non-response. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing.</p> | |
| Comparison groups | Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 499 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 12.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.34 |
| upper limit | 20.78 |

Secondary: IGA-CHE TS at Week 12

| | |
|--|-----------------------|
| End point title | IGA-CHE TS at Week 12 |
| End point description: | |
| The Investigator's Global Assessment for chronic hand eczema (IGA-CHE) is an instrument used in clinical trials to rate the severity of the participant's global chronic hand eczema (CHE) and is based on a 5-point scale ranging from 0 (clear) to 4 (severe). IGA-CHE treatment success (IGA-CHE TS) is defined as an IGA-CHE score of 0 (clear) or 1 (almost clear) with a ≥ 2 -step improvement from baseline. | |
| End point type | Secondary |
| End point timeframe: | |
| 12 weeks | |

| End point values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | | |
|-----------------------------|----------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 250 | 253 | | |
| Units: Participants | 68 | 42 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Delgocitinib cream 20 mg/g vs alitretinoin |
| Statistical analysis description: | |
| The difference in response rates was analysed using the Cochran-Mantel-Haenszel test stratified by hyperkeratotic/non-hyperkeratotic subtype. Missing data was imputed as non-response. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing. | |
| Comparison groups | Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 503 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 10.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.31 |
| upper limit | 17.87 |

Secondary: Change in HESD Itch Score (Weekly Average) From Baseline to Week 12

| | |
|--|---|
| End point title | Change in HESD Itch Score (Weekly Average) From Baseline to Week 12 |
| End point description: | |
| The Hand Eczema Symptom Diary (HESD) is an eDiary in which participants will assess the worst severity of 6 individual signs and symptoms of CHE over the past 24 hours using an 11-point numeric rating scale throughout the trial on a daily basis. This endpoint will only assess the 'itch' component. | |
| End point type | Secondary |
| End point timeframe: | |
| 12 weeks | |

| End point values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | | |
|----------------------------------|----------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 238 | 238 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | -3.0 (± 0.22) | -2.4 (± 0.21) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Delgocitinib cream 20 mg/g vs alitretinoin |
| Statistical analysis description: | |
| The change from baseline was analysed using an ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing. | |
| Comparison groups | Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.005 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.12 |
| upper limit | -0.2 |

Secondary: Change in HESD Pain Score (Weekly Average) From Baseline to Week 12

| | |
|------------------------|--|
| End point title | Change in HESD Pain Score (Weekly Average) From Baseline to Week 12 |
| End point description: | The Hand Eczema Symptom Diary (HESD) is an eDiary in which participants will assess the worst severity of 6 individual signs and symptoms of CHE over the past 24 hours using an 11-point numeric rating scale throughout the trial on a daily basis. This endpoint will only assess the 'pain' component. |
| End point type | Secondary |
| End point timeframe: | 12 weeks |

| End point values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | | |
|----------------------------------|----------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 238 | 238 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | -2.9 (± 0.23) | -2.3 (± 0.23) | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Delgocitinib cream 20 mg/g vs alitretinoin |
| Statistical analysis description: | The change from baseline was analysed using an ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing. |
| Comparison groups | Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 476 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.018 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.08 |
| upper limit | -0.1 |

Secondary: AUC of HECSI-90 From Baseline up to Week 24

| | |
|---|---|
| End point title | AUC of HECSI-90 From Baseline up to Week 24 |
| End point description: | |
| <p>The Hand Eczema Severity Index (HECSI) is an instrument used in clinical trials to rate the severity of 6 clinical signs (erythema, infiltration/papulation, vesicles, fissures, scaling, and oedema) and the extent of the lesions in each of the 5 hand regions (fingertips, fingers [except fingertips], palm of hands, back of hands, and wrists) by use of standard scales. The HECSI score will range from 0 (lowest possible score) to 360 (highest possible score). HECSI-90 is defined as at least 90% improvement in HECSI score from baseline. The area under the curve (AUC) at participant level will be determined as follows: 1 will be assigned when response is observed and 0 otherwise. The AUC is interpreted as number of days with 90% reduction in HECSI score until Week 24.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| 24 weeks | |

| End point values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | | |
|----------------------------------|----------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 250 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | 51.1 (± 4.11) | 43.5 (± 4.22) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Delgocitinib cream 20 mg/g vs alitretinoin |
| Statistical analysis description: | |
| <p>The AUC was analysed using a robust ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing.</p> | |
| Comparison groups | Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 499 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | 14.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.81 |
| upper limit | 22.86 |

Secondary: AUC of Change From Baseline in DLQI Score up to Week 24

| | |
|---|---|
| End point title | AUC of Change From Baseline in DLQI Score up to Week 24 |
| End point description: | |
| <p>The Dermatology Life Quality Index (DLQI) is a validated questionnaire consisting of 10 items addressing the participant's perception of the impact of their skin disease on different aspects of their quality of life over the last week. The DLQI score is the sum of the 10 items (score ranging from 0 to 30). The area under the curve (AUC) at patient level will be determined from the change from baseline in DLQI score estimated piecewise from Week 0 to Week 24. Differences will be analysed with opposite sign to interpret positive area as improvement in scores and negative area as worsening.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| 24 weeks | |

| End point values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | | |
|----------------------------------|----------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 230 | 236 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | 1124.7 (± 61.37) | 790.7 (± 62.67) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Delgocitinib cream 20 mg/g vs alitretinoin |
| Statistical analysis description: | |
| <p>The AUC was analysed using a robust ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing.</p> | |
| Comparison groups | Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 466 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | 334 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 195.69 |
| upper limit | 472.26 |

Secondary: Change in HECSI Score From Baseline to Week 24

| | |
|---|--|
| End point title | Change in HECSI Score From Baseline to Week 24 |
| End point description: | |
| The Hand Eczema Severity Index (HECSI) is an instrument used in clinical trials to rate the severity of 6 clinical signs (erythema, infiltration/papulation, vesicles, fissures, scaling, and oedema) and the extent of the lesions in each of the 5 hand regions (fingertips, fingers [except fingertips], palm of hands, back of hands, and wrists) by use of standard scales. The HECSI score will range from 0 (lowest possible score) to 360 (highest possible score). | |
| End point type | Secondary |
| End point timeframe: | |
| 24 weeks | |

| End point values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | | |
|----------------------------------|----------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 250 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard error) | -69.6 (± 3.78) | -45.1 (± 3.77) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Delgocitinib cream 20 mg/g vs alitretinoin |
| Statistical analysis description: | |
| The change from baseline was analysed using an ANCOVA model with effects of treatment group, hyperkeratotic/non-hyperkeratotic subtype and baseline value of the score. Missing data was imputed with WOCF. Data after initiation of rescue treatment or permanent discontinuation of IMP was treated as missing. | |
| Comparison groups | Delgocitinib Cream 20 mg/g v Alitretinoin Capsules 30 mg Per Capsule |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 499 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[1] |
| P-value | < 0.001 ^[2] |
| Method | ANCOVA |
| Parameter estimate | Mean difference (net) |
| Point estimate | -24.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -32.55 |
| upper limit | -16.36 |

Notes:

[1] - Non-inferiority (margin=10) was tested before superiority.

[2] - Non-inferiority (margin=10) p-value <0.001, superiority p-value <0.001

Secondary: Number of Treatment-emergent AEs From Baseline up to Week 26

| | |
|-----------------|--|
| End point title | Number of Treatment-emergent AEs From Baseline up to Week 26 |
|-----------------|--|

End point description:

An adverse event (AE) will be considered treatment emergent if started after the first application of investigational medicinal product (IMP), or if started before the first application of IMP and worsened in severity after first dose of IMP.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

26 weeks

| End point values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | | |
|-----------------------------|----------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 253 | 247 | | |
| Units: events | 280 | 620 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Treatment-emergent SAEs From Baseline up to Week 26

| | |
|-----------------|---|
| End point title | Number of Treatment-emergent SAEs From Baseline up to Week 26 |
|-----------------|---|

End point description:

A serious adverse event (SAE) will be considered treatment emergent if started after the first application of investigational medicinal product (IMP), or if started before the first application of IMP and worsened in severity after first dose of IMP.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

26 weeks

| End point values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | | |
|-----------------------------|----------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 253 | 247 | | |
| Units: events | 5 | 12 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of AEs Leading to IMP Discontinuation up to Week 24

| | | |
|---|--|--|
| End point title | Number of AEs Leading to IMP Discontinuation up to Week 24 | |
| End point description: | | |
| The investigational medicinal product (IMP) will be discontinued permanently in case of an AE that, in the opinion of the investigator or sponsor's medical expert, contraindicates further dosing. The investigator will assess the relationship between investigational medicinal product (IMP) and the adverse event (AE). | | |
| End point type | Secondary | |
| End point timeframe: | | |
| 24 weeks | | |

| End point values | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | | |
|-----------------------------|----------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 253 | 247 | | |
| Units: events | 4 | 44 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to Week 24

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------------|
| Reporting group title | Delgocitinib Cream 20 mg/g |
|-----------------------|----------------------------|

Reporting group description:

Twice-daily topical application for up to 24 weeks.

Delgocitinib: Cream for topical application 20 mg/g.

There was a possibility to stop treatment after 12 or 16 weeks if IGA 0/1 was obtained.

| | |
|-----------------------|---|
| Reporting group title | Alitretinoin Capsules 30 mg Per Capsule |
|-----------------------|---|

Reporting group description:

1 capsule per day for up to 24 weeks

Toctino: 1 capsule Toctino 30 mg per day; optional reduction to 10 mg per day in case unacceptable adverse reactions to the higher dose occur

| Serious adverse events | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | |
|---|-------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 253 (1.98%) | 12 / 247 (4.86%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Investigations | | | |
| Blood potassium increased | | | |
| subjects affected / exposed | 1 / 253 (0.40%) | 0 / 247 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 253 (0.40%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign salivary gland neoplasm | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Deep vein thrombosis postoperative | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastrointestinal inflammation | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Prostatitis | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Mediastinal cyst | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 253 (0.00%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Hand dermatitis | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 253 (0.40%) | 0 / 247 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 1 / 253 (0.40%) | 0 / 247 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 1 / 253 (0.40%) | 0 / 247 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 253 (0.00%) | 1 / 247 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | Delgocitinib Cream 20 mg/g | Alitretinoin Capsules 30 mg Per Capsule | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 58 / 253 (22.92%) | 143 / 247 (57.89%) | |
| Investigations Blood triglycerides increased subjects affected / exposed occurrences (all) | 2 / 253 (0.79%) 2 | 7 / 247 (2.83%) 8 | |
| Vascular disorders Flushing subjects affected / exposed occurrences (all) | 0 / 253 (0.00%) 0 | 5 / 247 (2.02%) 6 | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Migraine subjects affected / exposed occurrences (all) | 1 / 253 (0.40%) 1 10 / 253 (3.95%) 19 2 / 253 (0.79%) 2 | 6 / 247 (2.43%) 6 79 / 247 (31.98%) 113 6 / 247 (2.43%) 7 | |
| Eye disorders Dry eye subjects affected / exposed occurrences (all) | 0 / 253 (0.00%) 0 | 7 / 247 (2.83%) 7 | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Lip dry subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) | 0 / 253 (0.00%) 0 0 / 253 (0.00%) 0 1 / 253 (0.40%) 1 | 5 / 247 (2.02%) 5 8 / 247 (3.24%) 8 14 / 247 (5.67%) 15 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|-------------------------|-------------------------|--|
| Epistaxis subjects affected / exposed occurrences (all) | 1 / 253 (0.40%) 1 | 5 / 247 (2.02%) 6 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis atopic subjects affected / exposed occurrences (all) | 1 / 253 (0.40%) 1 | 5 / 247 (2.02%) 5 | |
| Eczema subjects affected / exposed occurrences (all) | 2 / 253 (0.79%) 2 | 5 / 247 (2.02%) 6 | |
| Erythema subjects affected / exposed occurrences (all) | 1 / 253 (0.40%) 1 | 9 / 247 (3.64%) 10 | |
| Dry skin subjects affected / exposed occurrences (all) | 3 / 253 (1.19%) 3 | 9 / 247 (3.64%) 9 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain subjects affected / exposed occurrences (all) | 2 / 253 (0.79%) 2 | 6 / 247 (2.43%) 6 | |
| Infections and infestations | | | |
| COVID-19 subjects affected / exposed occurrences (all) | 5 / 253 (1.98%) 5 | 9 / 247 (3.64%) 9 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 30 / 253 (11.86%) 38 | 34 / 247 (13.77%) 46 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 6 / 253 (2.37%) 8 | 8 / 247 (3.24%) 8 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 253 (0.40%) 1 | 10 / 247 (4.05%) 11 | |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 253 (0.00%) | 9 / 247 (3.64%) | |
| occurrences (all) | 0 | 10 | |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 3 / 253 (1.19%) | 6 / 247 (2.43%) | |
| occurrences (all) | 3 | 7 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 08 April 2022 | The protocol was amended in order to implement changes from local amendments (UK and Canada). |
| 24 June 2022 | The protocol was amended in order to add the patient reported outcomes PGI-S and PGI-C. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported