# Clinical trial results:
# Aprepitant – effect and safety in treatment of atopic dermatitis

## Summary

| | |
|---|---|
| EudraCT number | 2013-002029-40 |
| Trial protocol | SE |
| Global end of trial date | 31 March 2015 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 10 April 2021 |
| First version publication date | 10 April 2021 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 1001 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Karolinska Institutet |
| Sponsor organisation address | 17177, Stockholm, Sweden, |
| Public contact | Dep of dermatology, Karolinska Univ, Karolinska institutet, klas.nordlind@karolinska.se |
| Scientific contact | Dep of dermatology, Karolinska Univ, Karolinska institutet, klas.nordlind@karolinska.se |

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 March 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 March 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 March 2015 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To investigate the effect of Aprepitant (Emend) on atpoic dermatitis and prutitus.

Protection of trial subjects:

The protocol was approved by the local ethics committee and by the Medical Products Agency. Safety was assessed by recording adverse events at the second visit. The patients could also contact the clinic at any time during the treatment period if they observed any suspected side-effects.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 October 2013 |
| 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 | Sweden: 39 |
| Worldwide total number of subjects | 39 |
| EEA total number of subjects | 39 |

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) | 39 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The patients were recruited from dermatology clinics in the Stockholm area and examined at the Department of Dermatology, Karolinska University Hospital, Solna, Stockholm, Sweden, between October 2013 to March 2015.

### Pre-assignment

Screening details:

Patients had a moderate–severe (SCORAD > 20) AD and diagnosis was determined according to the Williams criteria. Exclusion criteria: other concomitant diseases or medications (except for contraceptives), skin type 5–6 according to Fitzpatrick, skin infections, pregnancy, breast-feeding. The washout period for prior systemic treatment was 2 months.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Treatment group |

Arm description:

The patients received 80 mg/day of aprepitant orally for 7 days in addition to standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer.
21 participants were enrolled, but 2 of those patients interrupted study treatment due to adverse events, specifically experienced transient side-effects, such as dizziness, impotence, headache (1 case) and lack of reactivity, dyspnoea and palpitations (the second case). Those 2 patients are not included in the baseline characteristics or analysis that is presented here.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Aprepitant |
| Investigational medicinal product code | SUB20017 |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

80 mg/day of aprepitant orally for 7 days.

| | |
|---|---|
| Investigational medicinal product name | Hydrocortisone butyrate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Topical use |

Dosage and administration details:

Standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden).

| | |
|---|---|
| **Arm title** | Control group |

Arm description:

Standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer.

| | |
|---|---|
| Arm type | Standard topical treatment |

| | |
|---|---|
| Investigational medicinal product name | Hydrocortisone butyrate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Topical use |

Dosage and administration details:

Standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden).

| **Number of subjects in period 1** | Treatment group | Control group |
|---|---|---|
| Started | 19 | 20 |
| Completed | 19 | 20 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Treatment group |
| Reporting group description: | |
| The patients received 80 mg/day of aprepitant orally for 7 days in addition to standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer.<br>21 participants were enrolled, but 2 of those patients interrupted study treatment due to adverse events, specifically experienced transient side-effects, such as dizziness, impotence, headache (1 case) and lack of reactivity, dyspnoea and palpitations (the second case). Those 2 patients are not included in the baseline characteristics or analysis that is presented here. | |
| Reporting group title | Control group |
| Reporting group description: | |
| Standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer. | |

| Reporting group values | Treatment group | Control group | Total |
|---|---|---|---|
| Number of subjects | 19 | 20 | 39 |
| Age categorical<br>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) | 19 | 20 | 39 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 30.8 | 29.3 | |
| standard deviation | ± 8.4 | ± 9.2 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 7 | 16 | 23 |
| Male | 12 | 4 | 16 |
| OSCORAD | | | |
| OSCORAD = objective SCORing of Atopic Dermatitis | | | |
| Units: Score | | | |
| arithmetic mean | 40.5 | 37.0 | |
| standard deviation | ± 12.0 | ± 11.3 | - |
| Visual analogue scale<br>Units: Score | | | |
| arithmetic mean | 5.5 | 6.7 | |
| standard deviation | ± 2.1 | ± 2.2 | - |
| IgE levels<br>Units: kU/l | | | |

| | | | |
|---|---|---|---|
| arithmetic mean | 903.7 | 876.5 | |
| standard deviation | ± 1.391 | ± 1.934 | - |
| Scratching movements | | | |
| Units: Registered number daily | | | |
| arithmetic mean | 77.3 | 65.0 | |
| standard deviation | ± 97.9 | ± 100.9 | - |
| Montgomery Åsberg Depression Rating Scale | | | |
| Units: Score | | | |
| arithmetic mean | 5.6 | 9.3 | |
| standard deviation | ± 4.9 | ± 8.9 | - |
| Hospital Anxiety and Depressive scale | | | |
| Units: Score | | | |
| arithmetic mean | 3.4 | 6.6 | |
| standard deviation | ± 4.1 | ± 4.8 | - |
| Substance P | | | |
| Units: pmol/g | | | |
| arithmetic mean | 98.7 | 105.6 | |
| standard deviation | ± 54.4 | ± 46.5 | - |

## End points

### End points reporting groups

| Reporting group title | Treatment group |
|---|---|
| Reporting group description: | |
| The patients received 80 mg/day of aprepitant orally for 7 days in addition to standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer.<br>21 participants were enrolled, but 2 of those patients interrupted study treatment due to adverse events, specifically experienced transient side-effects, such as dizziness, impotence, headache (1 case) and lack of reactivity, dyspnoea and palpitations (the second case). Those 2 patients are not included in the baseline characteristics or analysis that is presented here. | |
| Reporting group title | Control group |
| Reporting group description: | |
| Standard topical treatment with a moderately strong steroid cream (hydrocortisone butyrate; Locoid®, LEO Pharma AB, Malmö, Sweden) and a moisturizer. | |

### Primary: OSCORAD Post-treatment

| End point title | OSCORAD Post-treatment |
|---|---|
| End point description: | |
| Objective SCORing of Atopic Dermatitis, arbitrary units (range 0–83) | |
| End point type | Primary |
| End point timeframe: | |
| Day 7 of treatment. | |

| End point values | Treatment group | Control group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | 32.0 (± 11.2) | 26.7 (± 14.7) | | |

### Statistical analyses

| Statistical analysis title | Difference OSCORAD post-treatment |
|---|---|
| Statistical analysis description: | |
| Difference in OSCORAD between treatment and control after 7 days of treatment. | |
| Comparison groups | Treatment group v Control group |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | t-test, 2-sided |

## Secondary: Visual analogue scale Post-treatment

| End point title | Visual analogue scale Post-treatment |
|---|---|
| End point description: | |
| Visual analogue scale, arbitrary units (range 0–10). | |
| End point type | Secondary |
| End point timeframe: | |
| Day 7 of treatment. | |

| End point values | Treatment group | Control group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | 3.8 (± 2.2) | 4.1 (± 3.0) | | |

### Statistical analyses

| Statistical analysis title | Difference VAS post-treatment |
|---|---|
| Statistical analysis description: | |
| Difference in Visual Analogue Scale between treatment and control after 7 days of treatment. | |

| Comparison groups | Treatment group v Control group |
|---|---|
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | t-test, 2-sided |

## Secondary: IgE levels Post-treatment

| End point title | IgE levels Post-treatment |
|---|---|
| End point description: | |

| End point type | Secondary |
|---|---|
| End point timeframe: | |
| Day 7 of treatment. | |

| End point values | Treatment group | Control group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: kE/l | | | | |
| arithmetic mean (standard deviation) | 937.9 (± 1.403) | 821.1 (± 1.754) | | |

**Statistical analyses**

| Statistical analysis title | Difference IgE levels post treatment |
|---|---|
| Statistical analysis description:<br>Difference in IgE levels between treatment and control after 7 days of treatment. | |
| Comparison groups | Treatment group v Control group |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Wilcoxon (Mann-Whitney) |

**Secondary: Scratching movements Post-treatment**

| End point title | Scratching movements Post-treatment |
|---|---|
| End point description: | |
| End point type | Secondary |
| End point timeframe:<br>Day 7 of treatment. | |

| End point values | Treatment group | Control group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: Registered number daily | | | | |
| arithmetic mean (standard deviation) | 48.3 (± 62.6) | 34.7 (± 45.0) | | |

**Statistical analyses**

| Statistical analysis title | Difference Scratching movements post-treatment |
|---|---|
| Statistical analysis description:<br>Difference in Scratching movements between treatment and control after 7 days of treatment. | |
| Comparison groups | Treatment group v Control group |

| | |
|---|---|
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | t-test, 2-sided |

## Secondary: Montgomery Åsberg Depression Rating Scale Post-treatment

| | |
|---|---|
| End point title | Montgomery Åsberg Depression Rating Scale Post-treatment |

End point description:

Montgomery Åsberg Depression Rating Scale, arbitrary units (range 0–54).

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

End point timeframe:

Day 7 of treatment.

| End point values | Treatment group | Control group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | 4.0 (± 5.3) | 6.5 (± 5.9) | | |

### Statistical analyses

| Statistical analysis title | Difference Depression scale post-treatment |
|---|---|

Statistical analysis description:

Difference in Montgomery Åsberg Depression Rating Scale between treatment and control after 7 days of treatment.

| | |
|---|---|
| Comparison groups | Treatment group v Control group |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | t-test, 2-sided |

## Secondary: HAD Post-treatment

| | |
|---|---|
| End point title | HAD Post-treatment |

End point description:

Hospital Anxiety and Depressive scale, arbitrary units (range 0–21).

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

End point timeframe:

Day 7 of treatment.

| End point values | Treatment group | Control group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | 3.5 (± 3.2) | 4.8 (± 3.7) | | |

**Statistical analyses**

| Statistical analysis title | Difference HAD post-treatment |
|---|---|
| Statistical analysis description:<br>Difference in HAD between treatment and control after 7 days of treatment. | |
| Comparison groups | Treatment group v Control group |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | t-test, 2-sided |

**Secondary: Substance P Post-treatment**

| End point title | Substance P Post-treatment |
|---|---|
| End point description: | |
| End point type | Secondary |
| End point timeframe:<br>Day 7 of treatment. | |

| End point values | Treatment group | Control group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: pmol/g | | | | |
| arithmetic mean (standard deviation) | 97.6 (± 50.3) | 91.0 (± 32.7) | | |

**Statistical analyses**

| Statistical analysis title | Difference Substance P post-treatment |
|---|---|

Statistical analysis description:

Difference in Substance P between treatment and control after 7 days of treatment.

| | |
|---|---|
| Comparison groups | Treatment group v Control group |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | t-test, 2-sided |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Study start to day 7 of treatment.

Adverse event reporting additional description:

Recording of adverse events was done at the second visit (day 7 of treatment). The patients could also contact the clinic at any time during the treatment period if they observed any suspected side-effects. No frequency threshold was used, as all adverse events that arise were reported.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | ICD |
| Dictionary version | 10-SE |

### Reporting groups

| | |
|---|---|
| Reporting group title | Treatment group |
| Reporting group description: - | |
| Reporting group title | Control group |

Reporting group description: -

| Serious adverse events | Treatment group | Control group | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 20 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | Treatment group | Control group | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 13 / 21 (61.90%) | 0 / 20 (0.00%) | |
| Product issues | | | |
| Headache, fatigue, dizziness, elevated liver enzymes, palpitations, dyspnoea... | Additional description: 13/21 participants in treatment reported trancient AE: headache, fatigue, dizziness, elevated liver enzymes, palpitations, dyspnoea, altered ability to react, obstipation, stomach-ache, periocular dermatitis, erectile dysfunction, lack of reactivity. | | |
| subjects affected / exposed | 13 / 21 (61.90%) | 0 / 20 (0.00%) | |
| occurrences (all) | 13 | 0 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Patients in this study generally did not have worse than moderate pruritus, which may have had an impact on the results. There were different sex distributions in the 2 groups, thus it cannot be excluded that aprepitant exerts sex-specific effects.

Notes:

## Online references

http://www.ncbi.nlm.nih.gov/pubmed/29182791