



Clinical trial results:

RANDOMISED, PLACEBO-CONTROLLED, DOUBLE-BLIND EFFICACY STUDY OF THE EMOLLIENT V0034CR IN ADDITION TO A MODERATELY POTENT CORTICOSTEROID IN THE ACUTE PHASE OF TREATMENT OF ATOPIC DERMATITIS IN INFANTS.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2005-002803-18 |
| Trial protocol | FR FI EE LV DE |
| Global end of trial date | 22 June 2006 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 11 May 2019 |
| First version publication date | 21 November 2018 |
| Version creation reason | • Correction of full data set Add full data set |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | V00034CR3041B |
|-----------------------|---------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Pierre Fabre Médicament |
| Sponsor organisation address | 45, Place Abel Gance, Boulogne, France, 92100 |
| Public contact | Alain DELARUE, M.D, Institut de recherche Pierre Fabre, +33 5.61.73.73.09, alain.delarue@pierre-fabre.com |
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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? | Yes |
| 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 | 25 September 2006 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 June 2006 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 June 2006 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the short term efficacy of the emollient V0034CR in addition to a moderately potent topical corticosteroid in the acute phase of treatment of atopic dermatitis, by reducing the disease severity.

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki and subsequent amendments thereto, the Good Clinical Practices (CPMP/ICH/135/95) and local legal regulations. An information letter was given to the parent(s) or guardian(s) of each patient to assist them with their decision. Parent(s) or guardian(s) signed a written consent form, which described the details and constraints of the study, as well as the right to withdraw at any point, anonymity, and the right to access the data. The parent(s) or guardian(s), the investigator each had a copy of the signed consent form, as well as the sponsor for which it was sealed in an envelope to maintain confidentiality.

Background therapy:

Corticosteroid treatment was used by the parents on the lesions until complete resolution of the inflammatory signs, mainly the resolution of erythema. For their child's body and scalp washing, parents used the foaming gel Klorane* provided by the sponsor (one 250 mL bottle for 3 weeks; batch F727; expiry date: 10/2007).

Way of life and cosmetic cares should not be changed. Food supplements that could modify the skin properties as well as swimming pool were not allowed.

Evidence for comparator:

Due to the natural evolution of the disease, the parallel groups design was the only one adapted to the study purpose. Very few emollients have been evaluated double blind, thus contributing to the lack of proofs of their efficacy. In order to evaluate the benefit of the emollient V0034CR, placebo was mandatory and justified. Furthermore, the use of a placebo was ethically acceptable since all patients received an active treatment by corticosteroids for treating inflammatory signs.

| | |
|---|------------------|
| Actual start date of recruitment | 19 November 2005 |
| 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 | Poland: 81 |
| Country: Number of subjects enrolled | Romania: 17 |
| Country: Number of subjects enrolled | Estonia: 88 |
| Country: Number of subjects enrolled | Finland: 3 |
| Country: Number of subjects enrolled | France: 28 |
| Country: Number of subjects enrolled | Germany: 23 |
| Country: Number of subjects enrolled | Latvia: 80 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 320 |
| EEA total number of subjects | 320 |

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) | 320 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 322 patients were included in the study and randomized in the two treatment groups (19 centres in 7 countries). Two patients (Vehicle group) prematurely withdrew without any treatment application and any evaluation after inclusion.

Pre-assignment

Screening details:

Patients, male or female infants, aged between 3 and 24 months, presenting with atopic dermatitis according to the diagnostic criteria of the UK Working party; with SCORAD 20 to 50; whose xerosis was > 1; requiring topical corticosteroid treatment, moderately potent, on the body and/or the face were screened.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Treatment period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Blinding implementation details:

The study products as well as their packaging and labelling were rigorously identical. The investigator, the hospital pharmacist if appropriate, the study monitor had a set of blind sealed envelopes corresponding to the treatments received and given to the patients. An envelope could be opened only in case of emergency and only if the knowledge of the product having been received was necessary to start appropriate treatment.

Arms

| | |
|--|---------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Vehicle arm |
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | Vehicle cream |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Cutaneous use |

Dosage and administration details:

When inflammatory lesions were present (disease exacerbation phases): application on the whole body, in the evening. When inflammatory lesions had disappeared: application on the whole body, morning and evening, with a gentle massage until complete penetration. Applications of the study product were done in thin layers with a sufficient amount of cream.

| | |
|--|--------------------|
| Arm title | V0034CR arm |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | V0034 CR 01B cream |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Cutaneous use |

Dosage and administration details:

When inflammatory lesions were present (disease exacerbation phases): application on the whole body, in the evening, with a gentle massage until complete penetration.

When inflammatory lesions had disappeared: application on the whole body, morning and evening.

Applications of the study product were done in thin layers with a sufficient amount of cream by a gentle massage until complete penetration.

| Number of subjects in period 1 | Vehicle arm | V0034CR arm |
|---------------------------------------|-------------|-------------|
| Started | 157 | 163 |
| Completed | 153 | 160 |
| Not completed | 4 | 3 |
| Adverse events | 1 | 1 |
| Lost to follow-up | 1 | - |
| Worsening | 1 | 1 |
| Parent's decision | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|-------------|
| Reporting group title | Vehicle arm |
| Reporting group description: - | |
| Reporting group title | V0034CR arm |
| Reporting group description: - | |

| Reporting group values | Vehicle arm | V0034CR arm | Total |
|--|----------------|----------------|-------|
| Number of subjects | 157 | 163 | 320 |
| Age categorical Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 157 | 163 | 320 |
| Age continuous Units: months arithmetic mean standard deviation | 11.3 ± 5.8 | 12.3 ± 6.0 | - |
| Gender categorical Units: Subjects | | | |
| Female | 60 | 72 | 132 |
| Male | 97 | 91 | 188 |
| Family history of atopy Units: Subjects | | | |
| Yes | 116 | 123 | 239 |
| No | 41 | 40 | 81 |
| IGA score at baseline Units: Subjects | | | |
| Mild disease | 63 | 65 | 128 |
| Moderate disease | 92 | 93 | 185 |
| Severe disease | 2 | 5 | 7 |
| Height Units: cm arithmetic mean standard deviation | 75.3 ± 8.8 | 75.3 ± 8.7 | - |
| Weight Units: kg arithmetic mean standard deviation | 9.69 ± 2.37 | 9.85 ± 2.33 | - |
| Age of first cutaneous lesions Units: months arithmetic mean standard deviation | 3.5 ± 2.7 | 4.0 ± 3.5 | - |
| SCORAD at baseline Units: not applicable arithmetic mean standard deviation | 34.0 ± 6.9 | 33.5 ± 7.4 | - |

End points

End points reporting groups

| | |
|--------------------------------|-------------|
| Reporting group title | Vehicle arm |
| Reporting group description: - | |
| Reporting group title | V0034CR arm |
| Reporting group description: - | |

Primary: Evolution of SCORAD between baseline and D22 (or endpoint)

| | |
|------------------------|---|
| End point title | Evolution of SCORAD between baseline and D22 (or endpoint) |
| End point description: | The change in SCORAD between D1 and D22 was compared between treatment groups by a covariance analysis using the baseline SCORAD as a covariate with the treatment and the centre effects. Drop-outs patients were included in the analyses on the APTe population except for two patients with no available assessment of the main efficacy criterion. If the evaluation at Visit 4 (D22) was missing, it was replaced by the last evaluation on treatment (Last Observation Carried Forward). |
| End point type | Primary |
| End point timeframe: | The SCORAD score was measured at baseline (Day 1) and at Day 22. |

| End point values | Vehicle arm | V0034CR arm | | |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 157 | 163 | | |
| Units: not applicable | | | | |
| arithmetic mean (standard deviation) | -22.06 (\pm 0.7) | -23.07 (\pm 0.7) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Primary analysis |
| Statistical analysis description: | Covariance analysis using baseline as a covariate with the treatment and the centre effects. |
| Comparison groups | V0034CR arm v Vehicle arm |
| Number of subjects included in analysis | 320 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2145 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the visit 2 (D8 +/- 1) to Visit 4 (D22 +/- 1).

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

Dictionary used

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

| | |
|--------------------|-----|
| Dictionary version | 7.1 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Vehicle arm |
|-----------------------|-------------|

Reporting group description: -

| | |
|-----------------------|--------------|
| Reporting group title | V0034 CR arm |
|-----------------------|--------------|

Reporting group description: -

| Serious adverse events | Vehicle arm | V0034 CR arm | |
|---|-----------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 163 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Gastrointestinal disorders | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 163 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 0.6 %

| Non-serious adverse events | Vehicle arm | V0034 CR arm | |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 27 / 157 (17.20%) | 31 / 163 (19.02%) | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 157 (2.55%) | 0 / 163 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Hyperthermia | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 163 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|--|----------------------|----------------------|--|
| Unevaluable event subjects affected / exposed occurrences (all) | 1 / 157 (0.64%) 1 | 0 / 163 (0.00%) 0 | |
| Eye disorders conjunctivitis subjects affected / exposed occurrences (all) | 0 / 157 (0.00%) 0 | 1 / 163 (0.61%) 1 | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 4 / 157 (2.55%) 4 | 0 / 163 (0.00%) 0 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 1 / 157 (0.64%) 1 | 0 / 163 (0.00%) 0 | |
| Constipation subjects affected / exposed occurrences (all) | 0 / 157 (0.00%) 0 | 1 / 163 (0.61%) 1 | |
| Enterocolitis subjects affected / exposed occurrences (all) | 1 / 157 (0.64%) 1 | 0 / 163 (0.00%) 0 | |
| Toothache subjects affected / exposed occurrences (all) | 1 / 157 (0.64%) 1 | 0 / 163 (0.00%) 0 | |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 157 (0.00%) 0 | 1 / 163 (0.61%) 1 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 4 / 157 (2.55%) 4 | 3 / 163 (1.84%) 3 | |
| Rhinitis allergic subjects affected / exposed occurrences (all) | 1 / 157 (0.64%) 1 | 1 / 163 (0.61%) 1 | |
| Skin and subcutaneous tissue disorders Dermatitis atopic | | | |

| | | | |
|---|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 157 (0.00%) 0 | 1 / 163 (0.61%) 1 | |
| Intertrigo subjects affected / exposed occurrences (all) | 1 / 157 (0.64%) 1 | 0 / 163 (0.00%) 0 | |
| Infections and infestations | | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 7 / 157 (4.46%) 7 | 6 / 163 (3.68%) 6 | |
| Viral infection subjects affected / exposed occurrences (all) | 4 / 157 (2.55%) 4 | 3 / 163 (1.84%) 3 | |
| Rhinitis subjects affected / exposed occurrences (all) | 0 / 157 (0.00%) 0 | 5 / 163 (3.07%) 5 | |
| Bronchitis subjects affected / exposed occurrences (all) | 1 / 157 (0.64%) 1 | 1 / 163 (0.61%) 1 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 157 (0.00%) 0 | 2 / 163 (1.23%) 2 | |
| Varicella subjects affected / exposed occurrences (all) | 0 / 157 (0.00%) 0 | 2 / 163 (1.23%) 2 | |
| Acute tonsillitis subjects affected / exposed occurrences (all) | 0 / 157 (0.00%) 0 | 1 / 163 (0.61%) 1 | |
| Bronchiolitis subjects affected / exposed occurrences (all) | 0 / 157 (0.00%) 0 | 1 / 163 (0.61%) 1 | |
| bronchitis acute subjects affected / exposed occurrences (all) | 1 / 157 (0.64%) 1 | 0 / 163 (0.00%) 0 | |
| Cystitis subjects affected / exposed occurrences (all) | 0 / 157 (0.00%) 0 | 1 / 163 (0.61%) 1 | |

| | | | |
|-----------------------------------|-----------------|-----------------|--|
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 163 (0.61%) | |
| occurrences (all) | 0 | 1 | |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 163 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 163 (0.61%) | |
| occurrences (all) | 0 | 1 | |
| Otitis media | | | |
| subjects affected / exposed | 1 / 157 (0.64%) | 0 / 163 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 163 (0.61%) | |
| occurrences (all) | 0 | 1 | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 163 (0.61%) | |
| occurrences (all) | 0 | 1 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 163 (0.61%) | |
| occurrences (all) | 0 | 1 | |
| Viral diarrhoea | | | |
| subjects affected / exposed | 0 / 157 (0.00%) | 1 / 163 (0.61%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 07 September 2005 | Modification of the Subject information leaflet and consent form (French version), following the CCPPRB remarks (during the session of August 17, 2005) |
| 29 November 2005 | Modification of the dates of study schedule |
| 29 November 2005 | Precisions for some non inclusion criteria, conditions of use of Locapred and withdrawal conditions (Germany) |
| 27 February 2006 | Modification of the dates of study schedule |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported