

**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	<ul style="list-style-type: none">• Correction of full data setAdd full data set

Trial information**Trial identification**

Sponsor protocol code	V00034CR3041B
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pierre Fabre Médicament
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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	11.3	12.3	-
standard deviation	± 5.8	± 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	75.3	75.3	-
standard deviation	± 8.8	± 8.7	-
Weight			
Units: kg			
arithmetic mean	9.69	9.85	-
standard deviation	± 2.37	± 2.33	-
Age of first cutaneous lesions			
Units: months			
arithmetic mean	3.5	4.0	-
standard deviation	± 2.7	± 3.5	-
SCORAD at baseline			
Units: not applicable			
arithmetic mean	34.0	33.5	-
standard deviation	± 6.9	± 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	7.1
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Reporting groups

Reporting group title	Vehicle arm
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Reporting group description: -

Reporting group title	V0034 CR arm
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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