



## Clinical trial results:

### Impact of the V0034CR 01B emollient on atopic dermatitis symptoms in children. A randomised, placebo-controlled, parallel-groups, double-blind study

#### Summary

EudraCT number	2008-003485-25
Trial protocol	LT FR EE DE PL LV IT
Global end of trial date	23 May 2009

#### Results information

Result version number	v1 (current)
This version publication date	01 December 2016
First version publication date	01 December 2016
Summary attachment (see zip file)	synopsis CSR V00034 CR 4 02 1B (Synopsis rapport V00034CR402 01B CSR Version 1 220110.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	V00034 CR 402 1B
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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
Sponsor organisation address	45, Place Abel Gance, Boulogne, France, 92100
Public contact	Elisabeth COPPEL , Pierre Fabre Medicament IRPF 3 av Hubert Curien-31100 Toulouse, elisabeth.coppel@pierre-fabre.com
Scientific contact	Elisabeth COPPEL , Pierre Fabre Medicament IRPF 3 av Hubert Curien-31100 Toulouse, elisabeth.coppel@pierre-fabre.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?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 January 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 May 2009
Global end of trial reached?	Yes
Global end of trial date	23 May 2009
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate, in children presenting with atopic dermatitis, the impact of a daily treatment by the emollient V0034CR 01B on the disease symptoms: evolution of the POEM (Patient-Oriented Eczema Measure) score.

Protection of trial subjects:

The trial was conducted according to Good Clinical Practices (CPMP/ICH/135/95), ICH E11, the Declaration of Helsinki and its subsequent amendments thereto and local legal regulations.

Due to the absence of risk with the products and the study procedures, patients were allowed to participate to another clinical trial after study termination.

The investigator registered side effects at each visit during clinical examination and questioning the parent(s)/guardian(s). At any time, if the patient's medical status required any other therapeutic (other than stated in protocol), the investigator could perform a final visit with a complete evaluation, then exclude the patient from the study and prescribe the appropriate treatment.

Background therapy:

During disease exacerbation phases (presence of inflammatory lesions), a moderately potent corticosteroid cream (Locapred®, desonide 0.1%) was allowed, used as follows:

- Locapred®: once a day (preferably in the evening) only on the lesions of the body and the face, Locapred® was used until complete resolution of the inflammatory signs. Conditions of use of Locapred® were explained to the parents.

\* When necessary, other treatments of atopic dermatitis signs/symptoms (antihistamines, antiseptics, zinc creams / ointments) were allowed and carefully notified.

\* Foaming gel Klorane® provided by the sponsor was allowed for children washing/cleansing.

Evidence for comparator: -

Actual start date of recruitment	30 October 2008
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	Romania: 86
Country: Number of subjects enrolled	Poland: 113
Country: Number of subjects enrolled	Estonia: 118
Country: Number of subjects enrolled	France: 35
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Italy: 2

Country: Number of subjects enrolled	Latvia: 117
Country: Number of subjects enrolled	Lithuania: 89
Worldwide total number of subjects	586
EEA total number of subjects	586

Notes:

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**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)	2
Children (2-11 years)	584
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:

591 patients were screened and 588 randomized and included. 2 patients did not take any treatment and therefore, the APT safety population was made of 586 patients.

### Pre-assignment

Screening details:

Main inclusion criteria were

- Age between 2 and 7 years,
- atopic dermatitis according to the diagnostic criteria of the UK Working Party,
- IGA score is  $\leq 1$  at inclusion,

### 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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Experimental Group
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	V0034CR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

One application bid (morning and evening) on the whole body including face.

When inflammatory lesions were present (disease exacerbation phases), a moderately potent corticosteroid was allowed, used as followed:

- Locapred®: once a day (preferably in the evening) only on the lesions of the body and the face,
- V0034CR : once a day (preferably in the morning) on the whole body including face.

<b>Arm title</b>	Vehicle Group
Arm description: -	
Arm type	Vehicle
Investigational medicinal product name	Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

One application bid (morning and evening) on the whole body including face.

When inflammatory lesions were present (disease exacerbation phases), a moderately potent corticosteroid was allowed, used as followed:

- Locapred®: once a day (preferably in the evening) only on the lesions of the body and the face,
- Vehicle: once a day (preferably in the morning) on the whole body including face.

<b>Number of subjects in period 1</b>	Experimental Group	Vehicle Group
Started	294	292
Completed	275	272
Not completed	19	20
Adverse event, non-fatal	11	6
Patient's or guardian's decision	7	5
Other reason	-	2
Worsening	1	6
Lack of efficacy	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Experimental Group
Reporting group description: -	
Reporting group title	Vehicle Group
Reporting group description: -	

Reporting group values	Experimental Group	Vehicle Group	Total
Number of subjects	294	292	586
Age categorical Units: Subjects			
Age continuous Units: months geometric mean full range (min-max)	50.4 14 to 95	52.1 16 to 94	-
Gender categorical Units: Subjects			
Female	145	151	296
Male	149	141	290
IGA score			
5-point Investigator's Global Assessment (IGA) tool of skin disease from 0 clear to 5 very severe disease			
Units: Subjects			
clear	111	119	230
almost clear	183	173	356
missing	0	0	0

### Subject analysis sets

Subject analysis set title	Safety data set
Subject analysis set type	Safety analysis
Subject analysis set description: Safety had to be analysed in all randomized patients having used at least once the study medication	
Subject analysis set title	Efficacy data set
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All Patients Treated data set for efficacy , i.e. all randomized patients having used at least once the study medication and for which the main criterion is assessed at least once after inclusion.	

Reporting group values	Safety data set	Efficacy data set	
Number of subjects	586	573	
Age categorical Units: Subjects			

Age continuous			
Units: months			
geometric mean	51.2		
full range (min-max)	14 to 95		
Gender categorical			
Units: Subjects			
Female	296		
Male	290		
IGA score			
5-point Investigator's Global Assessment (IGA) tool of skin disease from 0 clear to 5 very severe disease			
Units: Subjects			
clear	230		
almost clear	356		
missing	0		

## End points

### End points reporting groups

Reporting group title	Experimental Group
Reporting group description: -	
Reporting group title	Vehicle Group
Reporting group description: -	
Subject analysis set title	Safety data set
Subject analysis set type	Safety analysis
Subject analysis set description: Safety had to be analysed in all randomized patients having used at least once the study medication	
Subject analysis set title	Efficacy data set
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All Patients Treated data set for efficacy , i.e. all randomized patients having used at least once the study medication and for which the main criterion is assessed at least once after inclusion.	

### Primary: Mean POEM (Patient -Oriented Eczema Mesure) score

End point title	Mean POEM (Patient -Oriented Eczema Mesure) score
End point description: The POEM score is a fully validated self or parental assessment of the frequency of the most bothering symptoms impacting the quality of life of the patient. The POEM score consists of 7 main symptoms: itchiness, dryness, skin-bleeding, skin weeping/oozing, sleep disturbance, skin flakes and cracks. Each symptom is scored on a five grade scale from 0 to 4, resulting a maximum score 28, where: <ul style="list-style-type: none"><li>- 0: no symptoms during the last week;</li><li>- 1: one to two days of symptom's presence;</li><li>- 2: three to four days of symptom's presence;</li><li>- 3: five to six days of symptom's presence;</li><li>- 4: everyday presence of the symptoms.</li></ul>	
End point type	Primary
End point timeframe: Mean POEM score over the 12 weeks of treatment.	

End point values	Experimental Group	Vehicle Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	286		
Units: Score				
arithmetic mean (confidence interval 95%)	3.58 (3.14 to 4.01)	3.91 (3.48 to 4.35)		

### Statistical analyses

Statistical analysis title	Mean POEM score over 12 weeks
Statistical analysis description: Analysis of variance for the POEM score using a Mixed Model for Repeated Measures (MMRM) with treatment, country and visit as fixed effects and subject as random effect.	

Comparison groups	Experimental Group v Vehicle Group
Number of subjects included in analysis	573
Analysis specification	Pre-specified
Analysis type	superiority <sup>[1]</sup>
P-value	= 0.2343 <sup>[2]</sup>
Method	Mixed models analysis
Parameter estimate	Variance
Confidence interval	
level	95 %
sides	2-sided

Notes:

[1] - The initial POEM score was around 5.3/28 in both groups, which corresponds to atopic dermatitis of mild severity.

[2] - The results of the primary analysis (MMRM) exhibited a difference in favour of the study drug (-0.34) but the difference was not statistically significant (p=0.2343).

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

During the whole study period.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.0
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### Reporting groups

Reporting group title	Experimental Group
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Reporting group description: -

Reporting group title	Vehicle Group
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Reporting group description: -

<b>Serious adverse events</b>	Experimental Group	Vehicle Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 294 (1.02%)	9 / 292 (3.08%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 294 (0.00%)	1 / 292 (0.34%)	
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			
Ovarian cyst			
subjects affected / exposed	1 / 294 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 294 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Juvenile arthritis			
subjects affected / exposed	1 / 294 (0.34%)	0 / 292 (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			
Gastrointestinal candidiasis			
subjects affected / exposed	1 / 294 (0.34%)	0 / 292 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scarlet fever			
subjects affected / exposed	0 / 294 (0.00%)	2 / 292 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	0 / 294 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 294 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 294 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 294 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis bacterial			
subjects affected / exposed	0 / 294 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

bacterial			
subjects affected / exposed	0 / 294 (0.00%)	1 / 292 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral skin infection			
subjects affected / exposed	0 / 294 (0.00%)	1 / 292 (0.34%)	
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: 5 %

<b>Non-serious adverse events</b>	Experimental Group	Vehicle Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	159 / 294 (54.08%)	150 / 292 (51.37%)	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	25 / 294 (8.50%)	37 / 292 (12.67%)	
occurrences (all)	30	42	
Rhinitis			
subjects affected / exposed	25 / 294 (8.50%)	16 / 292 (5.48%)	
occurrences (all)	30	20	
Respiratory tract infection viral			
subjects affected / exposed	17 / 294 (5.78%)	15 / 292 (5.14%)	
occurrences (all)	18	17	
Bronchitis			
subjects affected / exposed	10 / 294 (3.40%)	17 / 292 (5.82%)	
occurrences (all)	11	18	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 September 2008	Substantial and general amendment. Following recommendations of Competent Authorities: - Addition of non inclusion criteria, - Addition of the warnings of associated treatment, - Modification in the "withdrawal criteria" section.
14 October 2008	Substantial and local amendment.  Following recommendations of Ethics Committee in Milan and Competent Authorities in Italy, change of phase of the study.
19 December 2008	Substantial and local amendment. Following recommendations of Competent Authorities in Czech Republic, Change of phase of the study.
10 February 2009	Substantial and general amendment. - Addition of a contractor in charge of Investigational Product management, - Correction of the Associate Clinical Study Coordinator contact details, - Addition of investigators

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported