Clinical trial results:
LONG-TERM MANAGEMENT OF ATOPIC DERMATITIS WITH THE EMOLLIENT V0034 CR. A RANDOMISED, PLACEBO-CONTROLLED, PARALLEL-GROUPS, DOUBLE-BLIND STUDY IN INFANTS AND CHILDREN

Summary

EudraCT number	2005-003396-21
Trial protocol	FR EE FI LV DE
Global end of trial date	07 November 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	• Changes to summary attachments Synopsis error

Trial information

Trial identification

Sponsor protocol code	V00034CR3071B

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	07 September 2006
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 September 2006
Global end of trial reached?	Yes
Global end of trial date	07 November 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the overall benefit of a regular treatment by the emollient V0034CR in the management of atopic dermatitis: reduction of corticosteroids consumption, reduction of flares

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.

Background therapy:

Corticosteroid treatment was used by the parents on the lesions where they appeared, 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: bottle 250 mL; batch F727; expiry date: 10/2007 or bottle 500 mL; batch F742; expiry date: 12/2007. Way of life and cosmetic cares should not be changed. Food supplements that could modify the skin properties. Just after being in a swimming pool, emollient should be applied once more.

Evidence for comparator:

Very few emollients have been evaluated double blind. In order to evaluate the effect of the emollient V0034 CR 01B, placebo was mandatory and justified. Furthermore, the use of a placebo (vehicle) was ethically acceptable since all patients received when necessary an active treatment by corticosteroids on one hand and because excipient topical formulations have also a well-known intrinsic activity that can improve the skin status.

Actual start date of recruitment	30 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	Estonia: 83
Country: Number of subjects enrolled	Finland: 20
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Latvia: 81
Country: Number of subjects enrolled	Poland: 84
Country: Number of subjects enrolled	Romania: 29
Worldwide total number of subjects	328
EEA total number of subjects	328

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)	98
Children (2-11 years)	230
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:

Twenty two centres in 7 countries screened and treated 328 patients, male or female children, aged between 3 months and 7 years, presenting with atopic dermatitis according to the diagnostic criteria of the UK Working party between the 30th of November 2005 and 07 September 2006.

Pre-assignment

Screening details:

Patients, male or female children, aged between 3 months and 7 years, presenting with atopic dermatitis according to the diagnostic criteria of the UK Working party, whose IGA score was < 1 at inclusion were screened. Patients in acute phase of AD or with a severe form of disease were excluded.

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 envelops corresponding to the treatments received and given to the patients. An envelope could be opened only in case of emergency (vital threatening, 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	V0034CR arm

Arm description:

160 patients were randomised in the V0034CR arm

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:

Application in thin layers with a sufficient amount of cream, with a gentle massage until penetration, on the whole body (including face), morning and evening; when inflammatory lesions were present (disease exacerbation phases): application on the whole body (including face), in the evening. The study was long enough (6 months) to have flares during one winter/spring season and thus to register corticosteroid consumption. Corticosteroid treatment was applied by the parents only on the inflammatory lesions until complete resolution of the inflammatory signs (if applicable).

Arm title	Vehicle arm

Arm description:

168 patients were randomised in the vehicle arm

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:

Application in thin layers with a sufficient amount of cream, with a gentle massage until penetration, on the whole body (including face), morning and evening; when inflammatory lesions were present (disease exacerbation phases): application on the whole body (including face), in the evening. The corticosteroid treatment was applied by the parents only on the inflammatory lesions until complete resolution of the inflammatory signs.

Number of subjects in period 1	V0034CR arm	Vehicle arm
Started	160	168
Completed	151	153
Not completed	9	15
Non serious AEs/SAEs	2	-
Patient's or guardian's decision	2	8
Insufficient response	2	2
Worsening	3	5

Baseline characteristics

Reporting groups	
Reporting group title	V0034CR arm
Reporting group description:	
160 patients were randomised in the V0034CR arm	
Reporting group title	Vehicle arm
Reporting group description:	
168 patients were randomised in the vehicle arm	

Reporting group values	V0034CR arm	Vehicle arm	Total
Number of subjects	160	168	328
Age categorical			
Units: Subjects			
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	50	48	98
Children (2-11 years)	110	120	230
Age continuous			
Units: months			
arithmetic mean	37.6	36.6	
standard deviation	± 22.0	± 21.3	-
Gender categorical			
Units: Subjects			
Female	75	89	164
Male	85	79	164
Family history of atopy			
Units: Subjects			
Yes	120	130	250
No	40	38	78
IGA score			
Units: Subjects			
Clear	49	72	121
Almost clear	111	96	207
Height			
Units: cm			
arithmetic mean	95.8	95.3	
standard deviation	± 16.6	± 15.3	-
Weight			
Units: kg			
arithmetic mean	15.2	14.49	
standard deviation	± 5.24	± 4.24	-
Age of first cutaneous lesion			
Units: months			
arithmetic mean	7.5	7.9	
standard deviation	± 0.096	± 0.08	-
Time between last flare and inclusion			
Units: days			
arithmetic mean	106.8	102.2	

standard deviation	± 150.9	± 139.6	-
SCORAD at baseline			
Units: not applicable			
arithmetic mean	16.4	15.9	
full range (min-max)	0 to 35	0 to 45	-

End points

End points reporting groups

Reporting group title	V0034CR arm
Reporting group description:	
160 patients were randomised in the V0034CR arm	
Reporting group title	Vehicle arm
Reporting group description:	
168 patients were randomised in the vehicle arm	

Primary: Number of days of application of corticosteroid.

End point title	Number of days of application of corticosteroid.

End point description:

The main criterion was the number of days of application of corticosteroid (percentage of the total number of days in the study). To take into account not only dropouts but also different durations in the study for completers, this number of days was expressed as a percentage of the total number of days in the study.
This percentage was compared between treatment groups using Cochran-Mantel-Haenszel (CMH) with modified ridit scores, adjusting for centre.

End point type	Primary

End point timeframe:

The number of days of application of corticosteroid was measured between the first visit of the study until the final visit (week 24)

End point values	V0034CR arm	Vehicle arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	160	168		
Units: percentage				
arithmetic mean (standard deviation)	5.4 (± 7.98)	7.74 (± 11.28)		

Statistical analyses

Statistical analysis title	Primary analysis

Statistical analysis description:

The main criteria (number of days of application of a moderately potent corticosteroids used for treating flares) was compared between treatment groups using Cochran-Mantel-Haenszel test (row mean scores) adjusting for centre, using modified ridit scores to get an extension of the Wilcoxon rank sum test.

Comparison groups	V0034CR arm v Vehicle arm

Number of subjects included in analysis	328
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.429
Method	Mantel-Haenszel
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 (W4) until the final visit Visit 6 (W24).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	8.1

Reporting groups	
Reporting group title	V0034 CR arm
Reporting group description: -	
Reporting group title	Vehicle arm
Reporting group description: -	

Serious adverse events	V0034 CR arm	Vehicle arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 160 (0.00%)	3 / 168 (1.79%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Ear and labyrinth disorders			
Otoplasty			
subjects affected / exposed	0 / 160 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 160 (0.00%)	1 / 168 (0.60%)	
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			
Respiratory tract infection			
subjects affected / exposed	0 / 160 (0.00%)	1 / 168 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			

subjects affected / exposed	0 / 160 (0.00%)	1 / 168 (0.60%)	
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 %

Non-serious adverse events	V0034 CR arm	Vehicle arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	88 / 160 (55.00%)	100 / 168 (59.52%)	
General disorders and administration site conditions			
general disorders and administration site conditions			
subjects affected / exposed	7 / 160 (4.38%)	11 / 168 (6.55%)	
occurrences (all)	7	11	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 160 (5.63%)	10 / 168 (5.95%)	
occurrences (all)	9	10	
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	12 / 160 (7.50%)	14 / 168 (8.33%)	
occurrences (all)	12	14	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	21 / 160 (13.13%)	14 / 168 (8.33%)	
occurrences (all)	21	14	
Rhinitis			
subjects affected / exposed	11 / 160 (6.88%)	14 / 168 (8.33%)	
occurrences (all)	11	14	
Pharyngitis			
subjects affected / exposed	13 / 160 (8.13%)	9 / 168 (5.36%)	
occurrences (all)	13	9	
Bronchitis			
subjects affected / exposed	9 / 160 (5.63%)	10 / 168 (5.95%)	
occurrences (all)	9	10	
Upper respiratory tract infection			

subjects affected / exposed	9 / 160 (5.63%)	10 / 168 (5.95%)	
occurrences (all)	9	10	
Ear infection			
subjects affected / exposed	6 / 160 (3.75%)	9 / 168 (5.36%)	
occurrences (all)	6	9	

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
20 January 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