Clinical trial results:
Efficacy of the V0034CR01B emollient on xerosis in children with atopic dermatitis. Randomised, vehicle-controlled, parallel-groups, double-blind study with an open label extension

Summary

EudraCT number	2011-003295-37
Trial protocol	FR EE LT PL
Global end of trial date	24 May 2012

Results information

Result version number	v1 (current)
This version publication date	18 February 2016
First version publication date	18 February 2016

Trial information

Trial identification

Sponsor protocol code	V00034CR3121B

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01467362
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pierre Fabre Medicament
Sponsor organisation address	45, Place Abel Gance, Boulogne, France, 92100
Public contact	Medical and/or Clinical Study Manager, Pierre Fabre Medicament, contact_essais_cliniques@pierre-fabre.com
Scientific contact	Medical and/or Clinical Study Manager, Pierre Fabre Medicament, contact_essais_cliniques@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	20 December 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 May 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of V0034CR01B cream on xerosis in children with atopic dermatitis in comparison with vehicle over 28 days.

Protection of trial subjects:

Medical and clinical examination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2011
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: 59
Country: Number of subjects enrolled	Estonia: 79
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Lithuania: 67
Country: Number of subjects enrolled	Romania: 26
Worldwide total number of subjects	249
EEA total number of subjects	249

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)	249
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:

251 patients were randomised but only 249 patients were randomised and treated. 2 patients did not take any treatment (1 withdrawn patient for parents decision in each arm); safety and efficacy population was composed of 249 patients.

Pre-assignment

Screening details:

Patients who met all inclusion criteria and none of exclusion criteria were randomised into 2 groups, V0034CR01B or vehicle, and during 28 days received treatment.
After this first period, according to the status of lesions and xerosis score, patients entered an open-label period for 56 days (V0034CR01B or started a treatment free follow-up).

Period 1

Period 1 title	Double-blind period Day 1 to Day 28
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental Group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Dexeryl®
Investigational medicinal product code	V0034CR01B
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

One application twice a day (morning and evening) on the whole body including face.

When inflammatory lesions were present (disease exacerbation phases), the product was applied once a day (in the morning) on the whole body including the face, and a moderately potent corticosteroid (Locapred®) was applied once a day (in the evening) only on the lesions of the body and the face.

Arm title	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 twice a day (morning and evening) on the whole body including face.

When inflammatory lesions were present (disease exacerbation phases), the product was applied once a day (in the morning) on the whole body including the face, and a moderately potent corticosteroid (Locapred®) was applied once a day (in the evening) only on the lesions of the body and the face.

Number of subjects in period 1	Experimental Group	Vehicle Group
Started	124	125
Completed	120	121
Not completed	4	4
Parents decision	2	-
Adverse event, non-fatal	1	3
Lack of efficacy	1	1

Period 2

Period 2 title	Open-label Period Day 28 to Day 56
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental Group

Arm description:

On Day 28, if patients had persisting lesions and/or xerosis score >1 at Day 28, the application of experimental treatment started (Patients from double-blind vehicle group) or continued (patients from double blind experimental group).

Arm type	Experimental
Investigational medicinal product name	Dexeryl®
Investigational medicinal product code	V0034CR01B
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

One application twice a day (morning and evening) on the whole body including face.

When inflammatory lesions were present (disease exacerbation phases), the product was applied once a day (in the morning) on the whole body including the face, and a moderately potent corticosteroid (Locapred®) was applied once a day (in the evening) only on the lesions of the body and the face.

Arm title	Treatment free follow-up Group

Arm description:

On Day 28, only patients without persisting lesions and xerosis score ≤ 1 started treatment free follow-up.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Experimental Group	Treatment free follow-up Group
Started	155	86
Completed	154	86
Not completed	1	0
Parents decision	1	-

Period 3

Period 3 title	Open-label Period Day 56 to Day 84
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental group

Arm description:

On day 56: if patients had persisting lesions and/or xerosis score >1 at D56, the application of experimental product started or continued. Patients treated with Experimental product between Day 28 and Day 56 could not started treatment free follow-up, even if their skin at Day 56 was free from lesions and xerosis score ≤1.

Arm type	Experimental
Investigational medicinal product name	Dexeryl®
Investigational medicinal product code	V0034CR01B
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

One application twice a day (morning and evening) on the whole body including face.

When inflammatory lesions were present (disease exacerbation phases), the product was applied once a day (in the morning) on the whole body including the face, and a moderately potent corticosteroid (Locapred®) was applied once a day (in the evening) only on the lesions of the body and the face.

Arm title	Treatment free follow-up Group

Arm description:

Only patients without persisting lesions and xerosis score ≤1 at Day 56 continued treatment free started at Day 28.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 3	Experimental group	Treatment free follow-up Group
Started	227	13
Completed	225	13
Not completed	2	0
Parents decision	1	-
Adverse event, non-fatal	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	124	125	249
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	4.04	4.05	
full range (min-max)	2 to 6.9	2 to 6.9	-
Gender categorical Units: Subjects			
Female	69	53	122
Male	55	72	127

Subject analysis sets	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

All randomised patients having received at least one application of the study treatment, used to perform the analysis of safety and efficacy.

Reporting group values	Full analysis set		
Number of subjects	249		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	4.05		
full range (min-max)	2 to 6.9		
Gender categorical Units: Subjects			
Female	122		
Male	127		

End points

End points reporting groups

Reporting group title	Experimental Group
Reporting group description: -	
Reporting group title	Vehicle Group
Reporting group description: -	
Reporting group title	Experimental Group
Reporting group description:	
On Day 28, if patients had persisting lesions and/or xerosis score >1 at Day 28, the application of experimental treatment started (Patients from double-blind vehicle group) or continued (patients from double blind experimental group).	
Reporting group title	Treatment free follow-up Group
Reporting group description:	
On Day 28, only patients without persisting lesions and xerosis score ≤ 1 started treatment free follow-up.	
Reporting group title	Experimental group
Reporting group description:	
On day 56: if patients had persisting lesions and/or xerosis score >1 at D56, the application of experimental product started or continued. Patients treated with Experimental product between Day 28 and Day 56 could not started treatment free follow-up, even if their skin at Day 56 was free from lesions and xerosis score ≤1.	
Reporting group title	Treatment free follow-up Group
Reporting group description:	
Only patients without persisting lesions and xerosis score ≤1 at Day 56 continued treatment free started at Day 28.	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomised patients having received at least one application of the study treatment, used to perform the analysis of safety and efficacy.	

Primary: Xerosis score : mean evolution over the different time-points of double-blind period

End point title	Xerosis score : mean evolution over the different time-points of double-blind period
End point description:	
The primary criterion was the change from baseline of the xerosis score over the different time-points of the double-blind period for patients included in the Full Analysis Set.	
End point type	Primary
End point timeframe:	
Baseline (Day 1), Day 7, Day 14, Day 21 and Day 28	

End point values	Experimental Group	Vehicle Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	125		
Units: not applicable				
least squares mean (standard error)	-0.93 (± 0.043)	-0.63 (± 0.043)		

Statistical analyses

Statistical analysis title	Adjusted mean difference in change (xerosis score)
Statistical analysis description:	
Analysis of the change from baseline to day 28 using a Mixed-effects Model for Repeated Measures (MMRM) (observed values from the mean changes in xerosis score at all time points up to day 28).	
Comparison groups	Experimental Group v Vehicle Group
Number of subjects included in analysis	249
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	-0.18
Variability estimate	Standard error of the mean
Dispersion value	0.061

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During the whole study period.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups	
Reporting group title	Double-blind period : Experimental Group
Reporting group description: -	
Reporting group title	Double blind : Vehicle group
Reporting group description: -	
Reporting group title	Open-Label Day 28 to Day 56 : Experimental group
Reporting group description: -	
Reporting group title	Open-Label Day 28 to Day 56 : Follow-up group
Reporting group description: -	
Reporting group title	Open-Label Day 56 to Day 84 : Experimental group
Reporting group description: -	
Reporting group title	Open-Label Day 56 to Day 84 : Follow-up group
Reporting group description: -	

Serious adverse events	Double-blind period : Experimental Group	Double blind : Vehicle group	Open-Label Day 28 to Day 56 : Experimental group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 124 (0.00%)	1 / 125 (0.80%)	0 / 155 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	0 / 124 (0.00%)	1 / 125 (0.80%)	0 / 155 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Open-Label Day 28 to Day 56 : Follow-up group	Open-Label Day 56 to Day 84 : Experimental group	Open-Label Day 56 to Day 84 : Follow-up group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 86 (0.00%)	0 / 227 (0.00%)	0 / 13 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	0 / 86 (0.00%)	0 / 227 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Double-blind period : Experimental Group	Double blind : Vehicle group	Open-Label Day 28 to Day 56 : Experimental group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 124 (27.42%)	42 / 125 (33.60%)	27 / 155 (17.42%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 124 (1.61%)	1 / 125 (0.80%)	1 / 155 (0.65%)
occurrences (all)	2	1	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 124 (1.61%)	3 / 125 (2.40%)	1 / 155 (0.65%)
occurrences (all)	4	4	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 124 (5.65%)	7 / 125 (5.60%)	5 / 155 (3.23%)
occurrences (all)	7	7	5
Rhinitis			
subjects affected / exposed	1 / 124 (0.81%)	5 / 125 (4.00%)	2 / 155 (1.29%)
occurrences (all)	1	5	2

Non-serious adverse events	Open-Label Day 28 to Day 56 : Follow-up group	Open-Label Day 56 to Day 84 : Experimental group	Open-Label Day 56 to Day 84 : Follow-up group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 86 (9.30%)	39 / 227 (17.18%)	2 / 13 (15.38%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 86 (1.16%)	7 / 227 (3.08%)	1 / 13 (7.69%)
occurrences (all)	1	7	1
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	0 / 86 (0.00%)	3 / 227 (1.32%)	1 / 13 (7.69%)
occurrences (all)	0	3	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 86 (1.16%)	6 / 227 (2.64%)	0 / 13 (0.00%)
occurrences (all)	1	6	0
Rhinitis			
subjects affected / exposed	1 / 86 (1.16%)	2 / 227 (0.88%)	1 / 13 (7.69%)
occurrences (all)	1	2	1

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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24267728