Clinical trial results:
Emollients in the management of atopic dermatitis in children: prevention of flares.

Summary

EudraCT number	2012-004621-24
Trial protocol	LT EE PL FR
Global end of trial date	12 February 2014

Results information

Result version number	v1 (current)
This version publication date	21 February 2016
First version publication date	21 February 2016

Trial information

Trial identification

Sponsor protocol code	V00034CR3131B

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01779258
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	06 June 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the ability of V0034CR to prevent flares after treatment of a previous flare by a topical corticosteroid.

Protection of trial subjects:

Medical and clinical examination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 February 2013
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	Estonia: 82
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Lithuania: 95
Country: Number of subjects enrolled	Romania: 87
Worldwide total number of subjects	347
EEA total number of subjects	347

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)	347
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:

347 patients were screened and 335 were randomised.

Pre-assignment

Screening details:

Patients were recruited during a flare, treated by a topical corticosteroid (run-in period Day-21 to Day0 - please see pre-assignment period), and randomised only when inflammatory lesions had cleared (treatment period).
So, only 335 patients were randomised to one of the 3 groups (V0034CR01B or Atopiclair® or No emollient treatment).

Pre-assignment period milestones

Number of subjects started	347
Number of subjects completed	335

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Non respect of eligibility criteria: 7
Reason: Number of subjects	Technical problem with IVRS: 1
Reason: Number of subjects	Eligibility criteria and parent's decision: 2
Reason: Number of subjects	Parent's or guardian's decision:consent withdrawal: 2

Period 1

Period 1 title	Treatment period (Day 1 to Day 84) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

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

During flares, the product was applied once a day (in the morning), and Locapred® was applied only to the lesions, once a day (in the evening).

Arm title	Active control group

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	Atopiclair®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

One application tid (morning, afternoon and evening) on areas of skin affected by atopic dermatitis (AD), that had been affected by AD in the past or could reasonbly be affected by AD during the course of the study.

During flares, the product was applied twice a day (in the morning and in the afternoon), and Locapred®was applied only to the lesions, once a day (in the evening).

Arm title	Reference group (no treatment)
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1[1]	Experimental Group	Active control group	Reference group (no treatment)
Started	111	116	108
Completed	110	111	95
Not completed	1	5	13
Efficacy concerns	-	4	5
Bad compliance	-	-	1
Parental demotivation to continue	-	1	-
Parent's decision	-	-	7
Family divorce	1	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Following the run-in period, only 335 patients were randomised to one of the 3 groups (V0034CR or Atopiclair® or No emollient treatment) (1:1:1 ratio).

Baseline characteristics

Reporting groups	
Reporting group title	Experimental Group
Reporting group description: -	
Reporting group title	Active control group
Reporting group description: -	
Reporting group title	Reference group (no treatment)
Reporting group description: -	

Reporting group values	Experimental Group	Active control group	Reference group (no treatment)
Number of subjects	111	116	108
Age categorical Units: Subjects			
Children (2-11 years)	111	116	108
Age continuous Units: years			
arithmetic mean	4.16	4.02	4.06
full range (min-max)	2.1 to 6.8	2 to 6.7	2 to 6.9
Gender categorical Units: Subjects			
Female	69	51	54
Male	42	65	54

Reporting group values	Total		
Number of subjects	335		
Age categorical Units: Subjects			
Children (2-11 years)	335		
Age continuous Units: years			
arithmetic mean			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	174		
Male	161		

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

Subject analysis set description:

Composed of all randomised patients, which consisted of all included patients who were assigned to a study group (experimental group, active control group or reference group) used to perform all the analyses of efficacy and safety.

Reporting group values	Full analysis set		
Number of subjects	335		
Age categorical Units: Subjects			
Children (2-11 years)	335		
Age continuous Units: years			
arithmetic mean	4.08		
full range (min-max)	2 to 6.9		
Gender categorical Units: Subjects			
Female	174		
Male	161		

End points

End points reporting groups

Reporting group title	Experimental Group
Reporting group description: -	
Reporting group title	Active control group
Reporting group description: -	
Reporting group title	Reference group (no treatment)
Reporting group description: -	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

Composed of all randomised patients, which consisted of all included patients who were assigned to a study group (experimental group, active control group or reference group) used to perform all the analyses of efficacy and safety.

Primary: Number of patients with at least one flare

End point title	Number of patients with at least one flare[1]

End point description:

End point type	Primary

End point timeframe:

From Baseline to Day 84.

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per protocole, Primary Efficacy Analysis was only between treatment group (V0034CR01B) and reference group (no emollient).

End point values	Experimental Group	Reference group (no treatment)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	108		
Units: patients	39	73		

Statistical analyses

Statistical analysis title	Percentage of patients with at least one flare
Comparison groups	Experimental Group v Reference group (no treatment)
Number of subjects included in analysis	219
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel

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	16.0

Reporting groups	
Reporting group title	Experimental Group
Reporting group description: -	
Reporting group title	Active control group
Reporting group description: -	
Reporting group title	Reference group (no treatment)
Reporting group description: -	

Serious adverse events	Experimental Group	Active control group	Reference group (no treatment)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 111 (1.80%)	1 / 116 (0.86%)	2 / 108 (1.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Adenoidectomy			
subjects affected / exposed	0 / 111 (0.00%)	1 / 116 (0.86%)	0 / 108 (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
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 111 (0.00%)	0 / 116 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 111 (0.90%)	0 / 116 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			

subjects affected / exposed	1 / 111 (0.90%)	0 / 116 (0.00%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	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	Experimental Group	Active control group	Reference group (no treatment)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 111 (62.16%)	77 / 116 (66.38%)	79 / 108 (73.15%)
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	40 / 111 (36.04%)	61 / 116 (52.59%)	72 / 108 (66.67%)
occurrences (all)	69	88	131
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	8 / 111 (7.21%)	5 / 116 (4.31%)	7 / 108 (6.48%)
occurrences (all)	8	6	8
Rhinitis			
subjects affected / exposed	7 / 111 (6.31%)	2 / 116 (1.72%)	3 / 108 (2.78%)
occurrences (all)	8	2	4
Bronchitis			
subjects affected / exposed	6 / 111 (5.41%)	9 / 116 (7.76%)	7 / 108 (6.48%)
occurrences (all)	7	11	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 May 2013	General and substantial amendment: Due to the seasonality of the disease, the recruitment period was stopped the 28.02.2013. The number of patients to be randomized was not achieved. The aim of this amendment was to postpone the study end period to February 2014 with a new recruitment phase in September and October 2013. Furthermore, a clarification should be done in the protocol concerning the reporting and counting of the number of flares for a given patient.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported