



Clinical trial results:

Efficacy and tolerance of the emollient cream V0034 CR in the symptomatic treatment of ichthyosis in children. International, multicentric, randomised, controlled, double blind study, in parallel groups V0034 CR versus vehicle.

Summary

EudraCT number	2006-003369-14
Trial protocol	FI EE CZ NL DE LT FR LV IT ES
Global end of trial date	01 November 2007

Results information

Result version number	v1 (current)
This version publication date	10 December 2016
First version publication date	10 December 2016

Trial information

Trial identification

Sponsor protocol code	V00034 CR 309 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 Medicament
Sponsor organisation address	45, Place Abel Gance, Boulogne, France, 92100
Public contact	Elisabeth COPPEL, Centre de Recherche et Développement Clinique Pierre Fabre 3, Avenue Hubert CURIEN 31100 TOULOUSE, elisabeth.coppel@pierre-fabre.com
Scientific contact	Elisabeth COPPEL, Centre de Recherche et Développement Clinique Pierre Fabre 3, Avenue 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	25 June 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 November 2007
Global end of trial reached?	Yes
Global end of trial date	01 November 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of a 4-week treatment by the emollient V0034CR in reducing the disease severity assessed by a specified symptom sum score (SRRC: Scales Roughness Redness Cracks fissures score) on both legs.

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.

Patient underwent a health assessment at the start of the study and remains under regular Medical control during the whole study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 2007
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	Czech Republic: 28
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Estonia: 50
Country: Number of subjects enrolled	Finland: 16
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Latvia: 38
Country: Number of subjects enrolled	Lithuania: 30
Country: Number of subjects enrolled	Poland: 40
Country: Number of subjects enrolled	Tunisia: 30
Worldwide total number of subjects	265
EEA total number of subjects	235

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)	36
Children (2-11 years)	146
Adolescents (12-17 years)	83
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 265 patients were included in the study and randomized in the two treatment groups. The study was performed in 12 countries and involved 21 centres. Among randomized patients, a total of 9 patients (3.4%) did not complete the study 3 (2.3%) in Vehicle group and 6 (4.5%) in V0034CR group. The main reason was lost to follow-up

Pre-assignment

Screening details:

Patients under 18 years suffering from a non-bullous form of ichthyosis with SRRC global score ≥ 4 and scaling SRRC ≥ 2 on both external faces of the legs.

A double-blind period (V0034CR or vehicle) during 4 weeks followed by an open label period with all patients treated by V0034 CR for 8 weeks.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	V0034

Arm description: -

Arm type	Experimental
Investigational medicinal product name	V0034
Investigational medicinal product code	V0034 CR
Other name	Dexeryl
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Twice a day on the whole body, in the morning and the evening for 4 weeks

Arm title	Vehicle
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Twice a day on the whole body in the morning and in the evening during 4 weeks

Number of subjects in period 1^[1]	V0034	Vehicle
Started	131	130
Completed	131	130

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: of the 265 enrolled and randomized patients worldwide, 9 patients (3.4%) did not complete the study; Mean reason for non completion was lost of follow up

Period 2

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

Arms

Arm title	V0034-8 weeks
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	V0034
Investigational medicinal product code	V0034 CR
Other name	Dexeryl
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Twice a day on the whole body, in the morning and the evening for 4 weeks

Number of subjects in period 2^[2]	V0034-8 weeks
Started	258
Completed	258

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: only subjects treated by V0034 CR were enrolled in the open label 4week follow up period

Baseline characteristics

Reporting groups

Reporting group title	V0034
Reporting group description: -	
Reporting group title	Vehicle
Reporting group description: -	

Reporting group values	V0034	Vehicle	Total
Number of subjects	131	130	261
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	9.18	8.52	
full range (min-max)	0.1 to 17.9	0.2 to 17.9	-

Gender categorical Units: Subjects			
Female	43	48	91
Male	88	82	170

type of ichthyosis Units: Subjects			
Ichthyosis vulgaris	78	81	159
X linked recessive ichthyosis	15	21	36
Non erythrodermic ichthyosis	22	15	37
Other	16	13	29

Scaling score			
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Visual evaluation of scaling symptom on a five-point scale:
 0 Absent
 1 Slight: small scales only, surface lightly dull in colour
 2 Moderate: small scales in combination with larger scales (>0.05mm), surface opaque or whitish
 3 Severe: larger and large scales (flakes >1mm) are prominent, surface whitish
 4 Extreme: larger flakes covering almost the entire skin surface in the examination field

Units: Subjects			
absent	0	0	0
slight	0	0	0
moderate	48	43	91
severe	62	72	134
extreme	21	15	36

SRRC score			
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Four symptoms, scaling, roughness, redness and cracks on both legs were rated on a five-grade scale from 0 absent to 4 extreme. The SRRC score was the sum of these four symptom grades. The maximum score was 16.

Units: decimal			
arithmetic mean	7.47	7.12	
full range (min-max)	4 to 14	3 to 13	-

Subject analysis sets

Subject analysis set title	Safety data set
Subject analysis set type	Safety analysis
Subject analysis set description: All randomised patients having taken at least one dose of study treatment.	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description: All randomised patients having taken at least one dose of study treatment and with at least one post baseline evaluation of the primary efficacy criterion.	
Subject analysis set title	Full Analysis Set excluding one country
Subject analysis set type	Full analysis
Subject analysis set description: All randomised patients having taken at least one dose of study treatment and with at least one post baseline evaluation of the primary efficacy criterion, excluding patients from Tunisia (because unexpected results in this country- 100% responders in both groups).	

Reporting group values	Safety data set	Full analysis set	Full Analysis Set excluding one country
Number of subjects	262	261	231
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean full range (min-max)	8.84 0.1 to 17.9	8.85 0.1 to 17.9	8.68 0.1 to 17.9
Gender categorical Units: Subjects			
Female	91	91	79
Male	171	170	152
type of ichthyosis Units: Subjects			
Ichthyosis vulgaris		159	
X linked recessive ichthyosis		36	
Non erythrodermic ichthyosis		37	
Other		29	
Scaling score			
Visual evaluation of scaling syptom on a five-point scale: 0 Absent 1 Slight: small scales only, surface lightly dull in colour 2 Moderate: small scales in combination with larger scales (>0.05mm), surface opaque or whitish 3 Severe: larger and large scales (flakes >1mm) are prominent, surface whitish Scaling (visual evaluation) 4 Extreme: larger flakes covering almost the entire skin surface in the examination field			
Units: Subjects			
absent		0	
slight		0	
moderate		91	
severe		134	
extreme		36	

SRRC score			
Four symptoms, scaling, roughness, redness and cracks on both legs were rated on a five-grade scale from 0 absent to 4 extreme. The SRRC score was the sum of these four symptom grades. The maximum score was 16.			
Units: decimal			
arithmetic mean		7.3	
full range (min-max)		3 to 14	

End points

End points reporting groups

Reporting group title	V0034
Reporting group description: -	
Reporting group title	Vehicle
Reporting group description: -	
Reporting group title	V0034-8 weeks
Reporting group description: -	
Subject analysis set title	Safety data set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomised patients having taken at least one dose of study treatment.	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomised patients having taken at least one dose of study treatment and with at least one post baseline evaluation of the primary efficacy criterion.	
Subject analysis set title	Full Analysis Set excluding one country
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomised patients having taken at least one dose of study treatment and with at least one post baseline evaluation of the primary efficacy criterion, excluding patients from Tunisia (because unexpected results in this country- 100% responders in both groups).	

Primary: Patients having a 50% reduction of the SRRC score (Scaling, Roughness, Redness, Cracks fissures score) on FAS including all countries

End point title	Patients having a 50% reduction of the SRRC score (Scaling, Roughness, Redness, Cracks fissures score) on FAS including all countries
End point description:	
The primary efficacy criterion was the response to treatment defined by a decrease of at least 50% of the SRRC score on the external face of legs (mean of the 2 legs) between baseline and Day 28.	
The main analysis of the primary efficacy criterion was performed on the FAS population (All countries) using the Cochran Mantel Haenszel test stratified by centre.	
End point type	Primary
End point timeframe:	
From baseline to Day 28	

End point values	V0034	Vehicle	Full analysis set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	131	130	261	
Units: Patient	85	65	150	

Statistical analyses

Statistical analysis title	Primary efficacy analysis
Statistical analysis description: Responses to treatment defined by a decrease of at least 50% of the SRRC score (mean of the 2 legs) between the 2 arms were compared using the Cochran-Mantel-Haenszel (CMH) test stratified by type of ichthyosis	
Comparison groups	Vehicle v V0034
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	= 0.008 ^[2]
Method	Cochran-Mantel-Haenszel

Notes:

[1] - The CMH test was performed on the FAS including all countries to assess whether the response (i. e. decrease in the SRRC score by at least 50% on Day 28) was independent of treatment (explanatory variable) when adjusting for group of countries.

[2] - The difference between the two treatment groups was statistically significant (p=0.008) adjusted for pooled centres.

Primary: Patients having a 50% reduction of the SRRC score (Scaling, Roughness, Redness, Cracks fissures score) on FAS excluding one country

End point title	Patients having a 50% reduction of the SRRC score (Scaling, Roughness, Redness, Cracks fissures score) on FAS excluding one country ^[3]
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End point description:

The main analysis of the primary efficacy criterion was performed also on the FAS excluding Tunisia, using the Cochran Mantel Haenszel test stratified by centre.
(Thirty patients from two centres were excluded from FAS analysis because of doubtful drug administration and results, with a 100% of responders in both groups.)

End point type	Primary
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End point timeframe:

From Baseline to Day 28

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No analysis has been performed

Statistical analyses

No statistical analyses for this end point

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	8.1
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Reporting groups

Reporting group title	Vehicle group
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Reporting group description: -

Reporting group title	Experimental Group
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Reporting group description: -

Serious adverse events	Vehicle group	Experimental Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 130 (2.31%)	2 / 132 (1.52%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Congenital, familial and genetic disorders			
Ichthyosis	Additional description: Exacerbation of known ichthyosis (post-study).		
subjects affected / exposed	1 / 130 (0.77%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Talipes correction			
subjects affected / exposed	1 / 130 (0.77%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 130 (0.00%)	1 / 132 (0.76%)	
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 / 130 (0.00%)	1 / 132 (0.76%)	
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			
Asthma			
subjects affected / exposed	1 / 130 (0.77%)	0 / 132 (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: 5 %

Non-serious adverse events	Vehicle group	Experimental Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 130 (20.00%)	30 / 132 (22.73%)	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 130 (6.92%)	9 / 132 (6.82%)	
occurrences (all)	9	12	
Rhinitis			
subjects affected / exposed	12 / 130 (9.23%)	6 / 132 (4.55%)	
occurrences (all)	13	6	
Pharyngitis			
subjects affected / exposed	7 / 130 (5.38%)	2 / 132 (1.52%)	
occurrences (all)	8	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 November 2006	Substantial-general - all countries: Life style change in the information consent form following a discrepancy between protocol and Information consent.
11 December 2006	Substantial-local amendment (Czech Republic): Precision of one non inclusion criteria and modification of Inform consent Form . The protocol was modified with the addition of "pregnancy test" where appropriate.
14 March 2007	Substantial-general - all countries: Modification of the dates of study schedule

Notes:

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/22118417>