Clinical trial results:
A placebo controlled evaluation of a developmental gel for the treatment of atopic eczema.

Summary

EudraCT number	2011-004184-79
Trial protocol	GB
Global end of trial date	08 April 2014

Results information

Result version number	v1 (current)
This version publication date	12 July 2016
First version publication date	31 July 2015

Trial information

Trial identification

Sponsor protocol code	NIAD-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Dermal Laboratories Limited
Sponsor organisation address	Tatmore Place, Gosmore, Hitchin, United Kingdom, SG4 7QR
Public contact	Amanda Wigens, Dermal Laboratories Limited, 0044 01462458866, clinical@dermal.co.uk
Scientific contact	Amanda Wigens, Dermal Laboratories Limited, 0044 01462458866, clinical@dermal.co.uk

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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 April 2014
Global end of trial reached?	Yes
Global end of trial date	08 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to find out whether the 4% nicotinamide gel (NIAD Gel) offers therapeutically relevant treatment of mild to moderate atopic eczema compared to placebo, using a bilateral (within subject comparison) study design. If the active gel is beneficial in treating the very itchy, red and inflamed 'flared' atopic eczema skin areas, this may help us develop a new product which can help reduce the impact of atopic eczema on the lives of patients and their families.

This study was powered for two endpoints: the difference between the improvement from baseline Investigator Global Assessment (IGA) for the NIAD Gel treated areas compared to the Placebo treated areas after the 4 weeks treatment period, and the change from baseline Three Item Severity Score (TISS = erythema + oedema + excoriation) for the NIAD treated areas compared to the Placebo treated areas after the 4 week treatment period.

Protection of trial subjects:

Topical application of the product was consistent with standard care. The main risk to the participants presented by this research was that of the treatment (active and placebo) not working. This was mitigated by the chosen study design and methodology, which restricted the application of both active and placebo gels to relatively small areas of the body while allowing other topical treatments to continue elsewhere. Also, reported placebo effects are not uncommon in similar studies, therefore significant worsening of the skin condition on the treatment areas was not likely.

Background therapy:

The use of the IMPs was restricted to the patient's volar forearms only. Elsewhere, they were allowed to carry on applying their usual topical treatments to manage their eczema.

Evidence for comparator:

Use of a placebo comparison involving limited treatment areas only (the volar forearms) was chosen because this offers the advantages of scientific rigor (from placebo control) whilst also permitting patients to continue using their normal eczema treatments elsewhere; thereby minimising ethical issues associated with a placebo.

Actual start date of recruitment	10 June 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	United Kingdom: 54
Worldwide total number of subjects	54
EEA total number of subjects	54

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)	0
Adolescents (12-17 years)	7
Adults (18-64 years)	47
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Potential participants were primarily identified from a review of the study centre's patient volunteer database. In addition, a study poster/advert was displayed in local GP surgeries and other locations, in order to publicise the study to the wider community.

Pre-assignment

Screening details:

68 patients were screened of which 54 were consented and randomised into the study. Of these, 51 patients were included in the Intention-To-Treat (ITT) population used in the outcome analysis.

Period 1

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

Arms

Arm title	Active and Placebo

Arm description:

Bilateral design - all patients received active and placebo.

Arm type	Active and Placebo
Investigational medicinal product name	NIAD Gel
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

The product was applied topically three times daily for four weeks. Patients were asked to apply a sufficient amount of gel to ensure complete coverage of the treatment area in the left or right volar forearm (from the front of the wrist to just above the creases of the elbow) with a thin film of the product.

Investigational medicinal product name	Placebo Gel
Investigational medicinal product code	PL1
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

The product was applied topically three times daily for four weeks. Patients were asked to apply a sufficient amount of gel to ensure complete coverage of the treatment area in the other volar forearm (from the front of the wrist to just above the creases of the elbow) with a thin film of the product.

Number of subjects in period 1	Active and Placebo
Started	54
Baseline to 2 weeks	50
2 weeks to 4 weeks	50
Completed	50
Not completed	4
No longer able to attend appointments	2
Lost to follow-up	1
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial
Reporting group description:	
All randomised patients.	

Reporting group values	Overall trial	Total	
Number of subjects	54	54	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	7	7	
Adults (18-64 years)	47	47	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	37	37	
Male	17	17	
Ethnic group Units: Subjects			
Caucasian	52	52	
Asian	2	2	
Solar skin type Units: Subjects			
White (always burns never tans)	14	14	
White (usually burns tans with difficulty)	11	11	
Cream (sometimes mild burn gradually tans)	27	27	
Brown (rarely burns tans with ease)	1	1	
Dark brown (very rarely burns tans very easily)	1	1	
Black (never burns tans very easily)	0	0	

Subject analysis sets	
Subject analysis set title	ITT analysis set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intention-to-treat (ITT) analysis set.	
Subject analysis set title	N/A (bilateral study design)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Bilateral design - all patients received active and placebo.

Reporting group values	ITT analysis set	N/A (bilateral study design)	
Number of subjects	51	51	
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	6		
Adults (18-64 years)	45		
From 65-84 years	0		
85 years and over	0		
Gender categorical Units: Subjects			
Female	34		
Male	17		
Ethnic group Units: Subjects			
Caucasian	49		
Asian	2		
Solar skin type Units: Subjects			
White (always burns never tans)	12		
White (usually burns tans with difficulty)	10		
Cream (sometimes mild burn gradually tans)	27		
Brown (rarely burns tans with ease)	1		
Dark brown (very rarely burns tans very easily)	1		
Black (never burns tans very easily)	0		

End points

End points reporting groups

Reporting group title	Active and Placebo
Reporting group description: Bilateral design - all patients received active and placebo.	
Subject analysis set title	ITT analysis set
Subject analysis set type	Intention-to-treat
Subject analysis set description: Intention-to-treat (ITT) analysis set.	
Subject analysis set title	N/A (bilateral study design)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Bilateral design - all patients received active and placebo.	

Primary: Baseline improvement IGA, NIAD arm minus Placebo arm

End point title	Baseline improvement IGA, NIAD arm minus Placebo arm
End point description: The primary endpoint is the difference between the improvement from baseline Investigator Global Assessment (IGA) for the NIAD Gel treated areas compared to the Placebo treated areas after the 4 weeks treatment period.	
End point type	Primary
End point timeframe: Difference in improvement from baseline to final assessment (after 4 weeks of treatment).	

End point values	ITT analysis set	N/A (bilateral study design)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	51	51[1]		
Units: percent				
number (not applicable)				
-2 (placebo arm improved more)	0	0		
-1 (placebo arm improved more)	12	0		
0 (both arms same improvement)	57	0		
+1 (NIAD arm improved more)	25	0		
+2 (NIAD arm improved more)	4	0		
Missing	2	0		

Notes:

[1] - Bilateral design - all patients received active and placebo.

Attachments (see zip file)	Primary outcome/Figure - primary.pdf

Statistical analyses

Statistical analysis title	Primary outcome
Statistical analysis description: The number of subjects included in this analysis is 51 (not 102), this is because it is a bilateral study.	
Comparison groups	ITT analysis set v N/A (bilateral study design)

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.032 [3]
Method	Wilcoxon signed ranks test

Notes:

[2] - Analysed on a paired basis to reflect the bilateral study design.

[3] - Significant at 5% level (2-sided).

Secondary: Baseline improvement TISS, NIAD arm minus Placebo arm

End point title	Baseline improvement TISS, NIAD arm minus Placebo arm

End point description:

The secondary outcome is the change from baseline Three Item Severity Score (TISS) for the NIAD treated areas compared to the Placebo treated areas after the 4 week treatment period. TISS is the sum of the SCORAD intensity item scores for Erythema, Oedema/papulation and Excoriations/scratches (each on a 0 to 3 scale).

End point type	Secondary

End point timeframe:

Difference in improvement from baseline to final assessment (after 4 weeks of treatment).

End point values	ITT analysis set	N/A (bilateral study design)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	51	51[4]		
Units: Mean improvement in TISS score				
least squares mean (confidence interval 95%)				
NIAD minus Placebo (adjusted mean and 95% CI)	0.31 (0.01 to 0.61)	0 (0 to 0)		

Notes:

[4] - Bilateral design - all patients received active and placebo.

Statistical analyses

Statistical analysis title	Secondary outcome

Statistical analysis description:

This endpoint was analysed by fitting the data using a mixed model taking into account the bilateral study design, with baseline TISS as covariate, randomised group, arm and treatment as fixed effects and subject as a random effect. The treatment effect was assessed using the within subject error term and the arm effect was assessed using the between subject error term. The number of subjects included in this analysis is 51 (not 102), this is because it is a bilateral study.

Comparison groups	ITT analysis set v N/A (bilateral study design)
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04 [5]
Method	Mixed models analysis

Notes:

[5] - Significant at 5% level (2-sided).

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline to 6 weeks (this includes 2 weeks late onset).	
Assessment type	Systematic
Dictionary used	
Dictionary name	As reported in CRF
Dictionary version	N/A
Reporting groups	
Reporting group title	All randomised patients

Reporting group description: -

Serious adverse events	All randomised patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 54 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	All randomised patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 54 (37.04%)		
Skin and subcutaneous tissue disorders			
Worsening/flare of eczema	Additional description: Adverse events probably or possibly related to NIAD and/or Placebo.		
subjects affected / exposed	7 / 54 (12.96%)		
occurrences (all)	7		
Redness of skin/Dryness of skin/Itching/Increased papulation	Additional description: Adverse events probably or possibly related to NIAD and/or Placebo.		
subjects affected / exposed	8 / 54 (14.81%)		
occurrences (all)	14		
Stinging (or 'nip')	Additional description: Adverse events probably or possibly related to NIAD and/or Placebo.		
subjects affected / exposed	11 / 54 (20.37%)		
occurrences (all)	11		

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