Clinical trial results:
Choice Of Moisturiser in Eczema Treatment (COMET): A feasibility study of pragmatic, single blind, randomised clinical trial to compare the clinical and cost effectiveness of leave-on emollients in treatment of infant eczema in primary care

Summary

EudraCT number	2013-003001-26
Trial protocol	GB
Global end of trial date	31 August 2015

Results information

Result version number	v1 (current)
This version publication date	01 July 2018
First version publication date	01 July 2018

Trial information

Trial identification

Sponsor protocol code	2009

Additional study identifiers

ISRCTN number	ISRCTN21828118
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	NIHR RfPB: PB-PG-0712-28056, NIHR Portfolio: 134716, NHS REC: 13/SW/0297

Notes:

Sponsors

Sponsor organisation name	University of Bristol
Sponsor organisation address	Senate House, Tyndall Avenue, Bristol, United Kingdom, BS8 1TH
Public contact	Birgit Whitman, University of Bristol, +44 01173317130, birgit.whitman@bristol.ac.uk
Scientific contact	Birgit Whitman, University of Bristol, +44 01173317130, birgit.whitman@bristol.ac.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	04 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2015
Global end of trial reached?	Yes
Global end of trial date	31 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal research question for this feasibility study: Is it possible to recruit and retain participants from primary care into a four arm randomised control trial of emollients in children with eczema aged between 1 month and 5 years?

The principal research question for the main trial: "Which is the most clinically and cost effective primary emollient to use in infants with eczema?"

Protection of trial subjects:

The trial was conducted in compliance with the principles of the Declaration of Helsinki (1996), the principles of GCP and in accordance with all applicable regulatory requirements including but not limited to the Research Governance Framework and the Medicines for Human Use (Clinical Trial) Regulations 2004, as amended in 2006 and any subsequent amendments.

This protocol and related documents were reviewed by NRES Committee South West - Central Bristol Research Ethics (REC), and given Clinical Trial Authorisation by the Medicines and Healthcare products Regulatory Agency (MHRA).

An adult with parental responsibility gave written consent for the child to take part. The study was classified as a low risk (type A) medicines trial because participants were randomised to treatments that can be both bought over-the-counter and are prescribed on a daily basis.

The conduct of the study and the safety of participants were monitored by an independent Trial Steering/Data Monitoring Committee.

Background therapy:

All participants were allocated a study emollient. The study did not include a control arm, as it might be considered unethical to randomise a child with eczema to no emollient.

Evidence for comparator:

Participants were randomly allocated to one of four emollients (Aveeno® lotion, Diprobase® cream, Doublebase® gel, Hydromol® ointment) to use as their primary leave-on emollient with directions to 'Use twice daily and when required.' These were chosen because they represent each of the different formulations (lotion, cream, gel and ointment), are among the most commonly prescribed and vary in cost. In addition, Doublebase® and Diprobase® emerged as the most popular in a patient preference study and mechanistic studies have shown that these emollients enhance skin barrier function.

Actual start date of recruitment	03 February 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 197

Worldwide total number of subjects	197
EEA total number of subjects	197

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)	123
Children (2-11 years)	74
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:

Between July 2014 and April 2015, participants were recruited in primary care (general practice) via two pathways: 'self-referral' (usually in response to a letter sent by their practice inviting them to take part) or 'in consultation' (an approach during a surgery visit by GP/practice nurse, who also received consent and undertook randomisation).

Pre-assignment

Screening details:

GP searched their medical records for registered patients aged > 1 to <35 months with an eczema Read code; and screened the results excluding children: who no longer have eczema; known to be sensitive to one of the study emollients; whose parents unable to complete questionnaires; with adverse medical or social circumstances; or for other reasons.

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Blinding implementation details:

The Clinical Study Officer (CSO) was masked to the participant's treatment allocation: they had restricted access to the randomisation system meaning they could not identify which emollient had been assigned to which participant; and parents were asked not to disclose which treatment they are using, to hide the emollient container from view, and to maximise the amount of time between emollient application and the assessments taking place.

Arms

Are arms mutually exclusive?	Yes
Arm title	Lotion

Arm description:

Aveeno lotion

Arm type	Active comparator
Investigational medicinal product name	Aveeno lotion
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Cutaneous use

Dosage and administration details:

No maximum dose
Cutaneous use

Arm title	Cream

Arm description:

Diprobase cream

Arm type	Active comparator
Investigational medicinal product name	Diprobase Cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

No maximum dosage.
Cutaneous use

Arm title	Gel_
Arm description: Doublebase gel	
Arm type	Active comparator
Investigational medicinal product name	Doublebase gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use
Dosage and administration details: No maximum dose. Cutaneous use.	

Arm title	Ointment
Arm description: Hydromol ointment	
Arm type	Active comparator
Investigational medicinal product name	Hydromol ointment
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use
Dosage and administration details: No maximum dose. Cutaneous use	

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Only the observer was blinded; clinicians and parents/children taking part in the trial knew their allocation.

Number of subjects in period 1	Lotion	Cream	Gel_
Started	51	53	46
Completed	39	39	39
Not completed	12	14	7
Lost to follow-up	12	14	7

Number of subjects in period 1	Ointment
Started	47
Completed	34
Not completed	13
Lost to follow-up	13

Baseline characteristics

Reporting groups	
Reporting group title	Lotion
Reporting group description: Aveeno lotion	
Reporting group title	Cream
Reporting group description: Diprobase cream	
Reporting group title	Gel_
Reporting group description: Doublebase gel	
Reporting group title	Ointment
Reporting group description: Hydromol ointment	

Reporting group values	Lotion	Cream	Gel_
Number of subjects	51	53	46
Age categorical			
Age in months			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	30	29	30
Children (2-11 years)	21	24	16
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	17	26	19
Male	34	27	27
POEM			
Patient Orientated Eczema Measure			
Units: unit(s)			
arithmetic mean	8.3	8.5	9.7
standard deviation	± 5.9	± 6.5	± 5.4
EASI			
Eczema Area Severity Index			
Units: unit(s)			
arithmetic mean	2.8	3.5	2.7
standard deviation	± 3.6	± 4.1	± 4.2

Reporting group values	Ointment	Total	
Number of subjects	47	197	

Age categorical			
Age in months			
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)	34	123	
Children (2-11 years)	13	74	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	23	85	
Male	24	112	
POEM			
Patient Orientated Eczema Measure			
Units: unit(s)			
arithmetic mean	8.8		
standard deviation	± 5.7	-	
EASI			
Eczema Area Severity Index			
Units: unit(s)			
arithmetic mean	2.7		
standard deviation	± 3.3	-	

End points

End points reporting groups

Reporting group title	Lotion
Reporting group description: Aveeno lotion	
Reporting group title	Cream
Reporting group description: Diprobase cream	
Reporting group title	Gel_
Reporting group description: Doublebase gel	
Reporting group title	Ointment
Reporting group description: Hydromol ointment	

Primary: POEM

End point title	POEM[1]
End point description: 12 week follow-up questionnaire	
End point type	Primary
End point timeframe: 84 days	

Notes:

[1] - 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: This was a feasibility trial so no a priori primary outcome was specified.

End point values	Lotion	Cream	Gel_	Ointment
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	38	37	31
Units: unit(s)				
arithmetic mean (standard deviation)	3.7 (± 3.9)	5.2 (± 4.4)	3.9 (± 4.8)	4.4 (± 5.7)

Statistical analyses

No statistical analyses for this end point

Secondary: EASI

End point title	EASI
End point description: 3 month follow-up visit	
End point type	Secondary
End point timeframe: 84 days	

End point values	Lotion	Cream	Gel_	Ointment
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	39	38	32
Units: unit(s)				
arithmetic mean (standard deviation)	1.3 (± 1.6)	2.5 (± 2.9)	1.8 (± 5.3)	2.2 (± 2.9)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
3 months	
Adverse event reporting additional description:	
Adverse events were collected by means of a patient-completed diary; serious adverse events were reported directly to the trial team and the trial sponsor notified.	
Assessment type	Systematic

Dictionary used	
Dictionary name	No dictionary
Dictionary version	0

Reporting groups	
Reporting group title	Lotion
Reporting group description:	
Aveeno lotion	
Reporting group title	Cream
Reporting group description:	
Diprobase cream	
Reporting group title	Gel_
Reporting group description:	
Doublebase gel	
Reporting group title	Ointment
Reporting group description:	
Hydromol ointment	

Serious adverse events	Lotion	Cream	Gel_
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 51 (0.00%)	0 / 53 (0.00%)	0 / 46 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Skin and subcutaneous tissue disorders			
Skin infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 53 (0.00%)	0 / 46 (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

Serious adverse events	Ointment		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 47 (2.13%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Skin and subcutaneous tissue disorders			
Skin infection			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Lotion	Cream	Gel_
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 51 (50.98%)	30 / 53 (56.60%)	30 / 46 (65.22%)
Skin and subcutaneous tissue disorders			
All skin reactions	Additional description: Any of pruritis, rash, erythema, pain, dry skin or infection		
subjects affected / exposed	26 / 51 (50.98%)	30 / 53 (56.60%)	30 / 46 (65.22%)
occurrences (all)	107	90	89

Non-serious adverse events	Ointment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 47 (59.57%)		
Skin and subcutaneous tissue disorders			
All skin reactions	Additional description: Any of pruritis, rash, erythema, pain, dry skin or infection		
subjects affected / exposed	28 / 47 (59.57%)		
occurrences (all)	71		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 August 2014	Clarifying the adverse and serious adverse events that would be expected to be seen within the normal population of children within this age group; and the way we capture the information regarding AEs and SAEs.
06 December 2014	In addition to GCP-trained doctors, appropriately qualified health care professional who are GCP trained (with oversight from a medically qualified doctor) able to confirm eligibility. Change of eligibility criteria from "child aged between 1 month to 3 years with doctor diagnosed eczema" to "child aged between 1 month and 5 years of age with eczema (diagnosed by a doctor or an appropriately qualified health care professional with oversight from a medically qualified doctor)" Seeking to recruit children from an additional 14 general practices (so total of 30 practices), with only the first 16 practices doing the follow-up mail-outs. Distinction in interval between referral and baseline assessment between participants who enter the study via GP/PN and those who self-refer.

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/27852708