Clinical trial results:
A randomised placebo-controlled trial of oral and topical antibiotics for children with clinically infected eczema in the community: the ChildRen with Eczema, Antibiotic Management (CREAM) study

Summary

EudraCT number	2011-003591-37
Trial protocol	GB
Global end of trial date	25 March 2015

Results information

Result version number	v2 (current)
This version publication date	28 March 2019
First version publication date	23 July 2017
Version creation reason	• Correction of full data set Inconsistency in closure date - needed updating
Summary attachment (see zip file)	CREAM: NIHr HTA final report (CREAM FINAL NIHR HTA REPORT.pdf)

Trial information

Trial identification

Sponsor protocol code	SPON846-10

Additional study identifiers

ISRCTN number	ISRCTN96705420
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cardiff University
Sponsor organisation address	McKensie House, Newport Road, Cardiff, United Kingdom, CF24 0DE
Public contact	Trial Manager, Cardiff University, 44 02920687620, CREAM@cardiff.ac.uk
Scientific contact	Trial Manager, Cardiff University, 44 02920687665, CREAM@cardiff.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	29 April 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 March 2015
Global end of trial reached?	Yes
Global end of trial date	25 March 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Does the addition of oral or topical antibiotic treatment to treatment with corticosteroid cream, reduce eczema severity in children with suspected infected eczema in primary care?

Protection of trial subjects:

The IDMC for the CREAM trial was build-up to safeguard the interests of the CREAM trial participants, potential participants, investigator and sponsor; to assess the safety and efficacy of the trial interventions, and to monitor the trial's overall conduct, and protect its validity and credibility. Three IDMC meetings had been held (12th March 2012, 04th November 2013 and 07th May 2014). The IDMC received and reviewed the progress and accruing data of this trial and provided advice on the conduct of the trial to the Trial Steering Committee (TSC).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 July 2013
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: 113
Worldwide total number of subjects	113
EEA total number of subjects	113

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)	45
Children (2-11 years)	68
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:

General practitioner practices and dermatology clinic sites were recruited between 9 July 2013 and 21 October 2014. 32 GP sites and 1 dermatology clinic actively recruited one or more participants into the study.
Participants were recruited between 16 July 2013 and 28 November 2014. Of the 171 referred children, 113 were randomized.

Pre-assignment

Screening details:

1. Eligible patients identified by general practices and secondary care centres.
2. Research nurse checks eligibility.
3. Pharmacy randomises and dispenses medicine to research nurse

Pre-assignment period milestones

Number of subjects started	171[1]
Number of subjects completed	113

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Ineligible: 18
Reason: Number of subjects	Unable to participate because of time/resources: 28
Reason: Number of subjects	Declined to participate: 12

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number reported in the pre-assignment period include all participants screened for the study (171 in total). Enrolled and consented total = 113.
58 participants were either ineligible or declined to participate.

Period 1

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

Blinding implementation details:

Placebo products were matched to oral and topical antibiotic preparations. Participants, parents, clinicians
and research nurses remained blinded to treatment allocation.

Arms

Are arms mutually exclusive?	Yes
Arm title	Control_baseline

Arm description:

placebo oral and placebo topical cream treatment at baseline

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

Dosage and administration details:

The placebo antibiotic cream used in this study was manufactured to match the active treatment.
Apply medicine 3 times a day for 1 week

Investigational medicinal product name	Placebo oral solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution
Routes of administration	Oral use

Dosage and administration details:

supplied as granules for reconstitution

doses for each age group are -
• Children (2-5 years of age): 5ml four times a day
• Children under 2 years of age: 2.5ml four times a day

Arm title	Oral antibiotic_baseline

Arm description:

oral antibiotic and placebo topical cream at baseline

Arm type	Experimental
Investigational medicinal product name	flucloxacillin
Investigational medicinal product code	PL 20416/0077
Other name	
Pharmaceutical forms	Concentrate for oral suspension
Routes of administration	Oral use

Dosage and administration details:

granules for reconstitution in 100 ml to provide a concentration of 250 mg/5 ml.
the usual doses for each age group are -
• Children (2-5 years of age): 5ml four times a day
• Children under 2 years of age: 2.5ml four times a day

Investigational medicinal product name	Placebo topical cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

The placebo antibiotic cream used in this study was manufactured to match the active treatment.
Apply medicine 3 times a day for 1 week

Arm title	Topical antibiotic_baseline

Arm description:

topical antibiotic cream and placebo oral treatment at baseline

Arm type	Experimental
Investigational medicinal product name	Placebo oral solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution
Routes of administration	Oral use

Dosage and administration details:

supplied as granules for reconstitution

doses for each age group are -
• Children (2-5 years of age): 5ml four times a day
• Children under 2 years of age: 2.5ml four times a day

Investigational medicinal product name	Fuscidic acid cream 2%
Investigational medicinal product code	PL 00043/0065
Other name	
Pharmaceutical forms	Cream

Routes of administration	Topical use

Dosage and administration details:

apply topical cream medicine 3 times a day for 1 week

Number of subjects in period 1	Control_baseline	Oral antibiotic_baseline	Topical antibiotic_baseline
Started	40	36	37
Completed	40	36	37

Period 2

Period 2 title	2-week follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Control_week2

Arm description:

placebo oral and placebo topical cream treatment at week2

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

Dosage and administration details:

The placebo antibiotic cream used in this study was manufactured to match the active treatment.
Apply medicine 3 times a day for 1 week

Investigational medicinal product name	Placebo oral solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution
Routes of administration	Oral use

Dosage and administration details:

supplied as granules for reconstitution

doses for each age group are -
• Children (2-5 years of age): 5ml four times a day

• Children under 2 years of age: 2.5ml four times a day

Arm title	Oral antibiotic_week2
Arm description:	
oral antibiotic and placebo topical cream at week-2	
Arm type	Experimental
Investigational medicinal product name	Placebo topical cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use
Dosage and administration details:	
The placebo antibiotic cream used in this study was manufactured to match the active treatment. Apply medicine 3 times a day for 1 week	
Investigational medicinal product name	flucloxacillin
Investigational medicinal product code	PL 20416/0077
Other name	
Pharmaceutical forms	Concentrate for oral suspension
Routes of administration	Oral use
Dosage and administration details:	
granules for reconstitution in 100 ml to provide a concentration of 250 mg/5 ml. the usual doses for each age group are - • Children (2-5 years of age): 5ml four times a day • Children under 2 years of age: 2.5ml four times a day	
Arm title	Topical antibiotic_week2
Arm description:	
topical antibiotic cream and placebo oral treatment at week-2	
Arm type	Experimental
Investigational medicinal product name	Fuscidic acid cream 2%
Investigational medicinal product code	PL 00043/0065
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use
Dosage and administration details:	
apply topical cream medicine 3 times a day for 1 week	
Investigational medicinal product name	Placebo oral solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution
Routes of administration	Oral use
Dosage and administration details:	
supplied as granules for reconstitution doses for each age group are - • Children (2-5 years of age): 5ml four times a day • Children under 2 years of age: 2.5ml four times a day	

Number of subjects in period 2	Control_week2	Oral antibiotic_week2	Topical antibiotic_week2
Started	40	36	37
Completed	36	34	31
Not completed	4	2	6
Consent withdrawn by subject	2	1	5
Lost to follow-up	2	1	1

Period 3	
Period 3 title	4-week follow up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Control_week4

Arm description:

placebo oral and placebo topical cream treatment at week-4

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

Dosage and administration details:

The placebo antibiotic cream used in this study was manufactured to match the active treatment. Apply medicine 3 times a day for 1 week

Investigational medicinal product name	Placebo oral solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution
Routes of administration	Oral use

Dosage and administration details:

supplied as granules for reconstitution

doses for each age group are -
• Children (2-5 years of age): 5ml four times a day
• Children under 2 years of age: 2.5ml four times a day

Arm title	Oral antibiotic_week4

Arm description:

oral antibiotic and placebo topical cream at week-4

Arm type	Experimental

Investigational medicinal product name	Placebo topical cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

The placebo antibiotic cream used in this study was manufactured to match the active treatment.
Apply medicine 3 times a day for 1 week

Investigational medicinal product name	flucloxacillin
Investigational medicinal product code	PL 20416/0077
Other name	
Pharmaceutical forms	Concentrate for oral suspension
Routes of administration	Oral use

Dosage and administration details:

granules for reconstitution in 100 ml to provide a concentration of 250 mg/5 ml.
the usual doses for each age group are -
• Children (2-5 years of age): 5ml four times a day
• Children under 2 years of age: 2.5ml four times a day

Arm title	Topical antibiotic_week4

Arm description:

topical antibiotic cream and placebo oral treatment at week-4

Arm type	Experimental
Investigational medicinal product name	Fuscidic acid cream 2%
Investigational medicinal product code	PL 00043/0065
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

apply topical cream medicine 3 times a day for 1 week

Investigational medicinal product name	Placebo oral solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution
Routes of administration	Oral use

Dosage and administration details:

supplied as granules for reconstitution

doses for each age group are -
• Children (2-5 years of age): 5ml four times a day
• Children under 2 years of age: 2.5ml four times a day

Number of subjects in period 3	Control_week4	Oral antibiotic_week4	Topical antibiotic_week4
Started	36	34	31
Completed	35	33	30
Not completed	1	1	1
Consent withdrawn by subject	1	-	-
Lost to follow-up	-	1	1

Period 4

Period 4 title	3-month follow up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Control_month3

Arm description:

placebo oral and placebo topical cream treatment at month-3

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

Dosage and administration details:

The placebo antibiotic cream used in this study was manufactured to match the active treatment.
Apply medicine 3 times a day for 1 week

Investigational medicinal product name	Placebo oral solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution
Routes of administration	Oral use

Dosage and administration details:

supplied as granules for reconstitution

doses for each age group are -
• Children (2-5 years of age): 5ml four times a day
• Children under 2 years of age: 2.5ml four times a day

Arm title	Oral antibiotic_month3

Arm description:

oral antibiotic and placebo topical cream at month-3

Arm type	Experimental
Investigational medicinal product name	flucloxacillin
Investigational medicinal product code	PL 20416/0077
Other name	
Pharmaceutical forms	Concentrate for oral suspension
Routes of administration	Oral use

Dosage and administration details:

granules for reconstitution in 100 ml to provide a concentration of 250 mg/5 ml.
the usual doses for each age group are -
• Children (2-5 years of age): 5ml four times a day
• Children under 2 years of age: 2.5ml four times a day

Investigational medicinal product name	Placebo topical cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

The placebo antibiotic cream used in this study was manufactured to match the active treatment.
Apply medicine 3 times a day for 1 week

Arm title	Topical antibiotic_month3

Arm description:

topical antibiotic cream and placebo oral treatment at month-3

Arm type	Experimental
Investigational medicinal product name	Fuscidic acid cream 2%
Investigational medicinal product code	PL 00043/0065
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

apply topical cream medicine 3 times a day for 1 week

Investigational medicinal product name	Placebo oral solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules for oral solution
Routes of administration	Oral use

Dosage and administration details:

supplied as granules for reconstitution

doses for each age group are -
• Children (2-5 years of age): 5ml four times a day
• Children under 2 years of age: 2.5ml four times a day

Number of subjects in period 4	Control_month3	Oral antibiotic_month3	Topical antibiotic_month3
Started	35	33	30
Completed	25	28	21
Not completed	10	5	9
Lost to follow-up	10	5	9

Baseline characteristics

Reporting groups	
Reporting group title	Control_baseline
Reporting group description:	
placebo oral and placebo topical cream treatment at baseline	
Reporting group title	Oral antibiotic_baseline
Reporting group description:	
oral antibiotic and placebo topical cream at baseline	
Reporting group title	Topical antibiotic_baseline
Reporting group description:	
topical antibiotic cream and placebo oral treatment at baseline	

Reporting group values	Control_baseline	Oral antibiotic_baseline	Topical antibiotic_baseline
Number of subjects	40	36	37
Age categorical			
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)	15	15	15
Children (2-11 years)	25	21	22
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
Age continuous			
Age			
Units: years			
arithmetic mean	3.3	2.9	3
standard deviation	± 2.2	± 2.2	± 2.1
Gender categorical			
Units: Subjects			
Female	17	18	17
Male	23	18	20

Reporting group values	Total		
Number of subjects	113		
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)	45		
Children (2-11 years)	68		

Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Age			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	52		
Male	61		

Subject analysis sets

Subject analysis set title	analysis of primary outcome
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Our main (primary) analyses are intention-to-treat (ITT) analyses comparing POEM scores at 2 weeks in the
oral antibiotic group with the control (placebo) group, and in the topical antibiotic group with the control (placebo) group, and using all participants who have baseline and 2-week POEM scores (i.e. not using imputation for the primary ITT analysis). This was conducted using the analysis of covariance (ANCOVA) approach, controlling for baseline POEM score.

Subject analysis set title	analysis of secondary outcomes
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The analysis of POEM scores at 4 weeks and 3 months, EASI scores at 2 and 4 weeks, IDQoL, CDLQI and
DFI scores at 2 and 4 weeks and 3 months were also carried out using the ANCOVA approach. That is, we
used these scores as dependent variables, controlling for baseline scores and treatment arms, where the placebo group was set as the reference category. As these scores (EASI, IDQoL, CDLQI and DFI) were positively skewed and contained a number of zeros, we took the natural log transformation of the scores plus one. Therefore, the results of these analyses are presented as the percentage differences of the scores between treatment groups.

Reporting group values	analysis of primary outcome	analysis of secondary outcomes	
Number of subjects	113	113	
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)	45	45	
Children (2-11 years)	68	68	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	

Age continuous			
Age			
Units: years			
arithmetic mean	3.1	3.1	
standard deviation	± 2.1	± 2.1	
Gender categorical			
Units: Subjects			
Female	52	52	
Male	61	61	

End points

End points reporting groups

Reporting group title	Control_baseline
Reporting group description: placebo oral and placebo topical cream treatment at baseline	
Reporting group title	Oral antibiotic_baseline
Reporting group description: oral antibiotic and placebo topical cream at baseline	
Reporting group title	Topical antibiotic_baseline
Reporting group description: topical antibiotic cream and placebo oral treatment at baseline	
Reporting group title	Control_week2
Reporting group description: placebo oral and placebo topical cream treatment at week2	
Reporting group title	Oral antibiotic_week2
Reporting group description: oral antibiotic and placebo topical cream at week-2	
Reporting group title	Topical antibiotic_week2
Reporting group description: topical antibiotic cream and placebo oral treatment at week-2	
Reporting group title	Control_week4
Reporting group description: placebo oral and placebo topical cream treatment at week-4	
Reporting group title	Oral antibiotic_week4
Reporting group description: oral antibiotic and placebo topical cream at week-4	
Reporting group title	Topical antibiotic_week4
Reporting group description: topical antibiotic cream and placebo oral treatment at week-4	
Reporting group title	Control_month3
Reporting group description: placebo oral and placebo topical cream treatment at month-3	
Reporting group title	Oral antibiotic_month3
Reporting group description: oral antibiotic and placebo topical cream at month-3	
Reporting group title	Topical antibiotic_month3
Reporting group description: topical antibiotic cream and placebo oral treatment at month-3	
Subject analysis set title	analysis of primary outcome
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Our main (primary) analyses are intention-to-treat (ITT) analyses comparing POEM scores at 2 weeks in the
oral antibiotic group with the control (placebo) group, and in the topical antibiotic group with the control (placebo) group, and using all participants who have baseline and 2-week POEM scores (i.e. not using imputation for the primary ITT analysis). This was conducted using the analysis of covariance (ANCOVA)

approach, controlling for baseline POEM score.

Subject analysis set title	analysis of secondary outcomes
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The analysis of POEM scores at 4 weeks and 3 months, EASI scores at 2 and 4 weeks, IDQoL, CDLQI and
DFI scores at 2 and 4 weeks and 3 months were also carried out using the ANCOVA approach. That is, we
used these scores as dependent variables, controlling for baseline scores and treatment arms, where the placebo group was set as the reference category. As these scores (EASI, IDQoL, CDLQI and DFI) were positively skewed and contained a number of zeros, we took the natural log transformation of the scores plus one. Therefore, the results of these analyses are presented as the percentage differences of the scores between treatment groups.

Primary: POEM scores at 2-week

End point title	POEM scores at 2-week

End point description:

POEM scores can range from 0 to 28, and higher POEM scores represent worse eczema severity.

End point type	Primary

End point timeframe:

At 2 weeks following the baseline visit research nurses recorded
POEM.

End point values	Control_week2	Oral antibiotic_week 2	Topical antibiotic_week 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36	34	31	
Units: Range from 0 to 28				
arithmetic mean (standard error)	6.17 (± 5.97)	8.27 (± 7.33)	9.32 (± 6.17)	

Statistical analyses

Statistical analysis title	ANCOVA analysis of POEW at 2-week follow-up

Statistical analysis description:

Our main (primary) analyses are intention-to-treat (ITT) analyses comparing POEM scores at 2 weeks in the
oral antibiotic group with the control (placebo) group, and using all participants who have baseline and 2-week POEM scores (i.e. not using
imputation for the primary ITT analysis). This was conducted using the analysis of covariance (ANCOVA) approach, controlling for baseline POEM score.

Comparison groups	Oral antibiotic_week2 v Control_week2
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Mean difference (final values)
Point estimate	1.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.35
upper limit	4.4

Notes:

[1] - Owing to lower than expected recruitment rates the study was closed early, before the proposed reduced
target sample size was reached. Because of this, the analysis focuses on estimating effect sizes and confidence intervals (CIs) rather than tests of significance, which would have been undertaken if the sample size had been achieved.

Statistical analysis title	ANCOVA analysis of POEW at 2-week follow-up

Statistical analysis description:

Our main (primary) analyses are intention-to-treat (ITT) analyses comparing POEM scores at 2 weeks in the topical antibiotic group with the control
(placebo) group, and using all participants who have baseline and 2-week POEM scores (i.e. not using imputation for the primary ITT analysis). This was conducted using the analysis of covariance (ANCOVA) approach, controlling for baseline POEM score.

Comparison groups	Topical antibiotic_week2 v Control_week2
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other[2]
Parameter estimate	Mean difference (final values)
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.55
upper limit	4.53

Notes:

[2] - Owing to lower than expected recruitment rates the study was closed early, before the proposed reduced
target sample size was reached. Because of this, the analysis focuses on estimating effect sizes and confidence intervals (CIs) rather than tests of significance, which would have been undertaken if the sample size had been achieved.

Secondary: POEM at 4-week follow-up

End point title	POEM at 4-week follow-up

End point description:

POEM scores can range from 0 to 28, and higher POEM scores represent worse eczema severity.

End point type	Secondary

End point timeframe:

POEM score collect at week-4 follow up.

End point values	Control_week4	Oral antibiotic_week4	Topical antibiotic_week4	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	33	30	
Units: Range from 0 to 28				
arithmetic mean (standard deviation)	8.03 (± 5.95)	8.36 (± 7.71)	9.53 (± 5.89)	

Statistical analyses

No statistical analyses for this end point

Secondary: POEM at 3-month follow up

End point title	POEM at 3-month follow up

End point description:

POEM scores can range from 0 to 28, and higher POEM scores represent worse eczema severity.

End point type	Secondary

End point timeframe:

POEM scores collected at 3-month follow up.

End point values	Control_month 3	Oral antibiotic_month3	Topical antibiotic_month3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	28	21	
Units: Range from 0 to 28				
arithmetic mean (standard deviation)	7.72 (± 5.52)	7.86 (± 6.09)	7.86 (± 5.85)	

Statistical analyses

No statistical analyses for this end point

Secondary: EASI at 2-week follow-up

End point title	EASI at 2-week follow-up

End point description:

EASI scores range from 0 to 72, and higher scores represent more severe eczema.

End point type	Secondary

End point timeframe:

At 2 weeks following the baseline visit research nurses recorded EASI scores.

End point values	Control_week2	Oral antibiotic_week 2	Topical antibiotic_week 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	34	31	
Units: Range from 0 to 72				
arithmetic mean (standard deviation)	2.5 (± 5.64)	3.09 (± 3.59)	4.91 (± 5.65)	

Statistical analyses

No statistical analyses for this end point

Secondary: EASI at week-4 follow up

End point title	EASI at week-4 follow up

End point description:

EASI scores range from 0 to 72, and higher scores represent more severe eczema.

End point type	Secondary

End point timeframe:

At 4 weeks following the baseline visit research nurses recorded EASI scores.

End point values	Control_week4	Oral antibiotic_week 4	Topical antibiotic_week 4	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	33	30	
Units: Range from 0 to 72				
arithmetic mean (standard deviation)	4.01 (± 6.55)	3.23 (± 3.81)	4.98 (± 6.87)	

Statistical analyses

No statistical analyses for this end point

Secondary: DFI at 2-week follow up

End point title	DFI at 2-week follow up

End point description:

Impact on the family was measured using the DFI instrument, which includes 10 items each scored from 0 to 3. This results in a score from 0 to 30, with higher scores representing more severe impact on the family.

End point type	Secondary

End point timeframe:

DFI scores collected at week-2 follow-up.

End point values	Control_week2	Oral antibiotic_week 2	Topical antibiotic_week 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	34	31	
Units: Range from 0 to 30				
arithmetic mean (standard deviation)	2.6 (± 4.76)	3.69 (± 4.42)	4.84 (± 5.35)	

Statistical analyses

No statistical analyses for this end point

Secondary: DFI at 4-week follow-up

End point title	DFI at 4-week follow-up

End point description:

Impact on the family was measured using the DFI instrument, which includes 10 items each scored from 0 to 3. This results in a score from 0 to 30, with higher scores representing more severe impact on the family.

End point type	Secondary

End point timeframe:

DFI collected at week-4 follow-up.

End point values	Control_week4	Oral antibiotic_week 4	Topical antibiotic_week 4	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	33	30	
Units: Range from 0 to 30				
arithmetic mean (standard deviation)	3.11 (± 4.86)	3.52 (± 4.6)	4.23 (± 4.83)	

Statistical analyses

No statistical analyses for this end point

Secondary: DFI at 3-month follow-up

End point title	DFI at 3-month follow-up

End point description:

Impact on the family was measured using the DFI instrument, which includes 10 items each scored from 0 to 3. This results in a score from 0 to 30, with higher scores representing more severe impact on the family.

End point type	Secondary

End point timeframe:

DFI scores collected at 3-month follow up

End point values	Control_month 3	Oral antibiotic_month3	Topical antibiotic_month3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	25	20	
Units: Range form 0 to 30				
arithmetic mean (standard deviation)	3.5 (± 4.28)	3.46 (± 4.4)	4.1 (± 5.52)	

Statistical analyses

No statistical analyses for this end point

Secondary: IDQoL at week-2 follow-up

End point title	IDQoL at week-2 follow-up

End point description:

IDQoL scores include 10 items and have scores that range from 0 to 30, where higher scores represent more severe (worse) impact
on quality of life.

End point type	Secondary

End point timeframe:

IDQoL scores for children under 4 years old collected at week-2 follow-up

End point values	Control_week2	Oral antibiotic_week2	Topical antibiotic_week2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	25	22	
Units: Range from 0 to 30				
arithmetic mean (standard deviation)	6.07 (± 3.69)	6.74 (± 3.28)	7.19 (± 3)	

Statistical analyses

No statistical analyses for this end point

Secondary: IDQoL scores at week-4 follow-up

End point title	IDQoL scores at week-4 follow-up

End point description:

IDQoL scores include 10 items and have scores that range from 0 to 30, where higher scores represent more severe (worse) impact
on quality of life.

End point type	Secondary

End point timeframe:

IDQoL scores for children under 4 years old collected at week-4 follow-up

End point values	Control_week4	Oral antibiotic_week 4	Topical antibiotic_week 4	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	24	22	
Units: Range from 0 to 30				
arithmetic mean (standard deviation)	6.92 (± 3.74)	6.59 (± 3.23)	7.14 (± 2.96)	

Statistical analyses

No statistical analyses for this end point

Secondary: IDQoL scores at month-3 follow-up

End point title	IDQoL scores at month-3 follow-up

End point description:

IDQoL scores include 10 items and have scores that range from 0 to 30, where higher scores represent more severe (worse) impact
on quality of life.

End point type	Secondary

End point timeframe:

IDQoL scores for children under 4 years old collected at month-3 follow-up

End point values	Control_month 3	Oral antibiotic_mont h3	Topical antibiotic_mont h3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	18	15	
Units: Range from 0-30				
arithmetic mean (standard deviation)	7.25 (± 2.59)	6.01 (± 3.15)	6.67 (± 3.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: CDLQI at week-2 follow up

End point title	CDLQI at week-2 follow up

End point description:

CDLQI scores include 10 items and have scores that range from 0 to 30, where higher scores represent more severe (worse) impact
on quality of life.

End point type	Secondary

End point timeframe:

CDLQI scores for children over 4 years old collected at week-2 follow-up

End point values	Control_week2	Oral antibiotic_week 2	Topical antibiotic_week 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	9	9	
Units: Range from 0-30				
arithmetic mean (standard deviation)	1.82 (± 1.98)	4.07 (± 3.04)	5.88 (± 6.25)	

Statistical analyses

No statistical analyses for this end point

Secondary: CDLQI scores at week-4 follow-up

End point title	CDLQI scores at week-4 follow-up

End point description:

CDLQI scores include 10 items and have scores that range from 0 to 30, where higher scores represent more severe (worse) impact
on quality of life.

End point type	Secondary

End point timeframe:

CDLQI scores for children over 4 years old collected at week-2 follow-up

End point values	Control_week4	Oral antibiotic_week 4	Topical antibiotic_week 4	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	9	8	
Units: Range from 0-30				
arithmetic mean (standard deviation)	4.64 (± 5.89)	4.36 (± 4.79)	3.04 (± 2.22)	

Statistical analyses

No statistical analyses for this end point

Secondary: CDLQI scores at month-3 follow-up

End point title	CDLQI scores at month-3 follow-up

End point description:

CDLQI scores include 10 items and have scores that range from 0 to 30, where higher scores represent more severe (worse) impact

on quality of life.

End point type	Secondary

End point timeframe:

CDLQI scores for children over 4 years old collected at month-3 follow-up

End point values	Control_month 3	Oral antibiotic_mont h3	Topical antibiotic_mont h3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	6	6	
Units: Range from 0 to 30				
arithmetic mean (standard deviation)	6.18 (± 6.37)	5.57 (± 6.73)	4.61 (± 4.59)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Data on adverse effects were obtained from the daily symptom diaries and were available the first 4 weeks after enrollment. The daily symptom diary included potential adverse effects, with each symptom being rated from 0 to 6 by parents.

Adverse event reporting additional description:

In order to capture potential adverse effects related to treatment , we included the treatment period (the first 7 days) and the subsequent 2 days (i.e. the first 9 days). Patients were categorised as having that adverse event if any potential adverse symptom was rated as a 'slight problem' or worse (i.e. score of ≥ 2) in any of the first 9 days.

Assessment type	Systematic

Dictionary used

Dictionary name	Symptoms diary
Dictionary version	1.0

Reporting groups

Reporting group title	Control

Reporting group description:

placebo oral and placebo topical cream treatment

Reporting group title	Oral antibiotic

Reporting group description:

oral antibiotic and placebo topical cream

Reporting group title	Topical antibiotic

Reporting group description:

topical antibiotic cream and placebo oral treatment

Serious adverse events	Control	Oral antibiotic	Topical antibiotic
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 35 (0.00%)	0 / 33 (0.00%)	0 / 29 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Control	Oral antibiotic	Topical antibiotic
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 35 (37.14%)	10 / 33 (30.30%)	11 / 29 (37.93%)
Gastrointestinal disorders			
Nausea			

subjects affected / exposed	3 / 35 (8.57%)	2 / 33 (6.06%)	1 / 29 (3.45%)
occurrences (all)	3	2	1
Vomiting			
subjects affected / exposed	6 / 35 (17.14%)	4 / 33 (12.12%)	2 / 29 (6.90%)
occurrences (all)	6	4	2
Diarrhoea			
subjects affected / exposed	5 / 35 (14.29%)	5 / 33 (15.15%)	5 / 29 (17.24%)
occurrences (all)	5	5	5
Tummy Pain			
subjects affected / exposed	2 / 35 (5.71%)	3 / 33 (9.09%)	3 / 29 (10.34%)
occurrences (all)	2	3	3
Skin and subcutaneous tissue disorders			
New rash			
subjects affected / exposed	8 / 35 (22.86%)	4 / 33 (12.12%)	5 / 29 (17.24%)
occurrences (all)	8	4	5
Musculoskeletal and connective tissue disorders			
Joint Pain			
subjects affected / exposed	0 / 35 (0.00%)	1 / 33 (3.03%)	2 / 29 (6.90%)
occurrences (all)	0	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 December 2013	Update all aspects of the protocol to clarify changes to data collection: o photographs will no longer be taken at the baseline visit. o The week 1 visit will be stopped. Study Trial Packs (medication) will be collected at week 2 visit. Inclusion and exclusion criteria updated.

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/28289111