



## 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             | v1   |
| This version publication date     | 23 July 2017   |
| First version publication date    | 23 July 2017   |
| 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:

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**Results analysis stage**

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|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 29 April 2015    |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 09 December 2014 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 25 March 2015    |
| Was the trial ended prematurely?                     | Yes              |

Notes:

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**General information about the trial**

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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:

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**Population of trial subjects**

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**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:

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**Subjects enrolled per age group**

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|   |    |
|---|----|
| 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 <sup>[1]</sup> |
| 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 of subjects reported to have started the pre-assignment period are the numbers of referred patients (171 in total). The number of subjects reported to have completed the pre-assignment period are the numbers of recruited patients (113 in total).

### 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

|                  |                          |
|------------------|--------------------------|
| <b>Arm title</b> | 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

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | 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

| <b>Number of subjects in period 1</b> | Control_baseline | Oral<br>antibiotic_baseline | Topical<br>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           |
| <b>Arm title</b>             | 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

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | 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

|                  |                          |
|------------------|--------------------------|
| <b>Arm title</b> | 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           |
| <b>Arm title</b>             | 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

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | 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

|                  |                          |
|------------------|--------------------------|
| <b>Arm title</b> | Topical antibiotic_week4 |
|------------------|--------------------------|

Arm description:

topical antibiotic cream and placebo oral treatment at week-4

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Fusidic 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

| <b>Number of subjects in period 3</b> | 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                        |

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**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            |
| <b>Arm title</b>             | 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

|                  |                        |
|------------------|------------------------|
| <b>Arm title</b> | 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

|                  |                           |
|------------------|---------------------------|
| <b>Arm title</b> | Topical antibiotic_month3 |
|------------------|---------------------------|

Arm description:

topical antibiotic cream and placebo oral treatment at month-3

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Fusidic 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

| <b>Number of subjects in period 4</b> | 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:<br>placebo oral and placebo topical cream treatment at baseline    |                             |
| Reporting group title   | Oral antibiotic_baseline    |
| Reporting group description:<br>oral antibiotic and placebo topical cream at baseline           |                             |
| Reporting group title   | Topical antibiotic_baseline |
| Reporting group description:<br>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 | $\pm 2.1$ | $\pm 2.1$ |  |
| Gender categorical |           |           |  |
| Units: Subjects    |           |           |  |
| Female             | 52        | 52        |  |
| Male               | 61        | 61        |  |

---

## End points

### End points reporting groups

|   |                             |
|---|-----------------------------|
| Reporting group title   | Control_baseline            |
| Reporting group description:<br>placebo oral and placebo topical cream treatment at baseline  |                             |
| Reporting group title   | Oral antibiotic_baseline    |
| Reporting group description:<br>oral antibiotic and placebo topical cream at baseline   |                             |
| Reporting group title   | Topical antibiotic_baseline |
| Reporting group description:<br>topical antibiotic cream and placebo oral treatment at baseline   |                             |
| Reporting group title   | Control_week2               |
| Reporting group description:<br>placebo oral and placebo topical cream treatment at week2   |                             |
| Reporting group title   | Oral antibiotic_week2       |
| Reporting group description:<br>oral antibiotic and placebo topical cream at week-2   |                             |
| Reporting group title   | Topical antibiotic_week2    |
| Reporting group description:<br>topical antibiotic cream and placebo oral treatment at week-2   |                             |
| Reporting group title   | Control_week4               |
| Reporting group description:<br>placebo oral and placebo topical cream treatment at week-4  |                             |
| Reporting group title   | Oral antibiotic_week4       |
| Reporting group description:<br>oral antibiotic and placebo topical cream at week-4   |                             |
| Reporting group title   | Topical antibiotic_week4    |
| Reporting group description:<br>topical antibiotic cream and placebo oral treatment at week-4   |                             |
| Reporting group title   | Control_month3              |
| Reporting group description:<br>placebo oral and placebo topical cream treatment at month-3   |                             |
| Reporting group title   | Oral antibiotic_month3      |
| Reporting group description:<br>oral antibiotic and placebo topical cream at month-3  |                             |
| Reporting group title   | Topical antibiotic_month3   |
| Reporting group description:<br>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:<br>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_week2 | Topical antibiotic_week2 |  |
|----------------------------------|-----------------|-----------------------|--------------------------|--|
| 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 <sup>[1]</sup>                  |
| 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.

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | 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 <sup>[2]</sup>                     |
| 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<br>3 | Oral<br>antibiotic_month<br>h3 | Topical<br>antibiotic_month<br>h3 |  |
|--------------------------------------|--------------------|--------------------------------|-----------------------------------|--|
| 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_week2 | Topical antibiotic_week2 |  |
|--------------------------------------|-------------------|-----------------------|--------------------------|--|
| 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 ( $\pm$ 5.64) | 3.09 ( $\pm$ 3.59)    | 4.91 ( $\pm$ 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_week4 | Topical antibiotic_week4 |  |
|--------------------------------------|--------------------|-----------------------|--------------------------|--|
| 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 ( $\pm$ 6.55) | 3.23 ( $\pm$ 3.81)    | 4.98 ( $\pm$ 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_week2 | Topical antibiotic_week2 |  |
|--------------------------------------|-------------------|-----------------------|--------------------------|--|
| 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 ( $\pm$ 4.76) | 3.69 ( $\pm$ 4.42)    | 4.84 ( $\pm$ 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:<br>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:<br>DFI collected 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 30            |                    |                       |                          |  |
| arithmetic mean (standard deviation) | 3.11 ( $\pm$ 4.86) | 3.52 ( $\pm$ 4.6)     | 4.23 ( $\pm$ 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:<br>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:<br>DFI scores collected at 3-month follow up  |                          |

| End point values                     | Control_month<br>3 | Oral<br>antibiotic_mont<br>h3 | Topical<br>antibiotic_mont<br>h3 |  |
|--------------------------------------|--------------------|-------------------------------|----------------------------------|--|
| 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 ( $\pm$ 4.28)  | 3.46 ( $\pm$ 4.4)             | 4.1 ( $\pm$ 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:<br>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:<br>IDQoL scores for children under 4 years old collected at week-2 follow-up   |                           |

| End point values                     | Control_week2      | Oral<br>antibiotic_week<br>2 | Topical<br>antibiotic_week<br>2 |  |
|--------------------------------------|--------------------|------------------------------|---------------------------------|--|
| 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 ( $\pm$ 3.69) | 6.74 ( $\pm$ 3.28)           | 7.19 ( $\pm$ 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:<br>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_week4 | Topical antibiotic_week4 |  |
|--------------------------------------|--------------------|-----------------------|--------------------------|--|
| 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 ( $\pm$ 3.74) | 6.59 ( $\pm$ 3.23)    | 7.14 ( $\pm$ 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:<br>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:<br>IDQoL scores for children under 4 years old collected at month-3 follow-up  |                                   |

| End point values                     | Control_month3     | Oral antibiotic_month3 | Topical antibiotic_month3 |  |
|--------------------------------------|--------------------|------------------------|---------------------------|--|
| 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 ( $\pm$ 2.59) | 6.01 ( $\pm$ 3.15)     | 6.67 ( $\pm$ 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:<br>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<br>2 | Topical antibiotic_week<br>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<br>4 | Topical antibiotic_week<br>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<br>3 | Oral<br>antibiotic_mont<br>h3 | Topical<br>antibiotic_mont<br>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  $\geq 2$ ) 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<br>occurrences (all)  | 3 / 35 (8.57%)<br>3  | 2 / 33 (6.06%)<br>2  | 1 / 29 (3.45%)<br>1  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)  | 6 / 35 (17.14%)<br>6 | 4 / 33 (12.12%)<br>4 | 2 / 29 (6.90%)<br>2  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)   | 5 / 35 (14.29%)<br>5 | 5 / 33 (15.15%)<br>5 | 5 / 29 (17.24%)<br>5 |
| Tummy Pain<br>subjects affected / exposed<br>occurrences (all)  | 2 / 35 (5.71%)<br>2  | 3 / 33 (9.09%)<br>3  | 3 / 29 (10.34%)<br>3 |
| Skin and subcutaneous tissue disorders<br>New rash<br>subjects affected / exposed<br>occurrences (all)            | 8 / 35 (22.86%)<br>8 | 4 / 33 (12.12%)<br>4 | 5 / 29 (17.24%)<br>5 |
| Musculoskeletal and connective tissue disorders<br>Joint Pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 35 (0.00%)<br>0  | 1 / 33 (3.03%)<br>1  | 2 / 29 (6.90%)<br>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:<br>o photographs will no longer be taken at the baseline visit.<br>o The week 1 visit will be stopped. Study Trial Packs (medication) will be collected at week 2 visit.<br>Inclusion and exclusion criteria updated. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28289111>