



Clinical trial results:

A prospective single blind randomised controlled study to compare the outcomes of patients with diabetes and clinically non-infected ischaemic and neuropathic foot ulcers treated with and without oral antibiotics - KADFUT

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2010-022518-16 |
| Trial protocol | GB |
| Global end of trial date | 15 January 2014 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 27 August 2020 |
| First version publication date | 27 August 2020 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | KADFUT |
|-----------------------|--------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | King's College Hospital NHS Foundation Trust |
| Sponsor organisation address | Denmark Hill, London, United Kingdom, SE5 9RS |
| Public contact | Diabetic Foot Clinic, King's College Hospital , +44 020 3299 3223, mbates2@nhs.net |
| Scientific contact | Diabetic Foot Clinic, King's College Hospital , +44 020 3299 3223, mbates2@nhs.net |

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 | 13 August 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 15 January 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 January 2014 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The overall objective is to investigate whether antibiotics in the treatment of clinically clean neuropathic and ischaemic ulcers in diabetic foot patients could reduce the incidence of infection and therefore lead to improved outcomes .

Protection of trial subjects:

Patients are free to withdraw consent for study treatment and/or consent to participate in the study at any time and without the prejudice to further treatment. Patients who withdraw from study treatment, but are willing to continue to participate in the follow-up visits, should be followed according to the procedures outlined in the protocol.

Patients who develop clinical signs and symptoms of infection in their target or other foot ulcer will be withdrawn. At withdrawal data will be collected as described in the 'early termination visit' and patients followed up 14 days later as per the 'post treatment evaluation'.

Patients who develop drug related adverse events such as gastro intestinal side effects including diarrhoea and vomiting that continue for more than 72 hrs and prevent them from taking antibiotics will also be withdrawn from the study. Patients who develop previously unknown allergies to antibiotics will be withdrawn from the study.

Background therapy:

Standard of care treatment for diabetic foot ulceration without clinical signs of infection. It is generally recommended that patients with ulcers but no purulence should not be treated with antibiotics

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 30 April 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 16 |
| Worldwide total number of subjects | 16 |
| EEA total number of subjects | 16 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |

| | |
|--|----|
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 16 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patients were recruited over a period of 21 months at KCH.

First Patient first visit (FPFV) 30/04/2012.

Between January 2012 to October 2012 no recruitment took place.

The trial was terminated before the recruitment target was reached due to slow recruitment, lack of personnel and resources and recruitment had not taken place since 2013.

Pre-assignment

Screening details:

Patients with type 1 or 2 diabetes mellitus, who presented to the Diabetic Foot Clinic at KCH with clean neuropathic or ischaemic diabetic foot ulcers without clinical signs of infection. Patients were recruited over a period of 21 months. Including patients referred from GP surgeries, Primary Care Trusts and other hospitals.

Pre-assignment period milestones

| | |
|------------------------------|-------------------|
| Number of subjects started | 17 ^[1] |
| Number of subjects completed | 16 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|----------------|
| Reason: Number of subjects | screen fail: 1 |
|----------------------------|----------------|

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 pre-assignment period includes 1 screen fail who was not enrolled into the study

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Assessor ^[2] |

Blinding implementation details:

Both patients and the Chief Investigator will know the treatment group, however there will be a blinded research team for assessments. Patients will be advised that there will always be two teams of health care professionals monitoring them: the blinded team and the unblinded team. The patient will be asked not to inform the blinded team as to which group they belong.

Arms

| | |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Active group |

Arm description:

antibiotics + standard care

The IMPs are licensed antibiotics.

Amoxycillin 500mg /250mg capsules

Flucloxacillin 500mg/250mg capsules

Ciprofloxacin 500mg/250mg tablets

Metronidazole 400mg/200mg tablets

Clarithromycin 500mg/250mg tablets

The above antibiotics will be used for the initial treatment of the patient in the antibiotic group. On follow up visits, patients may continue with their initial antibiotics as prescribed or antibiotics may be adjusted according to the microbiology results of the ulcer culture and microbial sensitivity/resistance (see below). These results are reviewed weekly and antibiotics are changed if necessary.

Doxycycline 100mg capsules

Trimethoprim 200mg/100mg tablets

Sodium fusidate 250mg tablets

Rifampicin 300mg capsules

Co-amoxiclav 625mg/375mg tablets
 Co-trimoxazole 480mg
 Clindamycin 150mg capsules
 Linezolid 600mg tablets
 Ceftriaxone sodium 1Gm
 Ceftazidime pentahydrate 1Gm
 Teicoplanin 400mg/200mg

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | amoxicillin trihydrate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

1.5 g per day for up to 20 weeks

| | |
|--|-----------------------|
| Investigational medicinal product name | flucloxacillin sodium |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

2g per day for up to 20 weeks

| | |
|--|---------------|
| Investigational medicinal product name | metronidazole |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

1.2g per day for up to 20 weeks

| | |
|--|-----------------------------|
| Investigational medicinal product name | ciprofloxacin hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

1g per day for up to 20 weeks

| | |
|--|---------------------|
| Investigational medicinal product name | doxycycline hyclate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

100mg per day for up to 19 weeks

| | |
|--|--------------|
| Investigational medicinal product name | trimethoprim |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

400mg per day for up to 19 weeks

| | |
|--|-----------------|
| Investigational medicinal product name | sodium fusidate |
| Investigational medicinal product code | |
| Other name | |

| | |
|--|--|
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 1.5g per day for up to 19 weeks | |
| Investigational medicinal product name | rifampicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 1200 per day for up to 19 weeks | |
| Investigational medicinal product name | co-amoxiclav |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 1.875g per day for up to 19 weeks | |
| Investigational medicinal product name | clindamycin hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 1.2g per day for up to 19 weeks | |
| Investigational medicinal product name | clarithromycin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 1g per day for up to 20 weeks | |
| Investigational medicinal product name | ceftriaxone sodium |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 1g dissolved in 3.5 ml 1% lignocaine for up to 2 weeks | |
| Investigational medicinal product name | linezolid |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 1.2g per day for up to 4 weeks | |
| Investigational medicinal product name | ceftazidime pentahydrate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intramuscular use |

| | |
|--|-----------------------------------|
| Dosage and administration details: | |
| 3g dissolved in 3.0 ml 1% lignocaine per day for up to 2 weeks | |
| Investigational medicinal product name | teicoplanin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 400mg dissolved in 3.0mls sterile water per day for up to 2 weeks | |
| Investigational medicinal product name | co trimoxazole |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 1.920g per day for up to 19 weeks | |
| Arm title | Control group |
| Arm description: | |
| Received standard care for clinically non-infected ischaemic and neuropathic foot ulcers | |
| Arm type | standard of care |
| No investigational medicinal product assigned in this arm | |
| Notes: | |
| [2] - The roles blinded appear inconsistent with a simple blinded trial. | |
| Justification: There was a blinded research team who performed assessments. The patient and investigator were unblinded. | |

| Number of subjects in period 1 | Active group | Control group |
|--------------------------------|--------------|---------------|
| Started | 7 | 9 |
| Completed | 3 | 5 |
| Not completed | 4 | 4 |
| Adverse event, non-fatal | 4 | 4 |

Baseline characteristics

Reporting groups

| Reporting group title | Active group |
|--|---------------|
| Reporting group description: | |
| antibiotics + standard care | |
| The IMPs are licensed antibiotics. | |
| Amoxycillin 500mg /250mg capsules | |
| Flucloxacillin 500mg/250mg capsules | |
| Ciprofloxacin 500mg/250mg tablets | |
| Metronidazole 400mg/200mg tablets | |
| Clarithromycin 500mg/250mg tablets | |
| The above antibiotics will be used for the initial treatment of the patient in the antibiotic group. On follow up visits, patients may continue with their initial antibiotics as prescribed or antibiotics may be adjusted according to the microbiology results of the ulcer culture and microbial sensitivity/resistance (see below). These results are reviewed weekly and antibiotics are changed if necessary. | |
| Doxycycline 100mg capsules | |
| Trimethoprim 200mg/100mg tablets | |
| Sodium fusidate 250mg tablets | |
| Rifampicin 300mg capsules | |
| Co-amoxiclav 625mg/375mg tablets | |
| Co-trimoxazole 480mg | |
| Clindamycin 150mg capsules | |
| Linezolid 600mg tablets | |
| Ceftriaxone sodium 1Gm | |
| Ceftazidime pentahydrate 1Gm | |
| Teicoplanin 400mg/200mg | |
| Reporting group title | Control group |
| Reporting group description: | |
| Received standard care for clinically non-infected ischaemic and neuropathic foot ulcers | |

| Reporting group values | Active group | Control group | Total |
|--|--------------|---------------|-------|
| Number of subjects | 7 | 9 | 16 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 57 | 65.4 | |
| standard deviation | ± 7.1 | ± 10.6 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 1 | 0 | 1 |
| Male | 6 | 9 | 15 |

| | | | |
|--|-------|-------|----|
| Type of diabetes Units: Subjects | | | |
| Type 1 DM | 1 | 0 | 1 |
| Type 2 DM | 6 | 9 | 15 |
| Neuropathic: neuroischaemic Units: Subjects | | | |
| Neuropathic | 6 | 9 | 15 |
| Neuroischaemic | 1 | 0 | 1 |
| Target ulcer Units: Subjects | | | |
| Right Foot | 3 | 3 | 6 |
| Left Foot | 4 | 6 | 10 |
| Duration of diabetes Units: Years | | | |
| arithmetic mean | 14 | 13.7 | |
| standard deviation | ± 4.6 | ± 8.7 | - |
| Ulcer area at presentation Units: cm ² | | | |
| arithmetic mean | 1.2 | 2.1 | |
| standard deviation | ± 1.1 | ± 2.4 | - |

End points

End points reporting groups

| | |
|---|---------------|
| Reporting group title | Active group |
| Reporting group description: antibiotics + standard care The IMPs are licensed antibiotics. Amoxycillin 500mg /250mg capsules Flucloxacillin 500mg/250mg capsules Ciprofloxacin 500mg/250mg tablets Metronidazole 400mg/200mg tablets Clarithromycin 500mg/250mg tablets The above antibiotics will be used for the initial treatment of the patient in the antibiotic group. On follow up visits, patients may continue with their initial antibiotics as prescribed or antibiotics may be adjusted according to the microbiology results of the ulcer culture and microbial sensitivity/resistance (see below). These results are reviewed weekly and antibiotics are changed if necessary. Doxycycline 100mg capsules Trimethoprim 200mg/100mg tablets Sodium fusidate 250mg tablets Rifampicin 300mg capsules Co-amoxiclav 625mg/375mg tablets Co-trimoxazole 480mg Clindamycin 150mg capsules Linezolid 600mg tablets Ceftriaxone sodium 1Gm Ceftazidime pentahydrate 1Gm Teicoplanin 400mg/200mg | |
| Reporting group title | Control group |
| Reporting group description: Received standard care for clinically non-infected ischaemic and neuropathic foot ulcers | |

Primary: Healing at week 20

| | |
|---|-----------------------------------|
| End point title | Healing at week 20 ^[1] |
| End point description: patients in each group that are healed at 20 weeks. Healing will be defined as complete epithelialisation which should be present on 2 consecutive weeks. | |
| End point type | Primary |
| End point timeframe: week 20 | |

Notes:

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

Justification: In view of the low numbers of subjects recruited , Analysis of Efficacy Variables was not carried out

| End point values | Active group | Control group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 9 | | |
| Units: Subjects | | | | |
| Healed | 3 | 5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to healing of foot ulceration

| | |
|-----------------|------------------------------------|
| End point title | Time to healing of foot ulceration |
|-----------------|------------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to 20 weeks

| End point values | Active group | Control group | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3 | 5 | | |
| Units: Weeks | | | | |
| arithmetic mean (standard deviation) | | | | |
| Healed | 8.7 (± 6.5) | 6.8 (± 3.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: develop clinical signs of foot infection

| | |
|-----------------|--|
| End point title | develop clinical signs of foot infection |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to 20 weeks

| End point values | Active group | Control group | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 9 | | |
| Units: Subjects | | | | |
| Developed clinical signs of foot infection | 2 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of hospital admissions related to the foot ulcer

| | |
|------------------------|---|
| End point title | Number of hospital admissions related to the foot ulcer |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to 20 weeks | |

| End point values | Active group | Control group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 7 | | |
| Units: Subjects | | | | |
| Admitted to hospital | 0 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of amputations

| | |
|------------------------|-----------------------|
| End point title | Number of amputations |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to 20 weeks | |

| End point values | Active group | Control group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 9 | | |
| Units: Subjects | | | | |
| Amputations | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse effects of antibiotic treatment

| | |
|------------------------|---|
| End point title | Adverse effects of antibiotic treatment |
| End point description: | |
| End point type | Secondary |

End point timeframe:

Baseline to 20 weeks

| End point values | Active group | Control group | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 | 9 | | |
| Units: Subjects | | | | |
| Adverse event related to antibiotic treatment | 2 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to week 20

Adverse event reporting additional description:

Adverse events will be noted and assessed at weekly visits by the unblinded team

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 32 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Active group |
|-----------------------|--------------|

Reporting group description:

antibiotics + standard care

The IMPs are licensed antibiotics.

Amoxycillin 500mg /250mg capsules

Flucloxacillin 500mg/250mg capsules

Ciprofloxacin 500mg/250mg tablets

Metronidazole 400mg/200mg tablets

Clarithromycin 500mg/250mg tablets

The above antibiotics will be used for the initial treatment of the patient in the antibiotic group. On follow up visits, patients may continue with their initial antibiotics as prescribed or antibiotics may be adjusted according to the microbiology results of the ulcer culture and microbial sensitivity/resistance (see below). These results are reviewed weekly and antibiotics are changed if necessary.

Doxycycline 100mg capsules

Trimethoprim 200mg/100mg tablets

Sodium fusidate 250mg tablets

Rifampicin 300mg capsules

Co-amoxiclav 625mg/375mg tablets

Co-trimoxazole 480mg

Clindamycin 150mg capsules

Linezolid 600mg tablets

Ceftriaxone sodium 1Gm

Ceftazidime pentahydrate 1Gm

Teicoplanin 400mg/200mg

| | |
|-----------------------|---------------|
| Reporting group title | Control group |
|-----------------------|---------------|

Reporting group description:

Received standard care for clinically non-infected ischaemic and neuropathic foot ulcers

| Serious adverse events | Active group | Control group | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 9 (22.22%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Renal and urinary disorders | | | |
| acute renal failure | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 9 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---------------|----------------|--|
| Infections and infestations | | | |
| infected foot ulcer | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 9 (22.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Active group | Control group | |
|---|-----------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 7 (100.00%) | 7 / 9 (77.78%) | |
| Nervous system disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 9 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 9 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Haemorrhage | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 9 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 9 (11.11%) | |
| occurrences (all) | 2 | 1 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 9 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 9 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 9 (11.11%) | |
| occurrences (all) | 0 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|---------------------|---------------------|--|
| dry cough subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 0 | 0 / 9 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders Blister subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 2 / 9 (22.22%) 2 | |
| toe bruising subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 9 (11.11%) 1 | |
| Musculoskeletal and connective tissue disorders Osteoarthritis subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 9 (0.00%) 0 | |
| pain in hip subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 0 | 0 / 9 (0.00%) 0 | |
| Infections and infestations foot infection subjects affected / exposed occurrences (all) | 2 / 7 (28.57%) 2 | 3 / 9 (33.33%) 0 | |
| Cold/flu subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 0 | 0 / 9 (0.00%) 0 | |
| Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 3 | 0 / 9 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 20 December 2011 | <p>Protocol updated as follows:</p> <p>Inclusion Criteria:</p> <p>Contraception updated to ensure only contraception that is not affected by enzyme inducing antibacterials such as rifampicin is used. Alternatively a barrier method may be added to the original contraceptive method has been added.</p> <p>Exclusion Criteria:</p> <p>Patients who are allergic to Penicillin can be randomised into the trial.</p> <p>Duration of trial updated.</p> <p>Clarifications and administrative changes.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As it was only possible to recruit 17 patients to this study, it is not possible to reach a conclusion regarding the outcomes of patients with diabetes& clinically non-infected ischaemic&neuropathic foot ulcers treated with & without oral antibiotics

Notes: