



Clinical trial results:

A Multi-Dose, Double-Blind, Double-Dummy, Active Control, Randomized Clinical (Phase II) Study of Two Dosing Regimens of Finafloxacin for the Treatment of cUTI and/or Acute Pyelonephritis Requiring Hospitalisation

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2011-006041-14 |
| Trial protocol | PL |
| Global end of trial date | 15 June 2014 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 05 January 2017 |
| First version publication date | 05 January 2017 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | FINA-007 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01928433 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | MerLion Pharmaceuticals GmbH |
| Sponsor organisation address | Robert-Roessle-Str. 10, Berlin, Germany, 13125 |
| Public contact | Head of Regulatory Affairs, MerLion Pharmaceuticals GmbH, lueckermann@merlionpharma.de |
| Scientific contact | Head of Regulatory Affairs, MerLion Pharmaceuticals GmbH, lueckermann@merlionpharma.de |

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 | 30 October 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 15 June 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 June 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Evaluate the microbiological and clinical outcome of treatment with finafloxacin for 5 days versus finafloxacin for 10 days versus ciprofloxacin for 10 days

Protection of trial subjects:

Stringent ECG monitoring, patients will be excluded in case of any significant ECG abnormalities.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 08 December 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Poland: 192 |
| Country: Number of subjects enrolled | Germany: 33 |
| Worldwide total number of subjects | 225 |
| EEA total number of subjects | 225 |

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) | 144 |
| From 65 to 84 years | 75 |
| 85 years and over | 6 |

Subject disposition

Recruitment

Recruitment details:

First patient enrolled: 08 December 2012

Last patient completed: 15 June 2014

Countries: Germany and Poland

Pre-assignment

Screening details:

After signing the informed consent patient received screening no. If these patients are eligible to continue the study, based on the inclusion and exclusion criteria they will be assigned to one of the three treatment groups (Finafloxacin for 5 days, Finafloxacin for 10 days or Ciprofloxacin for 10 days) in a ratio of 1:1:1.

Period 1

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

Blinding implementation details:

Blinding was conducted using the double-blind, double-dummy technique.

Arms

| | |
|------------------------------|------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Group I -Finafloxacin 5 days |

Arm description:

Finafloxacin 800 mg intravenous (i.v.) once daily (o.d.) (infused over 60 mins [i.v. pump]) for at least 3 days (in-patient) followed by finafloxacin 800 mg tablets (as four 200 mg tablets) o.d. (outpatient): total treatment period of 5 days. For blinding the patients received additional 5 days oral placebo treatment.

| | |
|--|----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Finafloxacin hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Finafloxacin 800 mg intravenous (i.v.) once daily (o.d.) infused over 60 mins [i.v. pump] for at least 3 days.

| | |
|--|----------------------------|
| Investigational medicinal product name | Finafloxacin hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Finafloxacin 800 mg oral (as four 200 mg film-coated tablets) o.d. (outpatient).

| | |
|------------------|--------------------------------|
| Arm title | Group II -Finafloxacin 10 days |
|------------------|--------------------------------|

Arm description:

Finafloxacin 800 mg intravenous (i.v.) once daily (o.d.) (infused over 60 mins [i.v. pump]) for at least 3 days (in-patient) followed by finafloxacin 800 mg tablets (as four 200 mg tablets) o.d. (outpatient): total treatment period of 10 days.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|----------------------------|
| Investigational medicinal product name | Finafloxacin hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Finafloxacin 800 mg intravenous (i.v.) once daily (o.d.) infused over 60 mins [i.v. pump] for at least 3 days.

| | |
|--|----------------------------|
| Investigational medicinal product name | Finafloxacin hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Finafloxacin 800 mg oral (as four 200 mg film-coated tablets) o.d. (outpatient).

| | |
|------------------|-----------------------------------|
| Arm title | Group III - Ciprofloxacin 10 days |
|------------------|-----------------------------------|

Arm description:

Ciprofloxacin 400 mg i.v. two times daily (b.i.d.) for at least 3 days (in-patient) followed by ciprofloxacin 500 mg oral (as two 250 mg capsules each) (b.i.d.) two times daily (outpatient); total treatment period of 10 days.

| | |
|--|---------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Ciprofloxacin hydrogen sulphate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Ciprofloxacin 400 mg i.v. two times daily (b.i.d.) infused over approximately 60 mins (i.v. pump).

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

Dosage and administration details:

Ciprofloxacin 500 mg oral (as two 250 mg capsules each) (b.i.d.) two times daily (outpatient).

| Number of subjects in period 1 | Group I - Finafloxacin 5 days | Group II - Finafloxacin 10 days | Group III - Ciprofloxacin 10 days |
|----------------------------------|----------------------------------|------------------------------------|---|
| | | | |
| Started | 76 | 75 | 74 |
| Completed | 56 | 54 | 46 |
| Not completed | 20 | 21 | 28 |
| Consent withdrawn by subject | - | 4 | - |
| Adverse event, non-fatal | 5 | 2 | 5 |
| Other | 3 | 3 | 4 |
| Lost to follow-up | - | 2 | 3 |
| Negative screening urine culture | 7 | 6 | 10 |
| Lack of efficacy | 5 | 4 | 4 |

| | | | |
|--------------------|---|---|---|
| Protocol deviation | - | - | 2 |
|--------------------|---|---|---|

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------------------|
| Reporting group title | Group I -Finafloxacin 5 days |
|-----------------------|------------------------------|

Reporting group description:

Finafloxacin 800 mg intravenous (i.v.) once daily (o.d.) (infused over 60 mins [i.v. pump]) for at least 3 days (in-patient) followed by finafloxacin 800 mg tablets (as four 200 mg tablets) o.d. (outpatient): total treatment period of 5 days. For blinding the patients received additional 5 days oral placebo treatment.

| | |
|-----------------------|--------------------------------|
| Reporting group title | Group II -Finafloxacin 10 days |
|-----------------------|--------------------------------|

Reporting group description:

Finafloxacin 800 mg intravenous (i.v.) once daily (o.d.) (infused over 60 mins [i.v. pump]) for at least 3 days (in-patient) followed by finafloxacin 800 mg tablets (as four 200 mg tablets) o.d. (outpatient): total treatment period of 10 days.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Group III - Ciprofloxacin 10 days |
|-----------------------|-----------------------------------|

Reporting group description:

Ciprofloxacin 400 mg i.v. two times daily (b.i.d.) for at least 3 days (in-patient) followed by ciprofloxacin 500 mg oral (as two 250 mg capsules each) (b.i.d.) two times daily (outpatient); total treatment period of 10 days.

| Reporting group values | Group I - Finafloxacin 5 days | Group II - Finafloxacin 10 days | Group III - Ciprofloxacin 10 days |
|---|----------------------------------|------------------------------------|---|
| Number of subjects | 76 | 75 | 74 |
| 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) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 52 | 43 | 49 |
| From 65-84 years | 20 | 31 | 24 |
| 85 years and over | 4 | 1 | 1 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 54.6 | 58 | 51.1 |
| standard deviation | ± 19.63 | ± 19.28 | ± 20.82 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 64 | 62 | 59 |
| Male | 12 | 13 | 15 |

| Reporting group values | Total | | |
|---|-------|--|--|
| Number of subjects | 225 | | |
| 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) | 144 | | |
| From 65-84 years | 75 | | |
| 85 years and over | 6 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 185 | | |
| Male | 40 | | |

Subject analysis sets

| | |
|----------------------------|--------------------|
| Subject analysis set title | ITT |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Patients who provided written consent to participate and were randomized into the study.

| | |
|----------------------------|-----------------|
| Subject analysis set title | Safety Set |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All patients who met the definition of ITT population and who received at least one dose of study medication during the trial.

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | micro-ITT |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

All subjects who met the definition for the ITT population and who had a positive baseline bacterial pathogen on culture of urine that causes UTI against which the investigational drug had antibacterial activity.

| Reporting group values | ITT | Safety Set | micro-ITT |
|--|------|------------|-----------|
| Number of subjects | 225 | 223 | 193 |
| 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) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 144 | 143 | 123 |
| From 65-84 years | 75 | 74 | 65 |
| 85 years and over | 6 | 6 | 5 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 54.6 | 54.6 | 54.9 |

| | | | |
|--------------------|-------------|-------------|-------------|
| standard deviation | ± 20.03 | ± 20.08 | ± 19.99 |
|--------------------|-------------|-------------|-------------|

| | | | |
|--------------------|-----|-----|-----|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 185 | 183 | 157 |
| Male | 40 | 40 | 36 |

End points

End points reporting groups

| | |
|---|-----------------------------------|
| Reporting group title | Group I -Finafloxacin 5 days |
| Reporting group description: Finafloxacin 800 mg intravenous (i.v.) once daily (o.d.) (infused over 60 mins [i.v. pump]) for at least 3 days (in-patient) followed by finafloxacin 800 mg tablets (as four 200 mg tablets) o.d. (outpatient): total treatment period of 5 days. For blinding the patients received additional 5 days oral placebo treatment. | |
| Reporting group title | Group II -Finafloxacin 10 days |
| Reporting group description: Finafloxacin 800 mg intravenous (i.v.) once daily (o.d.) (infused over 60 mins [i.v. pump]) for at least 3 days (in-patient) followed by finafloxacin 800 mg tablets (as four 200 mg tablets) o.d. (outpatient): total treatment period of 10 days. | |
| Reporting group title | Group III - Ciprofloxacin 10 days |
| Reporting group description: Ciprofloxacin 400 mg i.v. two times daily (b.i.d.) for at least 3 days (in-patient) followed by ciprofloxacin 500 mg oral (as two 250 mg capsules each) (b.i.d.) two times daily (outpatient); total treatment period of 10 days. | |
| Subject analysis set title | ITT |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Patients who provided written consent to participate and were randomized into the study. | |
| Subject analysis set title | Safety Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All patients who met the definition of ITT population and who received at least one dose of study medication during the trial. | |
| Subject analysis set title | micro-ITT |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: All subjects who met the definition for the ITT population and who had a positive baseline bacterial pathogen on culture of urine that causes UTI against which the investigational drug had antibacterial activity. | |

Primary: Efficacy - Combined Endpoint at Test of Cure

| | |
|---|---|
| End point title | Efficacy - Combined Endpoint at Test of Cure ^[1] |
| End point description: The primary endpoint of this study was the clinical and microbiological response of patients with cUTI or pyelonephritis to treatment with finafloxacin for 5 days versus finafloxacin for 10 days versus ciprofloxacin for 10 days as a reference comparator at the Test of Cure (ToC) visit (Day 17) in the micro-ITT population. | |
| End point type | Primary |
| End point timeframe: Day 17 (+/-2) after treatment start. | |

Notes:

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

Justification: This study was not powered to perform formal inferential statistical analyses.

| End point values | Group I - Finafloxacin 5 days | Group II - Finafloxacin 10 days | Group III - Ciprofloxacin 10 days | |
|-----------------------------|-------------------------------------|---------------------------------------|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 64 | 68 | 61 | |
| Units: percent | | | | |
| number (not applicable) | 70.3 | 67.6 | 57.4 | |

Statistical analyses

No statistical analyses for this end point

Primary: Efficacy - Clinical Success at Test of Cure

| | |
|-----------------|--|
| End point title | Efficacy - Clinical Success at Test of Cure ^[2] |
|-----------------|--|

End point description:

The clinical response of patients with cUTI or pyelonephritis to treatment with finafloxacin for 5 days versus finafloxacin for 10 days versus ciprofloxacin for 10 days as a reference comparator at the Test of Cure (ToC) visit (Day 17) in the micro-ITT population.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Treatment start to day 17 (+/- 2)

Notes:

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

Justification: This study was not powered to perform formal inferential statistical analyses.

| End point values | Group I - Finafloxacin 5 days | Group II - Finafloxacin 10 days | Group III - Ciprofloxacin 10 days | |
|-----------------------------|-------------------------------------|---------------------------------------|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 64 | 68 | 61 | |
| Units: percent | | | | |
| number (not applicable) | 79.7 | 83.8 | 72.1 | |

Statistical analyses

No statistical analyses for this end point

Primary: Efficacy - Microbiological Success at Test of Cure

| | |
|-----------------|---|
| End point title | Efficacy - Microbiological Success at Test of Cure ^[3] |
|-----------------|---|

End point description:

The microbiological response of patients with cUTI or pyelonephritis to treatment with finafloxacin for 5 days versus finafloxacin for 10 days versus ciprofloxacin for 10 days as a reference comparator at the Test of Cure (ToC) visit (Day 17) in the micro-ITT population.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Treatment start to day 17 (+/- 2)

Notes:

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

Justification: This study was not powered to perform formal inferential statistical analyses.

| End point values | Group I - Finafloxacin 5 days | Group II - Finafloxacin 10 days | Group III - Ciprofloxacin 10 days | |
|-----------------------------|-------------------------------------|---------------------------------------|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 64 | 68 | 61 | |
| Units: percent | | | | |
| number (not applicable) | 71.9 | 70.6 | 59 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timepoint of written informed consent to End of Study Visit (Day 24).

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | Safety set (2%) |
|-----------------------|-----------------|

Reporting group description: -

| | |
|-----------------------|--------------|
| Reporting group title | Finafloxacin |
|-----------------------|--------------|

Reporting group description: -

| | |
|-----------------------|---------------|
| Reporting group title | Ciprofloxacin |
|-----------------------|---------------|

Reporting group description: -

| Serious adverse events | Safety set (2%) | Finafloxacin | Ciprofloxacin |
|---|-----------------|-----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 223 (3.59%) | 7 / 151 (4.64%) | 1 / 72 (1.39%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Ovarian adenoma | | | |
| subjects affected / exposed | 1 / 223 (0.45%) | 1 / 151 (0.66%) | 0 / 72 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 223 (0.90%) | 2 / 151 (1.32%) | 0 / 72 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 223 (0.45%) | 1 / 151 (0.66%) | 0 / 72 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 223 (0.45%) | 1 / 151 (0.66%) | 0 / 72 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Obstructive uropathy | | | |
| subjects affected / exposed | 1 / 223 (0.45%) | 0 / 151 (0.00%) | 1 / 72 (1.39%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pyonephrosis | | | |
| subjects affected / exposed | 1 / 223 (0.45%) | 1 / 151 (0.66%) | 0 / 72 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 2 / 223 (0.90%) | 2 / 151 (1.32%) | 0 / 72 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | Safety set (2%) | Finafloxacin | Ciprofloxacin |
|---|-------------------|-------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 58 / 223 (26.01%) | 55 / 151 (36.42%) | 39 / 72 (54.17%) |
| Investigations | | | |
| Blood pressure increased | | | |
| subjects affected / exposed | 6 / 223 (2.69%) | 4 / 151 (2.65%) | 2 / 72 (2.78%) |
| occurrences (all) | 8 | 5 | 3 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 15 / 223 (6.73%) | 9 / 151 (5.96%) | 6 / 72 (8.33%) |
| occurrences (all) | 19 | 10 | 9 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 13 / 223 (5.83%) | 8 / 151 (5.30%) | 5 / 72 (6.94%) |
| occurrences (all) | 16 | 11 | 5 |
| Nausea | | | |

| | | | |
|--|----------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 7 / 223 (3.14%) 7 | 6 / 151 (3.97%) 6 | 1 / 72 (1.39%) 1 |
| Abdominal pain subjects affected / exposed occurrences (all) | 6 / 223 (2.69%) 6 | 3 / 151 (1.99%) 3 | 3 / 72 (4.17%) 3 |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 6 / 223 (2.69%) 7 | 5 / 151 (3.31%) 6 | 1 / 72 (1.39%) 1 |
| Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all) | 5 / 223 (2.24%) 5 | 3 / 151 (1.99%) 3 | 2 / 72 (2.78%) 2 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 21 May 2013 | Update of the SmPC for Ciprofloxacin and new Informed Consent was submitted. |
| 25 April 2014 | Implementation of an administrative analysis. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported