



Clinical trial results:

A prospective Phase 3, double-blind, multicenter, randomized study of the efficacy and safety of sulopenem followed by sulopenem etzadroxil with probenecid versus ertapenem followed by ciprofloxacin and metronidazole or amoxicillin-clavulanate for treatment of complicated intra-abdominal infections in adults.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2017-003773-34 |
| Trial protocol | LV HU BG CZ |
| Global end of trial date | 02 October 2019 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 13 December 2021 |
| First version publication date | 13 December 2021 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | IT001-303 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03358576 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Iterum Therapeutics |
| Sponsor organisation address | 20 Research Parkway, Suite A, Old Saybrook, United States, 06475 |
| Public contact | Senior VP and head of Clinical Development, Senior VP and head of Clinical Development, 1 8608762690, saroin@iterumtx.com |
| Scientific contact | Senior VP and head of Clinical Development, Senior VP and head of Clinical Development, 1 8608762690, saroin@iterumtx.com |

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 | 08 December 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 02 October 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 October 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of sulopenem followed by sulopenem etzadroxil with probenecid versus ertapenem followed by ciprofloxacin and metronidazole or amoxicillin-clavulanate for treatment of complicated intra-abdominal infection in adults, on Day 28 (test of cure [TOC]) post randomization.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Patients, adopted by the General Assembly of the World Medical Association (2013), and in compliance with all International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial participants.

Background therapy: -

Evidence for comparator:

Ertapenem, the comparator chosen for this study, was approved by the US Food and Drug Administration (FDA) in 2001, for a number of serious infections, including complicated intra-abdominal infections and by the European Medicines Agency (EMA) for complicated intra-abdominal infections in 2002. Unlike sulopenem, however, it does not possess the advantage of being available in oral form; the step-down regimens chosen for those receiving ertapenem were ciprofloxacin + metronidazole or amoxicillin clavulanate, depending on the susceptibility of the pathogen(s) identified at baseline.

| | |
|---|-----------------|
| Actual start date of recruitment | 01 October 2018 |
| 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 | Bulgaria: 188 |
| Country: Number of subjects enrolled | Czechia: 17 |
| Country: Number of subjects enrolled | Estonia: 77 |
| Country: Number of subjects enrolled | Hungary: 46 |
| Country: Number of subjects enrolled | Latvia: 56 |
| Country: Number of subjects enrolled | Georgia: 83 |
| Country: Number of subjects enrolled | Russian Federation: 40 |
| Country: Number of subjects enrolled | Serbia: 17 |
| Country: Number of subjects enrolled | Ukraine: 118 |
| Country: Number of subjects enrolled | United States: 32 |
| Worldwide total number of subjects | 674 |
| EEA total number of subjects | 384 |

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) | 443 |
| From 65 to 84 years | 212 |
| 85 years and over | 19 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 91 study centers in Bulgaria, the Czech Republic, Estonia, Georgia, Hungary, Latvia, Russia, Serbia, Ukraine, and the United States. Study initiation date 28 November 2018.

Study completion date 02 October 2019.

Pre-assignment

Screening details:

A total of 707 potential patients were screened for enrollment. Of these, 33 failed the screening process; the most common reason for screening failure, occurring in 13 patients, was the lack of a cIAI diagnosis as defined in the protocol, ie, not meeting inclusion criterion number 3.

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 | Investigator, Monitor, Data analyst, Carer, Subject, Assessor |

Blinding implementation details:

This study was designed to be a double-blind study. The site pharmacist was unblinded in order to prepare the IV study medications and to select the appropriate oral follow on therapy for patients randomized to the ertapenem regimen.

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | Yes |
| Arm title | Sulopenem |

Arm description:

Patients randomized to sulopenem IV followed by oral sulopenem etzadroxil plus probenecid

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Sulopenem |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients with normal renal function who were randomized to the sulopenem treatment group were to receive 1000 mg sulopenem IV infused over 3 hours once daily for 5 days and a saline IV infusion over 30 minutes to simulate the comparator; Patients with severe renal impairment who were randomized to the sulopenem treatment group were to receive 250 mg sulopenem IV infused over 3 hours once daily for 5 days and a saline IV infusion over 30 minutes to simulate the comparator.

| | |
|------------------|-----------|
| Arm title | Ertapenem |
|------------------|-----------|

Arm description:

Patients randomized to ertapenem IV followed by oral ciprofloxacin plus metronidazole or oral amoxicillin-clavulanate

| | |
|--|----------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Ertapenem |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients with normal renal function who were randomized to the comparator treatment group were to

receive 1000 mg of ertapenem IV infused over 30 minutes once daily for 5 days and a saline IV infusion over 3 hours to simulate the sulopenem; Patients with severe renal impairment who were randomized to the comparator treatment group were to receive 500 mg ertapenem IV infused over 30 minutes once daily for 5 days and a saline IV infusion over 3 hours to simulate the sulopenem.

| Number of subjects in period 1 | Sulopenem | Ertapenem |
|---------------------------------------|-----------|-----------|
| Started | 338 | 336 |
| Completed | 312 | 311 |
| Not completed | 26 | 25 |
| Adverse event, serious fatal | 2 | 4 |
| Consent withdrawn by subject | 7 | 8 |
| Physician decision | 5 | 3 |
| Adverse event, non-fatal | 5 | 8 |
| Carbapenem-resistant pathogen | 3 | 1 |
| other | 3 | 1 |
| Lack of efficacy | 1 | - |

Baseline characteristics

Reporting groups

| | |
|---|-----------|
| Reporting group title | Sulopenem |
| Reporting group description: | |
| Patients randomized to sulopenem IV followed by oral sulopenem etzadroxil plus probenecid | |
| Reporting group title | Ertapenem |
| Reporting group description: | |
| Patients randomized to ertapenem IV followed by oral ciprofloxacin plus metronidazole or oral amoxicillin-clavulanate | |

| Reporting group values | Sulopenem | Ertapenem | Total |
|---------------------------------|-----------|-----------|-------|
| Number of subjects | 338 | 336 | 674 |
| Age categorical | | | |
| Adult patients ≥18 years of age | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 226 | 217 | 443 |
| From 65-84 years | 102 | 110 | 212 |
| 85 years and over | 10 | 9 | 19 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 160 | 155 | 315 |
| Male | 178 | 181 | 359 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 9 | 8 | 17 |
| Not Hispanic or Latino | 329 | 328 | 657 |
| Geographic Region | | | |
| Units: Subjects | | | |
| U.S. | 16 | 16 | 32 |
| Non-U.S. | 322 | 320 | 642 |
| Race | | | |
| Units: Subjects | | | |
| Black or African American | 1 | 3 | 4 |
| Asian | 0 | 1 | 1 |
| White | 337 | 332 | 669 |
| Baseline APACHE II Score | | | |
| Units: Score | | | |
| geometric mean | 6.6 | 6.8 | |
| standard deviation | ± 3.9 | ± 3.8 | - |

End points

End points reporting groups

| | |
|---|-----------------------------|
| Reporting group title | Sulopenem |
| Reporting group description: Patients randomized to sulopenem IV followed by oral sulopenem etzadroxil plus probenecid | |
| Reporting group title | Ertapenem |
| Reporting group description: Patients randomized to ertapenem IV followed by oral ciprofloxacin plus metronidazole or oral amoxicillin-clavulanate | |
| Subject analysis set title | Clinical Set 1 |
| Subject analysis set type | Per protocol |
| Subject analysis set description: microbiologic modified intention to treat population | |
| Subject analysis set title | Clinical set 2 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Intention to treat population | |
| Subject analysis set title | Clinical Set 3 |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: Modified intention to treat population | |
| Subject analysis set title | Clinical Set 4 |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Clinically evaluable at test of cure population | |
| Subject analysis set title | Clinical Set 5 |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Microbiologically evaluable at test of cure population | |

Primary: Clinical response

| | |
|--|-------------------|
| End point title | Clinical response |
| End point description: microbiologic modified intention to treat population | |
| End point type | Primary |
| End point timeframe: Test of cure [Day 28] | |

| End point values | Sulopenem | Ertapenem | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 249 | 266 | | |
| Units: Number of patients | | | | |
| Clinical success | 213 | 240 | | |
| Clinical failure | 27 | 17 | | |
| Indeterminate | 9 | 9 | | |

Statistical analyses

| Statistical analysis title | Statistical outcome |
|---|-----------------------|
| Statistical analysis description: Number & % of patients assessed as clinical cure/failure/indeterminate were determined in each treatment group in micro MITT population. Observed difference in % of patients with clinical cure at Day 28 was determined; 95% CI for observed difference was computed using Z statistic. The noninferior hypothesis test was a 1-sided test performed at 2.5% level of significance. If lower limit of 95% CI was greater than -10%, the noninferiority of sulopenem to the comparator group was to be concluded. | |
| Comparison groups | Ertapenem v Sulopenem |
| Number of subjects included in analysis | 515 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.025 |
| Method | t-test, 1-sided |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| lower limit | -10 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The investigator was to report all directly observed AEs and all AEs spontaneously reported by the study patient from the time that the patient provided informed consent through the Day 28 (TOC) Visit.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Sulopenem |
|-----------------------|-----------|

Reporting group description:

Patients randomized to sulopenem IV followed by oral sulopenem etzadroxil plus probenecid

| | |
|-----------------------|-----------|
| Reporting group title | Ertapenem |
|-----------------------|-----------|

Reporting group description:

Patients randomized to ertapenem IV followed by oral ciprofloxacin plus metronidazole or oral amoxicillin-clavulanate

| Serious adverse events | Sulopenem | Ertapenem | |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 25 / 335 (7.46%) | 12 / 333 (3.60%) | |
| number of deaths (all causes) | 4 | 4 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 335 (0.00%) | 1 / 333 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 335 (0.00%) | 1 / 333 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Ventricular fibrillation | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 1 / 335 (0.30%) | 1 / 333 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Sudden death | | | |
| subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 335 (0.60%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus paralytic | | | |
| subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal perforation | | | |
| subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Mesenteric artery thrombosis subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Volvulus of small bowel subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure subjects affected / exposed | 0 / 335 (0.00%) | 1 / 333 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Renal and urinary disorders | | | |
| Renal failure subjects affected / exposed | 0 / 335 (0.00%) | 1 / 333 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Infections and infestations | | | |
| Abdominal abscess subjects affected / exposed | 9 / 335 (2.69%) | 1 / 333 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver abscess subjects affected / exposed | 2 / 335 (0.60%) | 1 / 333 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendiceal abscess subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon gangrene | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Sulopenem | Ertapenem | |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 90 / 335 (26.87%) | 80 / 333 (24.02%) | |
| Investigations | | | |
| Blood pressure increased | | | |
| subjects affected / exposed | 1 / 335 (0.30%) | 5 / 333 (1.50%) | |
| occurrences (all) | 1 | 5 | |
| Injury, poisoning and procedural complications | | | |
| Post procedural haematoma | | | |
| subjects affected / exposed | 0 / 335 (0.00%) | 2 / 333 (0.60%) | |
| occurrences (all) | 0 | 2 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 335 (0.60%) | 2 / 333 (0.60%) | |
| occurrences (all) | 2 | 2 | |
| Cardiac disorders | | | |
| Atrial flutter | | | |
| subjects affected / exposed | 1 / 335 (0.30%) | 0 / 333 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 335 (0.60%) | 5 / 333 (1.50%) | |
| occurrences (all) | 2 | 5 | |
| Cardiac disorder | | | |
| subjects affected / exposed | 6 / 335 (1.79%) | 7 / 333 (2.10%) | |
| occurrences (all) | 6 | 7 | |

| | | | |
|---|------------------------|----------------------|--|
| Atrial fibrillation subjects affected / exposed occurrences (all) | 1 / 335 (0.30%) 1 | 3 / 333 (0.90%) 3 | |
| Leukocytosis subjects affected / exposed occurrences (all) | 2 / 335 (0.60%) 2 | 0 / 333 (0.00%) 0 | |
| Thrombocytosis subjects affected / exposed occurrences (all) | 1 / 335 (0.30%) 1 | 0 / 333 (0.00%) 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 15 / 335 (4.48%) 15 | 8 / 333 (2.40%) 8 | |
| Nausea subjects affected / exposed occurrences (all) | 12 / 335 (3.58%) 12 | 8 / 333 (2.40%) 8 | |
| Vomiting subjects affected / exposed occurrences (all) | 6 / 335 (1.79%) 6 | 5 / 333 (1.50%) 5 | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 4 / 335 (1.19%) 4 | 1 / 333 (0.30%) 1 | |
| Constipation subjects affected / exposed occurrences (all) | 4 / 335 (1.19%) 4 | 1 / 333 (0.30%) 1 | |
| Ileus subjects affected / exposed occurrences (all) | 1 / 335 (0.30%) 1 | 1 / 333 (0.30%) 1 | |
| Gastrointestinal hypomotility subjects affected / exposed occurrences (all) | 1 / 335 (0.30%) 1 | 1 / 333 (0.30%) 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion subjects affected / exposed occurrences (all) | 2 / 335 (0.60%) 2 | 2 / 333 (0.60%) 2 | |
| Pleurisy | | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 335 (0.30%) 1 | 2 / 333 (0.60%) 2 | |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 1 / 335 (0.30%) 1 | 2 / 333 (0.60%) 2 | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 3 / 335 (0.90%) 3 | 0 / 333 (0.00%) 0 | |
| Infections and infestations Postoperative wound infection subjects affected / exposed occurrences (all) | 4 / 335 (1.19%) 4 | 8 / 333 (2.40%) 8 | |
| Pneumonia subjects affected / exposed occurrences (all) | 3 / 335 (0.90%) 3 | 5 / 333 (1.50%) 5 | |
| Abdominal abscess subjects affected / exposed occurrences (all) | 6 / 335 (1.79%) 6 | 0 / 333 (0.00%) 0 | |
| Wound infection subjects affected / exposed occurrences (all) | 1 / 335 (0.30%) 1 | 4 / 333 (1.20%) 4 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 335 (0.00%) 0 | 2 / 333 (0.60%) 2 | |
| Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all) | 4 / 335 (1.19%) 4 | 6 / 333 (1.80%) 6 | |
| Hypophosphataemia subjects affected / exposed occurrences (all) | 5 / 335 (1.49%) 5 | 0 / 333 (0.00%) 0 | |
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 3 / 335 (0.90%) 3 | 1 / 333 (0.30%) 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

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| Initial review of primary efficacy tables raised concerns about imbalances that didn't have a reasonable medical explanation. This prompted reexamination of programming and ultimately reanalysis of database to address identified deficiencies. |
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Notes: