



Clinical trial results:

A Phase III, Multicentre, Randomised, Double-Blind, Comparative Study to Evaluate the Efficacy and Safety of Ceftaroline Fosamil (600 mg every 8 hours) Versus Vancomycin Plus Aztreonam in the Treatment of Patients With Complicated Bacterial Skin and Soft Tissue Infections With Evidence of Systemic Inflammatory Response or Underlying Comorbidities

Summary

| | |
|--------------------------|----------------------------------|
| EudraCT number | 2011-004013-16 |
| Trial protocol | GR BE CZ BG DE AT PL ES GB SK IT |
| Global end of trial date | 30 April 2015 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 01 February 2017 |
| First version publication date | 19 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | D3720C00001 |
|-----------------------|-------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | AstraZeneca AB |
| Sponsor organisation address | 151 85 Södertälje, Södertälje, Sweden, |
| Public contact | Jesus Gonzalez, AstraZeneca, UK +44 (0)7557 541 031 , Jesus.Gonzalez@astrazeneca.com |
| Scientific contact | Matthew Dryden, Royal Hampshire County Hospital, Department of Microbiology, UK +44 (0)1962 824451, Matthew.Dryden@hhft.nhs.uk |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 05 March 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 26 June 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 April 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess whether ceftaroline fosamil was non inferior to vancomycin plus aztreonam in the clinical cure rate at the TOC visit in both the MITT and CE analysis sets of adult patients with cSSTI.

Protection of trial subjects:

The study will be performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with the International Conference on Harmonisation (ICH) harmonised tripartite guideline E6(R1): Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy on Bioethics and Human Biological Samples.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 17 May 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 | Argentina: 10 |
| Country: Number of subjects enrolled | Australia: 1 |
| Country: Number of subjects enrolled | Belgium: 1 |
| Country: Number of subjects enrolled | Brazil: 16 |
| Country: Number of subjects enrolled | Bulgaria: 83 |
| Country: Number of subjects enrolled | Chile: 3 |
| Country: Number of subjects enrolled | China: 151 |
| Country: Number of subjects enrolled | Croatia: 46 |
| Country: Number of subjects enrolled | Czech Republic: 4 |
| Country: Number of subjects enrolled | France: 1 |
| Country: Number of subjects enrolled | Germany: 10 |
| Country: Number of subjects enrolled | Greece: 4 |
| Country: Number of subjects enrolled | Hong Kong: 6 |
| Country: Number of subjects enrolled | Israel: 16 |
| Country: Number of subjects enrolled | Italy: 2 |
| Country: Number of subjects enrolled | Mexico: 11 |
| Country: Number of subjects enrolled | Peru: 35 |

| | |
|--------------------------------------|--|
| Country: Number of subjects enrolled | Philippines: 5 |
| Country: Number of subjects enrolled | Poland: 3 |
| Country: Number of subjects enrolled | Romania: 21 |
| Country: Number of subjects enrolled | Russian Federation: 115 |
| Country: Number of subjects enrolled | South Africa: 22 |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 18 |
| Country: Number of subjects enrolled | Spain: 13 |
| Country: Number of subjects enrolled | Taiwan: 12 |
| Country: Number of subjects enrolled | Turkey: 14 |
| Country: Number of subjects enrolled | Ukraine: 29 |
| Country: Number of subjects enrolled | United States: 120 |
| Worldwide total number of subjects | 772 |
| EEA total number of subjects | 188 |

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) | 578 |
| From 65 to 84 years | 178 |
| 85 years and over | 16 |

Subject disposition

Recruitment

Recruitment details:

Overall, 802 patients were enrolled from 111 centres in 6 regions in this study. The first patient was enrolled on 17 May 2012 and the last patient last visit was on 26 June 2014.

Pre-assignment

Screening details:

None

Period 1

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

Blinding implementation details:

Individual treatment codes, indicating the treatment randomisation for each randomised patient, will be available to the investigators from the IVRS/IWRS. Routines for this will be described in the IVRS/IWRS user manual that will be provided to each centre.

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Ceftaroline fosamil at 600 mg every 8 hours (q8h) |

Arm description: -

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

Dosage and administration details:

Sterile crystalline powder in a single-dose, clear glass 20-mL vial,

| | |
|------------------|---------------------------|
| Arm title | Vancomycin Plus Aztreonam |
|------------------|---------------------------|

Arm description: -

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

Dosage and administration details:

Lyophilized powder, intravenous, dose strength (based on patient's

| | |
|--|----------------------------------|
| Investigational medicinal product name | Aztreonam |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Sterile powder containing approximately 1 gram of aztreonam per

| Number of subjects in period 1^[1] | Ceftaroline fosamil at 600 mg every 8 hours (q8h) | Vancomycin Plus Aztreonam |
|---|---|---------------------------|
| Started | 506 | 255 |
| Completed | 459 | 223 |
| Not completed | 47 | 32 |
| Adverse event, serious fatal | 3 | 2 |
| Consent withdrawn by subject | 16 | 6 |
| Lack of therapeutic response | 5 | 6 |
| Adverse event, non-fatal | 3 | 6 |
| Other | 3 | 1 |
| Lost to follow-up | 15 | 8 |
| Protocol deviation | 2 | 3 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Overall 802 patients were recruited, 772 patients were randomized, but only 761 patients had data for the study.

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---|
| Reporting group title | Ceftaroline fosamil at 600 mg every 8 hours (q8h) |
| Reporting group description: - | |
| Reporting group title | Vancomycin Plus Aztreonam |
| Reporting group description: - | |

| Reporting group values | Ceftaroline fosamil at 600 mg every 8 hours (q8h) | Vancomycin Plus Aztreonam | Total |
|---|---|------------------------------|-------|
| Number of subjects | 506 | 255 | 761 |
| 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) | 387 | 183 | 570 |
| From 65-84 years | 111 | 64 | 175 |
| 85 years and over | 8 | 8 | 16 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 52.6 | 53.6 | |
| standard deviation | ± 16.51 | ± 16.25 | - |
| Gender, Male/Female Units: Participants | | | |
| Female | 196 | 107 | 303 |
| Male | 310 | 148 | 458 |

End points

End points reporting groups

| | |
|--------------------------------|---|
| Reporting group title | Ceftaroline fosamil at 600 mg every 8 hours (q8h) |
| Reporting group description: - | |
| Reporting group title | Vancomycin Plus Aztreonam |
| Reporting group description: - | |

Primary: Clinical response at Test of Cure in MITT

| | |
|------------------------|---|
| End point title | Clinical response at Test of Cure in MITT |
| End point description: | The observed difference in the clinical cure rates at TOC (ceftaroline group minus vancomycin plus aztreonam group) in MITT |
| End point type | Primary |
| End point timeframe: | 7 to 20 days after the last dose of study drug |

| End point values | Ceftaroline fosamil at 600 mg every 8 hours (q8h) | Vancomycin Plus Aztreonam | | |
|-----------------------------|---|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 506 | 255 | | |
| Units: Participants | | | | |
| Clinical cure | 396 | 202 | | |
| Clinical failure | 58 | 34 | | |
| Indeterminate | 52 | 19 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Difference in clinical cure rates at TOC in MITT |
| Statistical analysis description: | Difference in clinical cure rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI. |
| Comparison groups | Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam |
| Number of subjects included in analysis | 761 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -0.95 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.9 |
| upper limit | 5.41 |

Primary: Clinical response at Test-of cure in CE

| | |
|---|---|
| End point title | Clinical response at Test-of cure in CE |
| End point description: The observed difference in the clinical cure rates at TOC (ceftaroline group minus vancomycin plus aztreonam group) in CE | |
| End point type | Primary |
| End point timeframe: 7 to 20 days after the last dose of study drug | |

| End point values | Ceftaroline fosamil at 600 mg every 8 hours (q8h) | Vancomycin Plus Aztreonam | | |
|-----------------------------|---|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 395 | 211 | | |
| Units: Participants | | | | |
| Clinical cure | 342 | 211 | | |
| Clinical failure | 53 | 31 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Difference in clinical cure rates at TOC in CE |
| Statistical analysis description: Difference in clinical cure rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI. | |
| Comparison groups | Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam |
| Number of subjects included in analysis | 606 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 1.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.32 |
| upper limit | 7.48 |

Secondary: Per patient microbiological response at TOC in mMITT

| | |
|-----------------|--|
| End point title | Per patient microbiological response at TOC in mMITT |
|-----------------|--|

End point description:

Difference in microbiological favorable response rate at TOC in mMITT

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

End point timeframe:

7 to 20 days after the last dose of study drug

| End point values | Ceftaroline fosamil at 600 mg every 8 hours (q8h) | Vancomycin Plus Aztreonam | | |
|-----------------------------|---|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 248 | 136 | | |
| Units: Participants | | | | |
| Favorable | 203 | 109 | | |
| Unfavorable | 17 | 17 | | |
| Indeterminate | 28 | 10 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Difference in favorable rates at TOC in mMITT |
|----------------------------|---|

Statistical analysis description:

Difference in favorable rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI.

| | |
|-------------------|---|
| Comparison groups | Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam |
|-------------------|---|

| | |
|---|-----|
| Number of subjects included in analysis | 384 |
|---|-----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|-------|
| Analysis type | other |
|---------------|-------|

| | |
|--------------------|----------------------|
| Parameter estimate | Risk difference (RD) |
|--------------------|----------------------|

| | |
|----------------|------|
| Point estimate | 1.71 |
|----------------|------|

Confidence interval

| | |
|-------|------|
| level | 95 % |
|-------|------|

| | |
|-------|---------|
| sides | 2-sided |
|-------|---------|

| | |
|-------------|-------|
| lower limit | -6.21 |
|-------------|-------|

| | |
|-------------|-------|
| upper limit | 10.39 |
|-------------|-------|

Secondary: Per-patient micro response at TOC for ME

| | |
|-----------------|--|
| End point title | Per-patient micro response at TOC for ME |
|-----------------|--|

End point description:

Difference in microbiological favorable response rate at TOC in ME

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 7 to 20 days after the last dose of study drug | |

| | | | | |
|-----------------------------|---|---------------------------|--|--|
| End point values | Ceftaroline fosamil at 600 mg every 8 hours (q8h) | Vancomycin Plus Aztreonam | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 181 | 112 | | |
| Units: Participants | | | | |
| Favorable | 167 | 98 | | |
| Unfavorable | 14 | 14 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Difference in favorable rates at TOC in ME |
| Statistical analysis description: | |
| Difference in favorable rates (Ceftaroline minus Vancomycin/Aztreonam).CI was calculated by unstratified Miettinen and Nurminen CI. | |
| Comparison groups | Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam |
| Number of subjects included in analysis | 293 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 4.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.11 |
| upper limit | 12.86 |

Secondary: Clinical response at EOT in MITT

| | |
|---|----------------------------------|
| End point title | Clinical response at EOT in MITT |
| End point description: | |
| The observed difference in the clinical cure rates at EOT (ceftaroline group minus vancomycin plus aztreonam group) in MITT | |
| End point type | Secondary |
| End point timeframe: | |
| On day of last dose of study drug (or + 1 day) | |

| | | | | |
|-----------------------------|--|------------------------------|--|--|
| End point values | Ceftaroline fosamil at 600 mg every 8 hours (q8h) | Vancomycin Plus Aztreonam | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 506 | 255 | | |
| Units: Participants | | | | |
| Clinical cure | 429 | 213 | | |
| Clinical failure | 44 | 29 | | |
| Indeterminate | 31 | 11 | | |
| Missing | 2 | 2 | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Difference in cure rates at EOT in MITT |
| Statistical analysis description: Difference in cure rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI. | |
| Comparison groups | Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam |
| Number of subjects included in analysis | 761 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 1.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.05 |
| upper limit | 7.06 |

Secondary: Clinical response at EOT in CE

| | |
|---|--------------------------------|
| End point title | Clinical response at EOT in CE |
| End point description: The observed difference in the clinical cure rates at EOT (ceftaroline group minus vancomycin plus aztreonam group) in CE | |
| End point type | Secondary |
| End point timeframe: On day of last dose of study drug (or +1 day) | |

| | | | | |
|-----------------------------|---|---------------------------|--|--|
| End point values | Ceftaroline fosamil at 600 mg every 8 hours (q8h) | Vancomycin Plus Aztreonam | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 395 | 211 | | |
| Units: Participants | | | | |
| Clinical cure | 356 | 184 | | |
| Clinical failure | 39 | 27 | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Difference in cure rates at EOT in CE |
| Statistical analysis description: Difference in cure rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI. | |
| Comparison groups | Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam |
| Number of subjects included in analysis | 606 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 2.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.19 |
| upper limit | 8.73 |

Secondary: clinical relapse rates at LFU in CE (patients with clinical cure at TOC)

| | |
|--|--|
| End point title | clinical relapse rates at LFU in CE (patients with clinical cure at TOC) |
| End point description: The observed difference in the clinical relapse rates at LFU (ceftaroline group minus vancomycin plus aztreonam group) in CE | |
| End point type | Secondary |
| End point timeframe: 21 to 42 days after the last dose of study drug | |

| | | | | |
|-----------------------------|---|---------------------------|--|--|
| End point values | Ceftaroline fosamil at 600 mg every 8 hours (q8h) | Vancomycin Plus Aztreonam | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 342 | 180 | | |
| Units: Participants | | | | |
| Relapse | 3 | 3 | | |

| | | | | |
|---------------|-----|-----|--|--|
| No relapse | 335 | 174 | | |
| Indeterminate | 3 | 3 | | |
| Missing | 1 | 0 | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Difference in relapse rates at LFU in CE |
| Statistical analysis description: | |
| Difference in relapse rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI. | |
| Comparison groups | Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam |
| Number of subjects included in analysis | 522 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -0.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.98 |
| upper limit | 1.18 |

Secondary: Early response at 48 to 72 hours of treatment in MITT

| | |
|---|---|
| End point title | Early response at 48 to 72 hours of treatment in MITT |
| End point description: | |
| The observed difference in the early success rates at 48 to 72 hours of treatment (ceftaroline group minus vancomycin plus aztreonam group) in MITT | |
| End point type | Secondary |
| End point timeframe: | |
| 48 to 72 hours after first dose of study drug | |

| | | | | |
|-----------------------------|---|---------------------------|--|--|
| End point values | Ceftaroline fosamil at 600 mg every 8 hours (q8h) | Vancomycin Plus Aztreonam | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 506 | 255 | | |
| Units: Participants | | | | |
| Success | 445 | 229 | | |
| Failure | 28 | 11 | | |
| Indeterminate | 33 | 15 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Difference in success rates at 48-72 hours in MITT |
| Statistical analysis description: Difference in success rates (Ceftaroline minus Vancomycin/Aztreonam). CI was calculated by unstratified Miettinen and Nurminen CI. | |
| Comparison groups | Ceftaroline fosamil at 600 mg every 8 hours (q8h) v Vancomycin Plus Aztreonam |
| Number of subjects included in analysis | 761 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -1.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.34 |
| upper limit | 3.15 |

Secondary: Per-pathogen microbiological response at TOC by baseline pathogen from site of skin infection in ME

| | |
|--|---|
| End point title | Per-pathogen microbiological response at TOC by baseline pathogen from site of skin infection in ME |
| End point description: Per-pathogen microbiological response at TOC by baseline pathogen from site of skin infection in ME analysis set | |
| End point type | Secondary |
| End point timeframe: 7 to 20 days after the last dose of study drug | |

| End point values | Ceftaroline fosamil at 600 mg every 8 hours (q8h) | Vancomycin Plus Aztreonam | | |
|--|--|------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 181 | 112 | | |
| Units: Participants | | | | |
| MSSA - Patients reported | 94 | 57 | | |
| MSSA - Favorable | 91 | 49 | | |
| MSSA - Unfavorable | 3 | 8 | | |
| MRSA - Patients reported | 25 | 15 | | |
| MRSA - Favorable | 22 | 12 | | |
| MRSA - Unfavorable | 3 | 3 | | |
| Streptococcus pyogenes - Patients reported | 15 | 7 | | |
| Streptococcus pyogenes - Favorable | 14 | 7 | | |
| Streptococcus pyogenes - Unfavorable | 1 | 0 | | |
| Streptococcus agalactiae - Patients reported | 6 | 9 | | |
| Streptococcus agalactiae - Favorable | 6 | 9 | | |

| | | | | |
|--|----|----|--|--|
| Streptococcus agalactiae - Unfavorable | 0 | 0 | | |
| Streptococcus dysgalactiae - Patients reported | 9 | 0 | | |
| Streptococcus dysgalactiae - Favorable | 9 | 0 | | |
| Streptococcus dysgalactiae - Unfavorable | 0 | 0 | | |
| Enterococcus faecalis - Patients reported | 6 | 5 | | |
| Enterococcus faecalis - Favorable | 5 | 4 | | |
| Enterococcus faecalis - Unfavorable | 1 | 1 | | |
| Escherichia coli - Patients reported | 12 | 10 | | |
| Escherichia coli - Favorable | 12 | 9 | | |
| Escherichia coli - Unfavorable | 0 | 1 | | |
| Klebsiella pneumoniae - Patients reported | 7 | 4 | | |
| Klebsiella pneumoniae - Favorable | 6 | 3 | | |
| Klebsiella pneumoniae - Unfavorable | 1 | 1 | | |
| Klebsiella oxytoca - Patients reported | 4 | 1 | | |
| Klebsiella oxytoca - Favorable | 4 | 1 | | |
| Klebsiella oxytoca - Unfavorable | 0 | 0 | | |
| Proteus mirabilis - Patients reported | 7 | 2 | | |
| Proteus mirabilis - Favorable | 6 | 2 | | |
| Proteus mirabilis - Unfavorable | 1 | 0 | | |
| Morganella morganii - Patients reported | 4 | 2 | | |
| Morganella morganii - Favorable | 4 | 2 | | |
| Morganella morganii - Unfavorable | 0 | 0 | | |
| Enterobacter cloacae - Patients reported | 4 | 5 | | |
| Enterobacter cloacae - Favorable | 4 | 5 | | |
| Enterobacter cloacae - Unfavorable | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from time of administration of the first dose of study therapy up to and including the TOC visit. Serious AEs were collected from time of signature of informed consent up to and including the LFU visit.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 17.0 |

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Vancomycin/Aztreonam |
|-----------------------|----------------------|

Reporting group description:

Vancomycin Plus Aztreonam

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Ceftaroline fosamil 600 mg 120 min IV |
|-----------------------|---------------------------------------|

Reporting group description: -

| Serious adverse events | Vancomycin/Aztreonam | Ceftaroline fosamil 600 mg 120 min IV | |
|---|----------------------|---------------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 15 / 255 (5.88%) | 31 / 506 (6.13%) | |
| number of deaths (all causes) | 2 | 3 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 2 / 506 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous thrombosis | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary haemosiderosis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Alcohol withdrawal syndrome | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Metal poisoning | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 3 / 506 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiomyopathy | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (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 | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Gastrointestinal disorders | | | |
| Anal fistula | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Drug eruption | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxic epidermal necrolysis | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Nephropathy toxic | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure acute | | | |
| subjects affected / exposed | 2 / 255 (0.78%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abdominal infection | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic gangrene | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gangrene | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 2 / 506 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia staphylococcal | | | |
| subjects affected / exposed | 1 / 255 (0.39%) | 0 / 506 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 255 (0.00%) | 1 / 506 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Vancomycin/Aztreonam | Ceftaroline fosamil 600 mg 120 min IV | |
|---|----------------------|---------------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 46 / 255 (18.04%) | 82 / 506 (16.21%) | |
| Investigations | | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 7 / 255 (2.75%) | 3 / 506 (0.59%) | |
| occurrences (all) | 7 | 3 | |

| | | | |
|---|--|--|--|
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 8 / 255 (3.14%) 8 | 7 / 506 (1.38%) 8 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 12 / 255 (4.71%) 13 | 17 / 506 (3.36%) 17 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 9 / 255 (3.53%) 9 | 10 / 506 (1.98%) 10 | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) | 5 / 255 (1.96%) 5 8 / 255 (3.14%) 8 11 / 255 (4.31%) 11 5 / 255 (1.96%) 5 | 12 / 506 (2.37%) 12 9 / 506 (1.78%) 9 20 / 506 (3.95%) 20 13 / 506 (2.57%) 15 | |
| Skin and subcutaneous tissue disorders Pruritus generalised subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) | 6 / 255 (2.35%) 6 6 / 255 (2.35%) 6 | 4 / 506 (0.79%) 4 10 / 506 (1.98%) 11 | |
| Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all) | 8 / 255 (3.14%) 9 | 14 / 506 (2.77%) 14 | |

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

None reported