



Clinical trial results:

A Multicenter, Randomized, Observer-Blinded, Active-Controlled Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of Ceftaroline Versus Ceftriaxone in Pediatric Subjects With Community-acquired Bacterial Pneumonia Requiring Hospitalization

Summary

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2012-002203-18 |
| Trial protocol | Outside EU/EEA HU GR ES PL BG |
| Global end of trial date | 14 April 2014 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 09 August 2018 |
| First version publication date | 09 August 2018 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | P903-31 |
|-----------------------|---------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Cerexa, Inc (a subsidiary of Allergan, plc) |
| Sponsor organisation address | 185 Hudson Street, Plaza 5, New Jersey, United States, NJ 07302-3908 |
| Public contact | Clinical Trial Registry Team, Cerexa, Inc (a subsidiary of Allergan, plc), +1 877-277-8566, CTRegistration@allergan.com |
| Scientific contact | Clinical Trial Registry Team, Cerexa, Inc (a subsidiary of Allergan, plc), +1 877-277-8566, CTRegistration@allergan.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000769-PIP01-09 |
| 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 | 17 October 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 April 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the safety and tolerability of ceftaroline versus ceftriaxone in pediatric subjects ages 2 months to < 18 years with CABP requiring hospitalization.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices and applicable regulatory requirements. Written informed consent from parent or legally acceptable representative and verbal informed assent from subject (if age appropriate and according to local requirements) were obtained before initiating study-related assessments or procedures.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 01 November 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: 23 |
| Country: Number of subjects enrolled | Spain: 5 |
| Country: Number of subjects enrolled | Bulgaria: 13 |
| Country: Number of subjects enrolled | Greece: 14 |
| Country: Number of subjects enrolled | Hungary: 65 |
| Country: Number of subjects enrolled | Ukraine: 20 |
| Country: Number of subjects enrolled | United States: 12 |
| Country: Number of subjects enrolled | Georgia: 9 |
| Worldwide total number of subjects | 161 |
| EEA total number of subjects | 120 |

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) | 30 |
| Children (2-11 years) | 121 |
| Adolescents (12-17 years) | 10 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 161 paediatric subjects between the ages of 2 months to < 18 years with Community-acquired Bacterial Pneumonia (CABP) were enrolled in 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 ^[1] |

Blinding implementation details:

At each study centre, at least 1 blinded investigator ("Blinded Observer") did not know the subject's treatment assignment and conducted clinical assessments (including efficacy and safety).

Arms

| | |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Ceftaroline fosamil |

Arm description:

122 subjects were randomised (ITT) to receive a minimum of 7 IV doses of ceftaroline fosamil (a minimum of 3 days of IV therapy). A switch to open-label oral study drug (amoxicillin clavulanate) was allowed on or after Study Day 4 if a subject met the protocol-specified criteria. A recommended total daily dose of up to 90 mg/kg/day amoxicillin clavulanate was to be divided equally every 12 hours. The total duration of study drug therapy was 5 to 14 days, inclusive.

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

Dosage and administration details:

IV ceftaroline fosamil was infused over 60 (\pm 10) minutes every 8 hours (q8h [\pm 1 hour]) as follows:

- Children \geq 6 months: ceftaroline fosamil 12 mg/kg for subjects weighing \leq 33 kg or 400 mg for subjects weighing $>$ 33 kg
- Children $<$ 6 months: ceftaroline fosamil 8 mg

| | |
|------------------|------------|
| Arm title | Comparator |
|------------------|------------|

Arm description:

39 subjects were randomised (ITT) to receive ceftriaxone for a minimum of 3 days of IV therapy. A switch to oral open-label study drug (amoxicillin clavulanate) was allowed on or after Study Day 4 if a subject met the protocol specified criteria. A recommended total daily dose of up to 90 mg/kg/day amoxicillin clavulanate was to be divided equally every 12h. The total duration of study drug therapy was 5 to 14 days, inclusive.

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

Dosage and administration details:

IV ceftriaxone at a total daily dose of 75 mg/kg/day up to a maximum of 4 g/day, was given in equally divided doses, each infused over 30 (\pm 10) minutes every 12 hours (q12h [\pm 2 hours]).

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Blinding of subject IV dosing regimens was not necessary because treatment was administered by unblinded study centre staff not involved in assessments of clinical response

| Number of subjects in period 1 | Ceftaroline fosamil | Comparator |
|---------------------------------------|---------------------|------------|
| Started | 122 | 39 |
| Completed | 116 | 38 |
| Not completed | 6 | 1 |
| Consent withdrawn by subject | 2 | - |
| Other reasons | 3 | - |
| Lost to follow-up | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall trial |
| Reporting group description: - | |

| Reporting group values | Overall trial | Total | |
|--|---------------|-------|--|
| Number of subjects | 161 | 161 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 30 | 30 | |
| Children (2-11 years) | 121 | 121 | |
| Adolescents (12-17 years) | 10 | 10 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 76 | 76 | |
| Male | 85 | 85 | |

Subject analysis sets

| | |
|--|-----------------------------|
| Subject analysis set title | Ceftaroline - Safety Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The safety set consists of all patients who received any amount of IV study drug. | |
| Subject analysis set title | Comparator - Safety Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The safety set consists of all patients who received any amount of IV study drug. | |
| Subject analysis set title | Ceftaroline - MITT Set |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: The MITT population consists of all randomized subjects who received any amount of IV study drug and who had a confirmed diagnosis of CABP. | |
| Subject analysis set title | Comparator - MITT Set |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: The MITT population consists of all randomized subjects who received any amount of IV study drug and who had a confirmed diagnosis of CABP. | |
| Subject analysis set title | Ceftaroline - mMITT Set |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: The mMITT Population includes subjects for whom at least 1 typical bacterial pathogen has been isolated | |

from an adequate microbiological specimen at baseline.

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | Comparator - mMITT Set |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

The mMITT Population includes subjects for whom at least 1 typical bacterial pathogen has been isolated from an adequate microbiological specimen at baseline.

| | |
|----------------------------|--|
| Subject analysis set title | Ceftaroline - Clinically Evaluable Set |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Clinically Evaluable (CE) population consists of all patients in the ITT population who also meet the minimal CABP disease criteria and all evaluability criteria.

| | |
|----------------------------|---------------------------------------|
| Subject analysis set title | Comparator - Clinically Evaluable Set |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The Clinically Evaluable (CE) population consists of all patients in the ITT population who also meet the minimal CABP disease criteria and all evaluability criteria.

| Reporting group values | Ceftaroline - Safety Set | Comparator - Safety Set | Ceftaroline - MITT Set |
|--|--------------------------|-------------------------|------------------------|
| Number of subjects | 121 | 39 | 107 |
| 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) | 23 | 7 | 23 |
| Children (2-11 years) | 90 | 30 | 77 |
| Adolescents (12-17 years) | 8 | 2 | 7 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

| Reporting group values | Comparator - MITT Set | Ceftaroline - mMITT Set | Comparator - mMITT Set |
|--|-----------------------|-------------------------|------------------------|
| Number of subjects | 36 | 24 | 9 |
| 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) | 6 | 4 | 2 |
| Children (2-11 years) | 28 | 19 | 7 |
| Adolescents (12-17 years) | 2 | 1 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |

| | | | |
|--------------------|--|--|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

| Reporting group values | Ceftaroline - Clinically Evaluable Set | Comparator - Clinically Evaluable Set | |
|---|--|---|--|
| Number of subjects | 98 | 36 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 23 | 6 | |
| Children (2-11 years) | 69 | 28 | |
| Adolescents (12-17 years) | 6 | 2 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Ceftaroline fosamil |
| Reporting group description: 122 subjects were randomised (ITT) to receive a minimum of 7 IV doses of ceftaroline fosamil (a minimum of 3 days of IV therapy). A switch to open-label oral study drug (amoxicillin clavulanate) was allowed on or after Study Day 4 if a subject met the protocol-specified criteria. A recommended total daily dose of up to 90 mg/kg/day amoxicillin clavulanate was to be divided equally every 12 hours. The total duration of study drug therapy was 5 to 14 days, inclusive. | |
| Reporting group title | Comparator |
| Reporting group description: 39 subjects were randomised (ITT) to receive ceftriaxone for a minimum of 3 days of IV therapy. A switch to oral open-label study drug (amoxicillin clavulanate) was allowed on or after Study Day 4 if a subject met the protocol specified criteria. A recommended total daily dose of up to 90 mg/kg/day amoxicillin clavulanate was to be divided equally every 12h. The total duration of study drug therapy was 5 to 14 days, inclusive. | |
| Subject analysis set title | Ceftaroline - Safety Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The safety set consists of all patients who received any amount of IV study drug. | |
| Subject analysis set title | Comparator - Safety Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The safety set consists of all patients who received any amount of IV study drug. | |
| Subject analysis set title | Ceftaroline - MITT Set |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: The MITT population consists of all randomized subjects who received any amount of IV study drug and who had a confirmed diagnosis of CABP. | |
| Subject analysis set title | Comparator - MITT Set |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: The MITT population consists of all randomized subjects who received any amount of IV study drug and who had a confirmed diagnosis of CABP. | |
| Subject analysis set title | Ceftaroline - mMITT Set |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: The mMITT Population includes subjects for whom at least 1 typical bacterial pathogen has been isolated from an adequate microbiological specimen at baseline. | |
| Subject analysis set title | Comparator - mMITT Set |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: The mMITT Population includes subjects for whom at least 1 typical bacterial pathogen has been isolated from an adequate microbiological specimen at baseline. | |
| Subject analysis set title | Ceftaroline - Clinically Evaluable Set |
| Subject analysis set type | Per protocol |
| Subject analysis set description: The Clinically Evaluable (CE) population consists of all patients in the ITT population who also meet the minimal CABP disease criteria and all evaluability criteria. | |
| Subject analysis set title | Comparator - Clinically Evaluable Set |
| Subject analysis set type | Per protocol |
| Subject analysis set description: The Clinically Evaluable (CE) population consists of all patients in the ITT population who also meet the minimal CABP disease criteria and all evaluability criteria. | |

Primary: Extent of exposure - Safety Set

| | |
|-----------------|--|
| End point title | Extent of exposure - Safety Set ^[1] |
|-----------------|--|

End point description:

Extent of exposure is defined as calendar days of exposure to study drug during the IV and oral treatment periods.

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

End point timeframe:

Extent of exposure has been evaluated from date of the first dose of study drug to date of the last dose of study drug + 1 day.

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: The primary objective of this study is to evaluate the safety and tolerability of ceftaroline in children and it is not powered for inferential statistical analysis.

| End point values | Ceftaroline - Safety Set | Comparator - Safety Set | | |
|-----------------------------|--------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 121 | 39 | | |
| Units: Number of patients | | | | |
| < 3 days | 2 | 0 | | |
| 3 - 5 days | 7 | 1 | | |
| 6 - 8 days | 36 | 8 | | |
| 9 - 15 days | 74 | 30 | | |
| > 15 days | 2 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Adverse Events - Safety Set

| | |
|-----------------|--|
| End point title | Adverse Events - Safety Set ^[2] |
|-----------------|--|

End point description:

The safety assessment includes monitoring of adverse events (AEs), serious adverse events, deaths, and discontinuations due to AEs, including cephalosporin class effects and additional AEs.

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

End point timeframe:

Adverse events have been reported from signing the ICF through the late-follow up visit (21 to 35 days after the last dose of any study drug [IV or oral]) or until 30 days after last dose of study drug, whichever occurred later.

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: The primary objective of this study is to evaluate the safety and tolerability of ceftaroline in children and it is not powered for inferential statistical analysis.

| End point values | Ceftaroline - Safety Set | Comparator - Safety Set | | |
|-----------------------------|--------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 121 | 39 | | |
| Units: Number of patients | | | | |
| Subjects with any TEAE | 55 | 18 | | |

| | | | | |
|--|----|---|--|--|
| Subjects with any study drug-related TEAEs | 12 | 3 | | |
| Subjects with any SAEs | 6 | 1 | | |
| Subjects with any study drug-related SAEs | 0 | 0 | | |
| Discontinuations due to any study drug due to AE | 3 | 0 | | |
| Discontinuations of IV study drug due to AE | 2 | 0 | | |
| Deaths | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Response at Study Day 4 - MITT Set

| | |
|--|---|
| End point title | Clinical Response at Study Day 4 - MITT Set |
| End point description: Clinical response at Study Day 4 is defined as improvement in at least 2 out of 7 symptoms (cough, dyspnoea, chest pain, sputum production, chills, feeling of warmth/feverish and exercise intolerance or lethargy) and have worsening in none. | |
| End point type | Secondary |
| End point timeframe: Clinical response at Study Day 4 has been evaluated from Study Day 1 (the first day of IV study drug administration) to Study Day 4. | |

| End point values | Ceftaroline - MITT Set | Comparator - MITT Set | | |
|-----------------------------|------------------------|-----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 107 | 36 | | |
| Units: Number of patients | | | | |
| Responder | 74 | 24 | | |
| Non-responder | 24 | 11 | | |
| Incomplete data | 9 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Stability at Study Day 4 - MITT Set

| | |
|--|--|
| End point title | Clinical Stability at Study Day 4 - MITT Set |
| End point description: Clinical stability at Study Day 4 is defined as meeting all of the following criteria: Afebrile (temperature $\leq 38.0^{\circ}\text{C}$); age-appropriate normal pulse and respiratory rates; oxygen saturation $\geq 92\%$ on room air; worsening of none of the following symptoms relative to baseline: cough, dyspnoea, chest pain, sputum production, chills or rigors, feeling feverish, and exercise intolerance or lethargy. | |

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Clinical stability at Study Day 4 has been evaluated from Study Day 1 (the first day of IV study drug administration) to Study Day 4. | |

| End point values | Ceftaroline - MITT Set | Comparator - MITT Set | | |
|-----------------------------|------------------------|-----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 107 | 36 | | |
| Units: Number of patients | | | | |
| Stability | 37 | 13 | | |
| No stability | 60 | 23 | | |
| Incomplete data | 10 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Response at Study Day 4 - mMITT Set

| | |
|--|--|
| End point title | Clinical Response at Study Day 4 - mMITT Set |
| End point description: | |
| Clinical response at Study Day 4 is defined as improvement in at least 2 out of 7 symptoms (cough, dyspnoea, chest pain, sputum production, chills, feeling of warmth/feverish and exercise intolerance or lethargy) and have worsening in none. | |
| End point type | Secondary |
| End point timeframe: | |
| Clinical Response at Study Day 4 has been evaluated from Study Day 1 (the first day of IV study drug administration) to Study Day 4. | |

| End point values | Ceftaroline - mMITT Set | Comparator - mMITT Set | | |
|-----------------------------|-------------------------|------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 24 | 9 | | |
| Units: Number of patients | | | | |
| Responder | 14 | 7 | | |
| Non-responder | 7 | 1 | | |
| Incomplete data | 3 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Stability at Study Day 4 - mMITT Set

| | |
|-----------------|---|
| End point title | Clinical Stability at Study Day 4 - mMITT Set |
|-----------------|---|

End point description:

Clinical stability at Study Day 4 is defined as meeting all of the following criteria: Afebrile (temperature $\leq 38.0^{\circ}\text{C}$); age-appropriate normal pulse and respiratory rates; oxygen saturation $\geq 92\%$ on room air; worsening of none of the following symptoms relative to baseline: cough, dyspnoea, chest pain, sputum production, chills or rigors, feeling feverish, and exercise intolerance or lethargy.

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

End point timeframe:

Clinical Stability at Study Day 4 has been evaluated from Study Day 1 (the first day of IV study drug administration) to Study Day 4.

| End point values | Ceftaroline - mMITT Set | Comparator - mMITT Set | | |
|-----------------------------|-------------------------|------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 24 | 9 | | |
| Units: Number of patients | | | | |
| Stability | 5 | 1 | | |
| No stability | 15 | 8 | | |
| Incomplete data | 4 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Outcome at TOC - MITT Set

| | |
|-----------------|------------------------------------|
| End point title | Clinical Outcome at TOC - MITT Set |
|-----------------|------------------------------------|

End point description:

Clinical Outcome at TOC is defined as assessment of clinical cure, clinical failure and indeterminate for the MITT population at Test-Of-Cure.

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

End point timeframe:

Clinical Outcome at Test-of-Cure (TOC) has been evaluated 8 to 15 days after administration of the last dose of any study drug [IV or PO].

| End point values | Ceftaroline - MITT Set | Comparator - MITT Set | | |
|-----------------------------|------------------------|-----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 107 | 36 | | |
| Units: Number of patients | | | | |
| Clinical cure | 94 | 32 | | |
| Clinical failure | 8 | 4 | | |
| Indeterminate | 5 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Outcome at TOC - Clinically Evaluable Set

| | |
|-----------------|--|
| End point title | Clinical Outcome at TOC - Clinically Evaluable Set |
|-----------------|--|

End point description:

Clinical Outcome at TOC is defined as assessment of clinical cure, clinical failure and indeterminate for the CE population at Test-Of-Cure.

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

End point timeframe:

Clinical Outcome at Test-of-Cure (TOC) has been evaluated 8 to 15 days after administration of the last dose of any study drug [IV or PO].

| End point values | Ceftaroline - Clinically Evaluable Set | Comparator - Clinically Evaluable Set | | |
|-----------------------------|--|---------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 98 | 36 | | |
| Units: Number of patients | | | | |
| Clinical cure | 90 | 32 | | |
| Clinical failure | 8 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of first dose of study drug through the late follow-up visit or 30 days after the last dose of IV or oral study drug, whichever occurred later.

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|---------------------------------|
| Reporting group title | Ceftaroline - Safety Population |
|-----------------------|---------------------------------|

Reporting group description: -

| | |
|-----------------------|--------------------------------|
| Reporting group title | Comparator - Safety Population |
|-----------------------|--------------------------------|

Reporting group description: -

| Serious adverse events | Ceftaroline - Safety Population | Comparator - Safety Population | |
|---|---------------------------------|--------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 121 (4.96%) | 1 / 39 (2.56%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary thrombosis | | | |
| subjects affected / exposed | 0 / 121 (0.00%) | 1 / 39 (2.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 121 (1.65%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious pleural effusion | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia respiratory syncytial viral | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 39 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 121 (0.83%) | 0 / 39 (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: 5 %

| Non-serious adverse events | Ceftaroline - Safety Population | Comparator - Safety Population | |
|---|---------------------------------|--------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 20 / 121 (16.53%) | 12 / 39 (30.77%) | |
| Blood and lymphatic system disorders | | | |
| Thrombocytosis | | | |
| subjects affected / exposed | 2 / 121 (1.65%) | 3 / 39 (7.69%) | |
| occurrences (all) | 2 | 3 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 121 (2.48%) | 2 / 39 (5.13%) | |
| occurrences (all) | 3 | 2 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 10 / 121 (8.26%) | 2 / 39 (5.13%) | |
| occurrences (all) | 10 | 2 | |
| Vomiting | | | |

| | | | |
|---|----------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 4 / 121 (3.31%) 4 | 2 / 39 (5.13%) 2 | |
| Infections and infestations Otitis media subjects affected / exposed occurrences (all) | 1 / 121 (0.83%) 1 | 3 / 39 (7.69%) 3 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 11 April 2012 | The following changes were implemented with Amendment 1: Clarification of the efficacy outcome measures of clinical response, clinical stability, and clinical and microbiological outcomes in the Modified Intent-to-Treat (MITT) and the Microbiological Modified Intent-to-Treat (mMITT) populations; updates to the dosing language; updates to the clinical laboratory tests; addition of a symptom questionnaire to be performed by the Blinded Observer and other clarifications. |
| 26 October 2012 | The following changes were implemented with Amendment 2: Change of Study Phase designation; updates to dosing regimen; change in criteria for switching to outpatient parenteral antimicrobial therapy (OPAT) and other clarifications. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported