



Clinical trial results:

An Open-Label, Randomized, Multicenter, Phase III Study of Ceftazidime-Avibactam (CAZ-AVI, formerly CAZ104) and Best Available Therapy for the Treatment of Infections Due to Ceftazidime Resistant Gram-Negative Pathogens

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2012-000726-21 |
| Trial protocol | BE DE CZ ES GR BG HU IT GB |
| Global end of trial date | 29 September 2014 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 27 April 2016 |
| First version publication date | 27 April 2016 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | D4280C00006 |
|-----------------------|-------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | AstraZeneca |
| Sponsor organisation address | 151 85 Södertälje, Södertälje, Sweden, |
| Public contact | Nell Moore, AstraZeneca, UK 44 788-411-5907, Nell.Moore@astrazeneca.com |
| Scientific contact | Leanne Gasink, AstraZeneca, USA 302-885-5550, Leanne.Gasink@astrazeneca.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 | 19 March 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 29 September 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 September 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To estimate the per-patient clinical response to ceftazidime-avibactam (CAZ-AVI, formerly CAZ104) and Best Available Therapy (BAT) at Test of Cure (TOC) in the treatment of selected serious infections caused by ceftazidime-resistant Gram-negative pathogens.

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 | 07 January 2013 |
| 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 | Bulgaria: 91 |
| Country: Number of subjects enrolled | Croatia: 12 |
| Country: Number of subjects enrolled | Czech Republic: 6 |
| Country: Number of subjects enrolled | Romania: 31 |
| Country: Number of subjects enrolled | Russian Federation: 74 |
| Country: Number of subjects enrolled | Turkey: 23 |
| Country: Number of subjects enrolled | Ukraine: 31 |
| Country: Number of subjects enrolled | France: 3 |
| Country: Number of subjects enrolled | Spain: 4 |
| Country: Number of subjects enrolled | United States: 9 |
| Country: Number of subjects enrolled | Argentina: 9 |
| Country: Number of subjects enrolled | Israel: 17 |
| Country: Number of subjects enrolled | Korea, Republic of: 5 |
| Country: Number of subjects enrolled | Mexico: 7 |
| Country: Number of subjects enrolled | Peru: 9 |
| Country: Number of subjects enrolled | South Africa: 2 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 333 |
| EEA total number of subjects | 147 |

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) | 159 |
| From 65 to 84 years | 163 |
| 85 years and over | 11 |

Subject disposition

Recruitment

Recruitment details:

A total of 333 patients were randomized in 53 centers in 16 countries: 306 patients had cUTI and 27 patients had cIAI. The first patient was randomized on 07 January 2013 and the last patient was randomized on 29 August 2014. One patient in the CAZ-AVI arm was randomized but did not receive study drug.

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

Arms

| | |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | cIAI:Best Available Therapy |

Arm description:

cIAI: Best Available Therapy Determinated by Investigator

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Investigator-determined BAT(protocol preferred BAT options: meropenem,imipenem,doripenem,tigecycline, and colistin (if colistin,metronidazole should be added) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Details for dose and frequency of administration of BAT can be found.

| | |
|------------------|------------------------------|
| Arm title | cIAI:CAZ-AVI + metronidazole |
|------------------|------------------------------|

Arm description:

cIAI:CAZ-AVI (2000 mg ceftazidime/500 mg avibactam) plus metronidazole (500 mg)

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

Dosage and administration details:

Metronidazole 500 mg/100 mL solution for infusion

| | |
|--|--|
| Investigational medicinal product name | CAZ-AVI (single-vial product supply) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Sterile crystalline powder, 2000 mg ceftazidime/500 mg avibactam for solution for infusion

| | |
|--|--|
| Arm title | cUTI:Best Available Therapy |
| Arm description: cUTI:Best Available Therapy Determinated by Investigator | |
| Arm type | Active comparator |
| Investigational medicinal product name | Investigator-determined BAT(protocol preferred BAT options: meropenem,imipenem,doripenem,tigecycline, and colistin (if colistin,metronidazole should be added) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Details for dose and frequency of administration of BAT can be found.

| | |
|--|--------------------------------------|
| Arm title | cUTI:CAZ-AVI |
| Arm description: cUTI: CAZ-AVI | |
| Arm type | Experimental |
| Investigational medicinal product name | CAZ-AVI (single-vial product supply) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Sterile crystalline powder, 2000 mg ceftazidime/500 mg avibactam for

| Number of subjects in period 1 | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy |
|---------------------------------------|-----------------------------|------------------------------|-----------------------------|
| Started | 15 | 12 | 153 |
| Completed | 13 | 12 | 148 |
| Not completed | 2 | 0 | 5 |
| Adverse event, serious fatal | 1 | - | 3 |
| Consent withdrawn by subject | 1 | - | 2 |
| Other Eligibility criteria | - | - | - |
| Lost to follow-up | - | - | - |

| Number of subjects in period 1 | cUTI:CAZ-AVI |
|---------------------------------------|--------------|
| Started | 153 |
| Completed | 143 |
| Not completed | 10 |
| Adverse event, serious fatal | 3 |
| Consent withdrawn by subject | 1 |
| Other Eligibility criteria | 2 |
| Lost to follow-up | 4 |

Baseline characteristics

Reporting groups

| | |
|---|------------------------------|
| Reporting group title | cIAI:Best Available Therapy |
| Reporting group description: cIAI: Best Available Therapy Determinated by Investigator | |
| Reporting group title | cIAI:CAZ-AVI + metronidazole |
| Reporting group description: cIAI:CAZ-AVI (2000 mg ceftazidime/500 mg avibactam) plus metronidazole (500 mg) | |
| Reporting group title | cUTI:Best Available Therapy |
| Reporting group description: cUTI:Best Available Therapy Determinated by Investigator | |
| Reporting group title | cUTI:CAZ-AVI |
| Reporting group description: cUTI: CAZ-AVI | |

| Reporting group values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy |
|--|-----------------------------|------------------------------|-----------------------------|
| Number of subjects | 15 | 12 | 153 |
| 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) | 7 | 10 | 79 |
| From 65-84 years | 7 | 2 | 71 |
| 85 years and over | 1 | 0 | 3 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 59.5 | 50.3 | 61 |
| standard deviation | ± 18.78 | ± 14.71 | ± 15.27 |
| Gender, Male/Female Units: Participants | | | |
| Female | 5 | 7 | 73 |
| Male | 10 | 5 | 80 |
| Age, Customized Units: Subjects | | | |
| 18-45 | 3 | 3 | 24 |
| 46-64 | 4 | 7 | 55 |
| 65-74 | 4 | 2 | 46 |
| 75-90 | 4 | 0 | 28 |

| Reporting group values | cUTI:CAZ-AVI | Total | |
|------------------------|--------------|-------|--|
| Number of subjects | 153 | 333 | |

| | | | |
|---|---------|-----|--|
| 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) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 63 | 159 | |
| From 65-84 years | 83 | 163 | |
| 85 years and over | 7 | 11 | |
| Age Continuous Units: Years | | | |
| arithmetic mean | 64.3 | | |
| standard deviation | ± 14.72 | - | |
| Gender, Male/Female Units: Participants | | | |
| Female | 67 | 152 | |
| Male | 86 | 181 | |
| Age, Customized Units: Subjects | | | |
| 18-45 | 20 | 50 | |
| 46-64 | 43 | 109 | |
| 65-74 | 50 | 102 | |
| 75-90 | 40 | 72 | |

End points

End points reporting groups

| | |
|---|------------------------------|
| Reporting group title | cIAI:Best Available Therapy |
| Reporting group description: | |
| cIAI: Best Available Therapy Determinated by Investigator | |
| Reporting group title | cIAI:CAZ-AVI + metronidazole |
| Reporting group description: | |
| cIAI:CAZ-AVI (2000 mg ceftazidime/500 mg avibactam) plus metronidazole (500 mg) | |
| Reporting group title | cUTI:Best Available Therapy |
| Reporting group description: | |
| cUTI:Best Available Therapy Determinated by Investigator | |
| Reporting group title | cUTI:CAZ-AVI |
| Reporting group description: | |
| cUTI: CAZ-AVI | |

Primary: Clinical response at Test of Cure (TOC) in Microbiological modified intent-to-treat (mMITT) analysis set

| | |
|---|---|
| End point title | Clinical response at Test of Cure (TOC) in Microbiological modified intent-to-treat (mMITT) analysis set ^[1] |
| End point description: | |
| Proportion of patients with clinical cure at the TOC visit in the mMITT analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible). | |
| End point type | Primary |
| End point timeframe: | |
| 6-12 days after last infusion of study therapy | |

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: No treatment comparisons were done in this study. No no statistical analysis section were entered.

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| Clinical cure | 6 | 8 | 129 | 132 |
| Clinical failure | 0 | 0 | 2 | 2 |
| Indeterminate | 5 | 2 | 6 | 10 |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response at End of treatment (EOT) in mMITT analysis set.

| | |
|-----------------|--|
| End point title | Clinical response at End of treatment (EOT) in mMITT analysis set. |
|-----------------|--|

End point description:

Proportion of patients with clinical cure at the EOT visit in the mMITT analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible).

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

End point timeframe:

28 hours after completion of last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| Clinical cure | 6 | 9 | 136 | 142 |
| Clinical failure | 0 | 0 | 0 | 0 |
| Indeterminate | 5 | 1 | 1 | 2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response at Follow-up 1 (FU1) in mMITT analysis set

| | |
|-----------------|--|
| End point title | Clinical response at Follow-up 1 (FU1) in mMITT analysis set |
|-----------------|--|

End point description:

Proportion of patients with clinical cure at the FU1 visit in the mMITT analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible).

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

End point timeframe:

cIAI: 27-37 calendar days from randomization/cUTI: 20-27 calendar days from randomization

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| Clinical cure | 6 | 8 | 121 | 127 |
| Clinical failure | 0 | 0 | 8 | 5 |

| | | | | |
|---------------|---|---|---|----|
| Indeterminate | 5 | 2 | 8 | 12 |
|---------------|---|---|---|----|

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response at Follow-up 2 (FU2) in mMITT analysis set

| | |
|---|--|
| End point title | Clinical response at Follow-up 2 (FU2) in mMITT analysis set |
| End point description: Proportion of patients with clinical cure at the FU2 visit in the mMITT analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible). | |
| End point type | Secondary |
| End point timeframe: cUTI only: 28-34 calendar days from randomization | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[2] | 0 ^[3] | 137 | 144 |
| Units: Participant | | | | |
| Clinical cure | | | 118 | 123 |
| Clinical failure | | | 13 | 11 |
| Indeterminate | | | 6 | 10 |

Notes:

[2] - cIAI patients: FU2 is not applicable.

[3] - cIAI patients: FU2 is not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response at EOT in Extended Microbiologically Evaluable (EME) at EOT analysis set.

| | |
|--|---|
| End point title | Clinical response at EOT in Extended Microbiologically Evaluable (EME) at EOT analysis set. |
| End point description: Proportion of patients with clinical cure at the EOT visit in the EME at EOT analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible). | |
| End point type | Secondary |
| End point timeframe: 28 hours after completion of last infusion of study therapy | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 9 | 127 | 134 |
| Units: Participant | | | | |
| Clinical cure | 5 | 9 | 127 | 134 |
| Clinical failure | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response at TOC in EME at TOC analysis set.

| | |
|-----------------|--|
| End point title | Clinical response at TOC in EME at TOC analysis set. |
|-----------------|--|

End point description:

Proportion of patients with clinical cure at the TOC visit in the EME at TOC analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible).

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

End point timeframe:

6-12 days after last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 8 | 122 | 128 |
| Units: Participant | | | | |
| Clinical cure | 5 | 8 | 120 | 126 |
| Clinical failure | 0 | 0 | 2 | 2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response at FU1 in EME at FU1 analysis set.

| | |
|-----------------|--|
| End point title | Clinical response at FU1 in EME at FU1 analysis set. |
|-----------------|--|

End point description:

Proportion of patients with clinical cure at the FU1 visit in EME at FU1 analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that

no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible).

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| cIAI: 27-37 calendar days from randomization/cUTI: 20-27 calendar days from randomization | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 7 | 118 | 124 |
| Units: Participant | | | | |
| Clinical cure | 5 | 7 | 110 | 120 |
| Clinical failure | 0 | 0 | 8 | 4 |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical response at FU2 in EME at FU2 analysis set

| | |
|--|---|
| End point title | Clinical response at FU2 in EME at FU2 analysis set |
| End point description: | |
| Proportion of patients with clinical cure at the FU2 visit in EME at FU2 analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary. | |
| End point type | Secondary |
| End point timeframe: | |
| cUTI only: 28-34 calendar days from randomization | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[4] | 0 ^[5] | 114 | 116 |
| Units: Participant | | | | |
| Clinical cure | | | 102 | 106 |
| Clinical failure | | | 12 | 10 |

Notes:

[4] - cIAI patients: FU2 is not applicable.

[5] - cIAI patients: FU2 is not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical cure at TOC by baseline Gram-negative pathogen in mMITT analysis set

| | |
|-----------------|---|
| End point title | Clinical cure at TOC by baseline Gram-negative pathogen in mMITT analysis set |
|-----------------|---|

End point description:

Proportion of patients with clinical cure at TOC visit by baseline pathogen ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients) in the mMITT analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible).

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

End point timeframe:

6-12 days after last infusion of study therapy

| End point values | cIAI: Best Available Therapy | cIAI: CAZ-AVI + metronidazole | cUTI: Best Available Therapy | cUTI: CAZ-AVI |
|--|------------------------------|-------------------------------|------------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| E. coli - Clinical cure (n=6, 4, 57, 59) | 2 | 3 | 54 | 53 |
| K. pneumoniae - Clinical cure (n=3, 5, 65, 55) | 2 | 3 | 61 | 54 |
| P. aeruginosa - clinical cure (n=1, 1, 5, 14) | 1 | 1 | 5 | 12 |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical cure at TOC by baseline Gram-negative pathogen in EME at TOC analysis set

| | |
|-----------------|--|
| End point title | Clinical cure at TOC by baseline Gram-negative pathogen in EME at TOC analysis set |
|-----------------|--|

End point description:

Proportion of patients with clinical cure at TOC visit by baseline Gram-negative pathogen ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients) in EME at TOC analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible).

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

End point timeframe:

6-12 days after last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|--|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 8 | 124 | 131 |
| Units: Participant | | | | |
| E. coli - Clinical cure (n=2, 3, 48, 52) | 2 | 3 | 47 | 51 |
| K. pneumoniae - Clinical cure (n=2, 3, 59, 53) | 2 | 3 | 59 | 53 |
| P. aeruginosa - Clinical cure (n=1, 1, 5, 12) | 1 | 1 | 5 | 12 |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical cure at TOC by previously failed treatment class in mMITT analysis set

| | |
|-----------------|---|
| End point title | Clinical cure at TOC by previously failed treatment class in mMITT analysis set |
|-----------------|---|

End point description:

Proportion of patients with clinical cure at TOC visit by previously failed treatment class in the mMITT analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible).

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

End point timeframe:

6-12 days after last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|--|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| At least 1 failed - Cure (n=4,7,12,7) | 3 | 7 | 12 | 6 |
| Antibiotics - Cure (n=0,1,0,0) | 0 | 1 | 0 | 0 |
| Carbapenems - Cure (n=1,0,1,2) | 0 | 0 | 1 | 1 |
| Comb of Sulf/Trime inc Deriv- Cure(n=0,0,2,0) | 0 | 0 | 2 | 0 |
| Combs Of Peni. Inc B-Lact. Inhib.- Cure(n=1,3,0,2) | 1 | 3 | 0 | 2 |
| Cortico,Po. Comb W/Antibio.- Cure(n=0,0,1,0) | 0 | 0 | 1 | 0 |
| First-Gen. Cephalosporins-Cure (n=0,0,2,0) | 0 | 0 | 2 | 0 |
| Fluoroquinolones - Cure (n=1,2,7,1) | 0 | 2 | 7 | 1 |
| Glycopeptide Antibacterials-Cure (n=1,0,0,0) | 0 | 0 | 0 | 0 |
| Imidazole Derivatives - Cure (n=2,3,0,0) | 1 | 3 | 0 | 0 |

| | | | | |
|--|---|---|---|---|
| Other Aminoglycosides-Cure (n=0,0,1,1) | 0 | 0 | 1 | 1 |
| Other Antibacterials-Cure (n=0,1,1,0) | 0 | 1 | 1 | 0 |
| Other Antibio. F. Topic. Use-Cure(n=0,0,1,0) | 0 | 0 | 1 | 0 |
| Penici. With Ext. Spectrum-Cure(n=0,1,0,0) | 0 | 1 | 0 | 0 |
| Third-Gen.Cephalosporins - Cure(n=2,4,3,2) | 2 | 4 | 3 | 2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical cure at EOT by previously failed treatment class in EME at EOT analysis set

| | |
|-----------------|--|
| End point title | Clinical cure at EOT by previously failed treatment class in EME at EOT analysis set |
|-----------------|--|

End point description:

Proportion of patients with clinical cure at EOT visit by previously failed treatment class in EME at EOT analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible).

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

End point timeframe:

28 hours after completion of last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|---|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 9 | 127 | 134 |
| Units: Participant | | | | |
| Antibiotics - Cure (n=0,1,0,0) | 0 | 1 | 0 | 0 |
| Carbapenems - Cure (n=0,0,1,1) | 0 | 0 | 1 | 1 |
| Comb of Sulf/Trime inc Deriv-Cure(n=0,0,2,0) | 0 | 0 | 2 | 0 |
| Combs Of Peni. Inc B-Lact. Inhib.-Cure(n=1,3,0,2) | 1 | 3 | 0 | 2 |
| Cortico,Po. Comb W/Antibio.-Cure(n=0,0,1,0) | 0 | 0 | 1 | 0 |
| First-Gen. Cephalosporins-Cure (n=0,0,2,0) | 0 | 0 | 2 | 0 |
| Fluoroquinolones - Cure (n=0,2,5,1) | 0 | 2 | 5 | 1 |
| Imidazole Derivatives - Cure (n=1,3,0,0) | 1 | 3 | 0 | 0 |
| Other Aminoglycosides-Cure (n=0,0,1,1) | 0 | 0 | 1 | 1 |
| Other Antibacterials-Cure (n=0,1,1,0) | 0 | 1 | 1 | 0 |
| Other Antibio. F. Topic. Use-Cure(n=0,0,1,0) | 0 | 0 | 1 | 0 |

| | | | | |
|--|---|---|---|---|
| Penici. With Ext. Spectrum-Cure(n=0,1,0,0) | 0 | 1 | 0 | 0 |
| Third-Gen.Cephalosporins - Cure(n=2,4,2,2) | 2 | 4 | 2 | 2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical cure at TOC by previously failed treatment class in EME at TOC analysis set

| | |
|-----------------|--|
| End point title | Clinical cure at TOC by previously failed treatment class in EME at TOC analysis set |
|-----------------|--|

End point description:

Proportion of patients with clinical cure at TOC visit by previously failed treatment class in EME at TOC analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible).

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

End point timeframe:

6-12 days after last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|---|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 8 | 122 | 128 |
| Units: Participant | | | | |
| Antibiotics - Cure (n=0,1,0,0) | 0 | 1 | 0 | 0 |
| Carbapenems - Cure (n=0,0,1,1) | 0 | 0 | 1 | 1 |
| Comb of Sulf/Trime inc Deriv-Cure(n=0,0,2,0) | 0 | 0 | 2 | 0 |
| Combs Of Peni. Inc B-Lact. Inhib.-Cure(n=1,3,0,2) | 1 | 3 | 0 | 2 |
| Cortico,Po. Comb W/Antibio.-Cure(n=0,0,1,0) | 0 | 0 | 1 | 0 |
| First-Gen. Cephalosporins-Cure (n=0,0,2,0) | 0 | 0 | 2 | 0 |
| Fluoroquinolones - Cure (n=0,2,5,1) | 0 | 2 | 5 | 1 |
| Imidazole Derivatives - Cure (n=1,3,0,0) | 1 | 3 | 0 | 0 |
| Other Aminoglycosides-Cure (n=0,0,0,1) | 0 | 0 | 0 | 1 |
| Other Antibacterials-Cure (n=0,1,1,0) | 0 | 1 | 1 | 0 |
| Other Antibio. F. Topic. Use-Cure(n=0,0,1,0) | 0 | 0 | 1 | 0 |
| Penici. With Ext. Spectrum-Cure(n=0,1,0,0) | 0 | 1 | 0 | 0 |
| Third-Gen.Cephalosporins - Cure(n=2,4,2,2) | 2 | 4 | 2 | 2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical cure at FU1 by previously failed treatment class in EME at FU1 analysis set

| | |
|-----------------|--|
| End point title | Clinical cure at FU1 by previously failed treatment class in EME at FU1 analysis set |
|-----------------|--|

End point description:

Proportion of patients with clinical cure at FU1 visit by previously failed treatment class in EME at FU1 analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary; for cIAI patients no drainage or surgical intervention after 96 hours from randomization is necessary (ie. drainage or surgical intervention up to 96 hours from randomization is permissible).

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

End point timeframe:

cIAI: 27-37 calendar days from randomization/cUTI: 20-27 calendar days from randomization

| End point values | cIAI: Best Available Therapy | cIAI: CAZ-AVI + metronidazole | cUTI: Best Available Therapy | cUTI: CAZ-AVI |
|--|------------------------------|-------------------------------|------------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 7 | 118 | 124 |
| Units: Participant | | | | |
| Antibiotics - Cure (n=0,1,0,0) | 0 | 1 | 0 | 0 |
| Carbapenems - Cure (n=0,0,1,1) | 0 | 0 | 1 | 1 |
| Comb of Sulf/Trime inc Deriv- Cure(n=0,0,1,0) | 0 | 0 | 1 | 0 |
| Combs Of Peni. Inc B-Lact. Inhib.- Cure(n=1,3,0,2) | 1 | 3 | 0 | 2 |
| Cortico,Po. Comb W/Antibio.- Cure(n=0,0,1,0) | 0 | 0 | 0 | 0 |
| First-Gen. Cephalosporins-Cure (n=0,0,2,0) | 0 | 0 | 2 | 0 |
| Fluoroquinolones - Cure (n=0,2,5,1) | 0 | 2 | 4 | 1 |
| Imidazole Derivatives - Cure (n=1,3,0,0) | 1 | 3 | 0 | 0 |
| Other Aminoglycosides-Cure (n=0,0,0,1) | 0 | 0 | 0 | 1 |
| Other Antibacterials-Cure (n=0,1,1,0) | 0 | 1 | 1 | 0 |
| Other Antibio. F. Topic. Use- Cure(n=0,0,1,0) | 0 | 0 | 1 | 0 |
| Penici. With Ext. Spectrum- Cure(n=0,1,0,0) | 0 | 1 | 0 | 0 |
| Third-Gen.Cephalosporins - Cure(n=2,4,1,2) | 2 | 4 | 0 | 2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical cure at FU2 by previously failed treatment class in EME at FU2 analysis set

| | |
|-----------------|--|
| End point title | Clinical cure at FU2 by previously failed treatment class in EME at FU2 analysis set |
|-----------------|--|

End point description:

Proportion of patients with clinical cure at FU2 visit by previously failed treatment class in EME at FU2 analysis set. Clinical cure: Complete resolution or significant improvement of signs and symptoms of the index infection such that no further antibacterial therapy (other than those allowed per protocol) is necessary.

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

End point timeframe:

cUTI only: 28-34 calendar days from randomization

| End point values | cIAI: Best Available Therapy | cIAI: CAZ-AVI + metronidazole | cUTI: Best Available Therapy | cUTI: CAZ-AVI |
|---|------------------------------|-------------------------------|------------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[6] | 0 ^[7] | 114 | 116 |
| Units: Participant | | | | |
| Carbapenems - Cure (n=1,0) | | | 0 | 0 |
| Comb of Sulf/Trime inc Deriv-Cure(n=1,0) | | | 0 | 0 |
| Combs Of Peni. Inc B-Lact. Inhib.-Cure(n=0,2) | | | 0 | 2 |
| Cortico,Po. Comb W/Antibio.-Cure(n=1,0) | | | 0 | 0 |
| First-Gen. Cephalosporins-Cure (n=2,0) | | | 2 | 0 |
| Fluoroquinolones - Cure (n=5,0) | | | 4 | 0 |
| Other Aminoglycosides-Cure (n=0,1) | | | 0 | 1 |
| Other Antibacterials-Cure (n=1,0) | | | 0 | 0 |
| Other Antibio. F. Topic. Use-Cure(n=1,0) | | | 1 | 0 |
| Third-Gen.Cephalosporins -Cure(n=1,1) | | | 0 | 1 |

Notes:

[6] - cIAI patients: FU2 is not applicable.

[7] - cIAI patients: FU2 is not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Per-patient microbiological response at EOT in mMITT analysis set

| | |
|---|---|
| End point title | Per-patient microbiological response at EOT in mMITT analysis set |
| End point description: | |
| Microbiological responses as per the protocol criteria: responses other than "indeterminate" were classified as "favorable" or "unfavorable." Favorable microbiological response assessments included "eradication" and "presumed eradication." Unfavorable microbiological response assessments included "persistence," "persistence with increasing minimum inhibitory concentration (MIC)," and "presumed persistence." Indeterminate microbiologic response assessments included cIAI patients where the clinical response was changed to indeterminate due to a Surgical Review Panel assessment of inadequate source control (ie, circumstances that preclude classification as eradication, presumed eradication, persistence, persistence with increasing MIC, and presumed persistence). | |
| End point type | Secondary |
| End point timeframe: | |
| 28 hours after completion of last infusion of study therapy | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| Favorable | 6 | 9 | 130 | 136 |
| Unfavorable | 0 | 0 | 1 | 1 |
| Indeterminate | 5 | 1 | 6 | 7 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-patient microbiological response at TOC in mMITT analysis set

| | |
|---|---|
| End point title | Per-patient microbiological response at TOC in mMITT analysis set |
| End point description: | |
| Microbiological responses as per the protocol criteria: responses other than "indeterminate" were classified as "favorable" or "unfavorable." Favorable microbiological response assessments included "eradication" and "presumed eradication." Unfavorable microbiological response assessments included "persistence," "persistence with increasing minimum inhibitory concentration (MIC)," and "presumed persistence." Indeterminate microbiologic response assessments included cIAI patients where the clinical response was changed to indeterminate due to a Surgical Review Panel assessment of inadequate source control (ie, circumstances that preclude classification as eradication, presumed eradication, persistence, persistence with increasing MIC, and presumed persistence). | |
| End point type | Secondary |
| End point timeframe: | |
| 6-12 days after last infusion of study therapy | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| Favorable | 6 | 8 | 88 | 118 |
| Unfavorable | 0 | 0 | 42 | 17 |
| Indeterminate | 5 | 2 | 7 | 9 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-patient microbiological response at FU1 in mMITT analysis set

| | |
|-----------------|---|
| End point title | Per-patient microbiological response at FU1 in mMITT analysis set |
|-----------------|---|

End point description:

Microbiological responses as per the protocol criteria: responses other than "indeterminate" were classified as "favorable" or "unfavorable." Favorable microbiological response assessments included "eradication" and "presumed eradication." Unfavorable microbiological response assessments included "persistence," "persistence with increasing minimum inhibitory concentration (MIC)," and "presumed persistence." Indeterminate microbiologic response assessments included cIAI patients where the clinical response was changed to indeterminate due to a Surgical Review Panel assessment of inadequate source control (ie, circumstances that preclude classification as eradication, presumed eradication, persistence, persistence with increasing MIC, and presumed persistence).

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

End point timeframe:

cUTI: 20-27 calendar days from randomization/cIAI: 27-37 calendar days from randomization

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| Favorable | 6 | 8 | 78 | 103 |
| Unfavorable | 0 | 0 | 50 | 29 |
| Indeterminate | 5 | 2 | 9 | 12 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-patient microbiological response at FU2 in mMITT analysis set

| | |
|-----------------|---|
| End point title | Per-patient microbiological response at FU2 in mMITT analysis set |
|-----------------|---|

End point description:

Microbiological responses as per the protocol criteria: responses other than "indeterminate" were classified as "favorable" or "unfavorable." Favorable microbiological response assessments included "eradication" and "presumed eradication." Unfavorable microbiological response assessments included "persistence," "persistence with increasing minimum inhibitory concentration (MIC)," and "presumed persistence." Indeterminate microbiologic response assessments included cIAI patients where the clinical response was changed to indeterminate due to a Surgical Review Panel assessment of inadequate source control (ie, circumstances that preclude classification as eradication, presumed eradication, persistence, persistence with increasing MIC, and presumed persistence).

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

End point timeframe:

cUTI only: 28-34 calendar days from randomization

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[8] | 0 ^[9] | 137 | 144 |
| Units: Participant | | | | |
| Favorable | | | 73 | 99 |
| Unfavorable | | | 54 | 35 |
| Indeterminate | | | 10 | 10 |

Notes:

[8] - cIAI patients: FU2 is not applicable.

[9] - cIAI patients: FU2 is not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Per-patient microbiological response at EOT in EME at EOT analysis set

| | |
|-----------------|--|
| End point title | Per-patient microbiological response at EOT in EME at EOT analysis set |
|-----------------|--|

End point description:

Microbiological responses as per the protocol criteria: responses other than "indeterminate" were classified as "favorable" or "unfavorable." Favorable microbiological response assessments included "eradication" and "presumed eradication." Unfavorable microbiological response assessments included "persistence," "persistence with increasing minimum inhibitory concentration (MIC)," and "presumed persistence." Indeterminate microbiologic response assessments included cIAI patients where the clinical response was changed to indeterminate due to a Surgical Review Panel assessment of inadequate source control (ie, circumstances that preclude classification as eradication, presumed eradication, persistence, persistence with increasing MIC, and presumed persistence).

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

End point timeframe:

28 hours after completion of last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 9 | 127 | 134 |
| Units: Participant | | | | |
| Favorable | 5 | 9 | 127 | 133 |
| Unfavorable | 0 | 0 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-patient microbiological response at TOC in EME at TOC analysis set

| | |
|-----------------|--|
| End point title | Per-patient microbiological response at TOC in EME at TOC analysis set |
|-----------------|--|

End point description:

Microbiological responses as per the protocol criteria: responses other than "indeterminate" were classified as "favorable" or "unfavorable." Favorable microbiological response assessments included "eradication" and "presumed eradication." Unfavorable microbiological response assessments included "persistence," "persistence with increasing minimum inhibitory concentration (MIC)," and "presumed persistence." Indeterminate microbiologic response assessments included cIAI patients where the clinical response was changed to indeterminate due to a Surgical Review Panel assessment of inadequate source control (ie, circumstances that preclude classification as eradication, presumed eradication, persistence, persistence with increasing MIC, and presumed persistence).

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

End point timeframe:

6-12 days after last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 8 | 124 | 131 |
| Units: Participant | | | | |
| Favorable | 5 | 8 | 84 | 114 |
| Unfavorable | 0 | 0 | 40 | 17 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-patient microbiological response at FU1 in EME at FU1 analysis set

| | |
|-----------------|--|
| End point title | Per-patient microbiological response at FU1 in EME at FU1 analysis set |
|-----------------|--|

End point description:

Microbiological responses as per the protocol criteria: responses other than "indeterminate" were classified as "favorable" or "unfavorable." Favorable microbiological response assessments included

"eradication" and "presumed eradication." Unfavorable microbiological response assessments included "persistence," "persistence with increasing minimum inhibitory concentration (MIC)," and "presumed persistence." Indeterminate microbiologic response assessments included cIAI patients where the clinical response was changed to indeterminate due to a Surgical Review Panel assessment of inadequate source control (ie, circumstances that preclude classification as eradication, presumed eradication, persistence, persistence with increasing MIC, and presumed persistence).

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

End point timeframe:

cUTI: 20-27 calendar days from randomization/cIAI: 27-37 calendar days from randomization

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 7 | 120 | 126 |
| Units: Participant | | | | |
| Favorable | 5 | 7 | 75 | 98 |
| Unfavorable | 0 | 0 | 45 | 28 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-patient microbiological response at FU2 in EME at FU2 analysis set

| | |
|-----------------|--|
| End point title | Per-patient microbiological response at FU2 in EME at FU2 analysis set |
|-----------------|--|

End point description:

Microbiological responses as per the protocol criteria: responses other than "indeterminate" were classified as "favorable" or "unfavorable." Favorable microbiological response assessments included "eradication" and "presumed eradication." Unfavorable microbiological response assessments included "persistence," "persistence with increasing minimum inhibitory concentration (MIC)," and "presumed persistence." Indeterminate microbiologic response assessments included cIAI patients where the clinical response was changed to indeterminate due to a Surgical Review Panel assessment of inadequate source control (ie, circumstances that preclude classification as eradication, presumed eradication, persistence, persistence with increasing MIC, and presumed persistence).

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

End point timeframe:

cUTI only: 28-34 calendar days from randomization

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|-----------------------------|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[10] | 0 ^[11] | 115 | 117 |
| Units: Participant | | | | |
| Favorable | | | 68 | 85 |
| Unfavorable | | | 47 | 32 |

Notes:

[10] - cIAI patients: FU2 is not applicable.

[11] - cIAI patients: FU2 is not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response of Gram-negative pathogen at EOT in mMITT analysis set

| | |
|-----------------|--|
| End point title | Per-pathogen microbiological response of Gram-negative pathogen at EOT in mMITT analysis set |
|-----------------|--|

End point description:

Proportion of patients with a favorable per-pathogen microbiological response for pathogens ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients): favourable microbiological response includes: Eradication Absence (or urine quantification $\leq 10^4$ CFU/ml for cUTI patients) of causative pathogen from an appropriately obtained specimen at the site of infection. If the patient was bacteremic at Screening, the bacteremia has also resolved. Presumed eradication where, repeat cultures were not performed/clinically indicated in a patient who had a clinical response of cure (specific to cIAI population).

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

End point timeframe:

28 hours after completion of last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|--|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| E. coli - Favorable (n=6, 4, 57, 59) | 2 | 3 | 53 | 57 |
| E. coli - Unfavorable (n=6, 4, 57, 59) | 0 | 0 | 0 | 0 |
| E. coli - Indeterminate (n=6, 4, 57, 59) | 4 | 1 | 4 | 2 |
| K. pneumoniae - Favorable (n=3, 5, 65, 55) | 2 | 4 | 61 | 52 |
| K. pneumoniae - Unfavorable (n=3, 5, 65, 55) | 0 | 0 | 1 | 0 |
| K. pneumoniae - Indeterminate (n=3, 5, 65, 55) | 1 | 1 | 3 | 3 |
| P. aeruginosa - Favorable (n=1, 1, 5, 14) | 1 | 1 | 5 | 14 |
| P. aeruginosa - Unfavorable (n=1, 1, 5, 14) | 0 | 0 | 0 | 0 |
| P. aeruginosa - Indeterminate (n=1, 1, 5, 14) | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response of Gram-negative pathogen at TOC in mMITT analysis set

| | |
|-----------------|--|
| End point title | Per-pathogen microbiological response of Gram-negative pathogen at TOC in mMITT analysis set |
|-----------------|--|

End point description:

Proportion of patients with a favorable per-pathogen microbiological response for pathogens ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients): favourable microbiological response includes: Eradication Absence (or urine quantification $< 10^4$ CFU/ml for cUTI patients) of causative pathogen from an appropriately obtained specimen at the site of infection. If the patient was bacteremic at Screening, the bacteremia has also resolved. Presumed eradication where, repeat cultures were not performed/clinically indicated in a patient who had a clinical response of cure (specific to cIAI population).

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

End point timeframe:

6-12 days after last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|--|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| E. coli - Favorable (n=6, 4, 57, 59) | 2 | 3 | 38 | 52 |
| E. coli - Unfavorable (n=6, 4, 57, 59) | 0 | 0 | 16 | 3 |
| E. coli - Indeterminate (n=6, 4, 57, 59) | 4 | 1 | 3 | 4 |
| K. pneumoniae - Favorable (n=3, 5, 65, 55) | 2 | 3 | 43 | 46 |
| K. pneumoniae - Unfavorable (n=3, 5, 65, 55) | 0 | 0 | 19 | 8 |
| K. pneumoniae - Indeterminate (n=3, 5, 65, 55) | 1 | 2 | 3 | 1 |
| P. aeruginosa - Favorable (n=1, 1, 5, 14) | 1 | 1 | 3 | 11 |
| P. aeruginosa - Unfavorable (n=1, 1, 5, 14) | 0 | 0 | 2 | 2 |
| P. aeruginosa - Indeterminate (n=1, 1, 5, 14) | 0 | 0 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response of Gram-negative pathogen at FU1 in mMITT analysis set

| | |
|-----------------|--|
| End point title | Per-pathogen microbiological response of Gram-negative pathogen at FU1 in mMITT analysis set |
|-----------------|--|

End point description:

Proportion of patients with a favorable per-pathogen microbiological response for pathogens ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients): favourable microbiological response includes: Eradication Absence (or urine quantification $< 10^4$ CFU/ml for cUTI patients) of causative pathogen

from an appropriately obtained specimen at the site of infection. If the patient was bacteremic at Screening, the bacteremia has also resolved. Presumed eradication where, repeat cultures were not performed/clinically indicated in a patient who had a clinical response of cure (specific to cIAI population).

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| cIAI: 27-37 calendar days from randomization/cUTI: 20-27 calendar days from randomization | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|--|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| E. coli - Favorable (n=6, 4, 57, 59) | 2 | 3 | 33 | 45 |
| E. coli - Unfavorable (n=6, 4, 57, 59) | 0 | 0 | 18 | 12 |
| E. coli - Indeterminate (n=6, 4, 57, 59) | 4 | 1 | 6 | 2 |
| K. pneumoniae - Favorable (n=3, 5, 65, 55) | 2 | 3 | 39 | 42 |
| K. pneumoniae - Unfavorable (n=3, 5, 65, 55) | 0 | 0 | 23 | 10 |
| K. pneumoniae - Indeterminate (n=3, 5, 65, 55) | 1 | 2 | 3 | 3 |
| P. aeruginosa - Favorable (n=1, 1, 5, 14) | 1 | 1 | 3 | 8 |
| P. aeruginosa - Unfavorable (n=1, 1, 5, 14) | 0 | 0 | 2 | 2 |
| P. aeruginosa - Indeterminate (n=1, 1, 5, 14) | 0 | 0 | 0 | 4 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response of Gram-negative pathogen at FU2 in mMITT analysis set

| | |
|-----------------|--|
| End point title | Per-pathogen microbiological response of Gram-negative pathogen at FU2 in mMITT analysis set |
|-----------------|--|

End point description:

Proportion of patients with a favorable per-pathogen microbiological response for pathogens ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients): favourable microbiological response includes: Eradication Absence (or urine quantification $\leq 10^4$ CFU/ml for cUTI patients) of causative pathogen from an appropriately obtained specimen at the site of infection. If the patient was bacteremic at Screening, the bacteremia has also resolved. Presumed eradication where, repeat cultures were not performed/clinically indicated in a patient who had a clinical response of cure (specific to cIAI population).

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| cUTI only: 28-34 calendar days from randomization | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|--|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[12] | 0 ^[13] | 137 | 144 |
| Units: Participant | | | | |
| E. coli - Favorable (n=0, 0, 57, 59) | | | 32 | 43 |
| E. coli - Unfavorable (n=0, 0, 57, 59) | | | 19 | 14 |
| E. coli - Indeterminate (n=0, 0, 57, 59) | | | 6 | 2 |
| K. pneumoniae - Favorable (n=0, 0, 65, 55) | | | 35 | 39 |
| K. pneumoniae - Unfavorable (n=0, 0, 65, 55) | | | 26 | 14 |
| K. pneumoniae - Indeterminate (n=0, 0, 65, 55) | | | 4 | 2 |
| P. aeruginosa - Favorable (n=0, 0, 5, 14) | | | 2 | 10 |
| P. aeruginosa - Unfavorable (n=0, 0, 5, 14) | | | 3 | 2 |
| P. aeruginosa - Indeterminate (n=0, 0, 5, 14) | | | 0 | 2 |

Notes:

[12] - cIAI patients: FU2 is not applicable.

[13] - cIAI patients: FU2 is not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response of Gram-negative pathogen at EOT in EME at EOT analysis set

| | |
|-----------------|---|
| End point title | Per-pathogen microbiological response of Gram-negative pathogen at EOT in EME at EOT analysis set |
|-----------------|---|

End point description:

Proportion of patients with a favorable per-pathogen microbiological response for pathogens ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients): favourable microbiological response includes: Eradication Absence (or urine quantification $< 10^4$ CFU/ml for cUTI patients) of causative pathogen from an appropriately obtained specimen at the site of infection. If the patient was bacteremic at Screening, the bacteremia has also resolved. Presumed eradication where, repeat cultures were not performed/clinically indicated in a patient who had a clinical response of cure (specific to cIAI population).

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

End point timeframe:

28 hours after completion of last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|--|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 9 | 127 | 134 |
| Units: Participant | | | | |
| E. coli - Favorable (n=2, 3, 51, 55) | 2 | 3 | 51 | 55 |
| E. coli - Unfavorable (n=2, 3, 51, 55) | 0 | 0 | 0 | 0 |
| K. pneumoniae - Favorable (n=2, 4, 60, 52) | 2 | 4 | 60 | 52 |
| K. pneumoniae - Unfavorable (n=2, 4, 60, 52) | 0 | 0 | 0 | 0 |
| P. aeruginosa - Favorable (n=1, 1, 5, 14) | 1 | 1 | 5 | 14 |
| P. aeruginosa - Unfavorable (n=1, 1, 5, 14) | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response of Gram-negative pathogen at TOC in EME at TOC analysis set

| | |
|-----------------|---|
| End point title | Per-pathogen microbiological response of Gram-negative pathogen at TOC in EME at TOC analysis set |
|-----------------|---|

End point description:

Proportion of patients with a favorable per-pathogen microbiological response for pathogens ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients): favourable microbiological response includes: Eradication Absence (or urine quantification $\leq 10^4$ CFU/ml for cUTI patients) of causative pathogen from an appropriately obtained specimen at the site of infection. If the patient was bacteremic at Screening, the bacteremia has also resolved. Presumed eradication where, repeat cultures were not performed/clinically indicated in a patient who had a clinical response of cure (specific to cIAI population).

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

End point timeframe:

6-12 days after last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|--|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 8 | 124 | 131 |
| Units: Participant | | | | |
| E. coli - Favorable (n=2, 3, 49, 53) | 2 | 3 | 34 | 50 |
| E. coli - Unfavorable (n=2, 3, 49, 53) | 0 | 0 | 15 | 3 |
| K. pneumoniae - Favorable (n=2, 3, 60, 53) | 2 | 3 | 42 | 45 |
| K. pneumoniae - Unfavorable (n=2, 3, 60, 53) | 0 | 0 | 18 | 8 |
| P. aeruginosa - Favorable (n=1, 1, 5, 13) | 1 | 1 | 3 | 11 |

| | | | | |
|---|---|---|---|---|
| P. aeruginosa - Unfavorable (n=1, 1, 5, 13) | 0 | 0 | 2 | 2 |
|---|---|---|---|---|

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response of Gram-negative pathogen at FU1 in EME at FU1 analysis set

| | |
|--|---|
| End point title | Per-pathogen microbiological response of Gram-negative pathogen at FU1 in EME at FU1 analysis set |
| End point description: Proportion of patients with a favorable per-pathogen microbiological response for pathogens ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients): favourable microbiological response includes: Eradication Absence (or urine quantification $\leq 10^4$ CFU/ml for cUTI patients) of causative pathogen from an appropriately obtained specimen at the site of infection. If the patient was bacteremic at Screening, the bacteremia has also resolved. Presumed eradication where, repeat cultures were not performed/clinically indicated in a patient who had a clinical response of cure (specific to cIAI population). | |
| End point type | Secondary |
| End point timeframe: cIAI: 27-37 calendar days from randomization/cUTI: 20-27 calendar days from randomization | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|--|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 7 | 120 | 126 |
| Units: Participant | | | | |
| E. coli - Favorable (n=2, 3, 46, 54) | 2 | 3 | 30 | 43 |
| E. coli - Unfavorable (n=2, 3, 46, 54) | 0 | 0 | 16 | 11 |
| K. pneumoniae - Favorable (n=2, 2, 59, 50) | 2 | 2 | 38 | 40 |
| K. pneumoniae - Unfavorable (n=2, 2, 59, 50) | 0 | 0 | 21 | 10 |
| P. aeruginosa - Favorable (n=1, 1, 5, 10) | 1 | 1 | 3 | 8 |
| P. aeruginosa - Unfavorable (n=1, 1, 5, 10) | 0 | 0 | 2 | 2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response of Gram-negative pathogen at FU2 in EME at FU2 analysis set

| | |
|-----------------|--|
| End point title | Per-pathogen microbiological response of Gram-negative |
|-----------------|--|

End point description:

Proportion of patients with a favorable per-pathogen microbiological response for pathogens ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients): favourable microbiological response includes: Eradication Absence (or urine quantification $< 10^4$ CFU/ml for cUTI patients) of causative pathogen from an appropriately obtained specimen at the site of infection. If the patient was bacteremic at Screening, the bacteremia has also resolved. Presumed eradication where, repeat cultures were not performed/clinically indicated in a patient who had a clinical response of cure (specific to cIAI population).

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

End point timeframe:

cUTI only: 28-34 calendar days from randomization

| End point values | cIAI: Best Available Therapy | cIAI: CAZ-AVI + metronidazole | cUTI: Best Available Therapy | cUTI: CAZ-AVI |
|--|------------------------------|-------------------------------|------------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[14] | 0 ^[15] | 115 | 117 |
| Units: Participant | | | | |
| E. coli - Favorable (n=44, 50) | | | 28 | 39 |
| E. coli - Unfavorable (n=44, 50) | | | 16 | 11 |
| K. pneumoniae - Favorable (n= 56, 46) | | | 33 | 32 |
| K. pneumoniae - Unfavorable (n=56, 46) | | | 23 | 14 |
| P. aeruginosa - Favorable (n=4, 11) | | | 2 | 9 |
| P. aeruginosa - Unfavorable (n=4, 11) | | | 2 | 2 |

Notes:

[14] - cIAI patients: FU2 is not applicable.

[15] - cIAI patients: FU2 is not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response of Gram-negative pathogen at TOC by CAZ-AVI MIC in mMITT analysis set

| | |
|-----------------|---|
| End point title | Per-pathogen microbiological response of Gram-negative pathogen at TOC by CAZ-AVI MIC in mMITT analysis set |
|-----------------|---|

End point description:

Proportion of patients with a favorable per-pathogen microbiological response for pathogens ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients): favourable microbiological response includes: Eradication Absence (or urine quantification $< 10^4$ CFU/ml for cUTI patients) of causative pathogen from an appropriately obtained specimen at the site of infection. If the patient was bacteremic at Screening, the bacteremia has also resolved. Presumed eradication where, repeat cultures were not performed/clinically indicated in a patient who had a clinical response of cure (specific to cIAI population).

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

End point timeframe:

6-12 days after last infusion of study therapy

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|--|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| E. coli (MIC: ≤0.008)-Favorable (n=0, 0, 1, 1) | 0 | 0 | 1 | 1 |
| E. coli (MIC: 0.03)-Favorable (n=0, 0, 0, 2) | 0 | 0 | 0 | 1 |
| E. coli (MIC: 0.06)-Favorable (n=1, 0, 3, 2) | 0 | 0 | 3 | 2 |
| E. coli (MIC: 0.12)-Favorable (n=4, 2, 20, 20) | 2 | 1 | 12 | 16 |
| E. coli (MIC: 0.25)-Favorable (n=0, 0, 15, 16) | 0 | 0 | 10 | 15 |
| E. coli (MIC: 0.5)-Favorable (n=0, 1, 8, 11) | 0 | 1 | 5 | 10 |
| E. coli (MIC: 1)-Favorable (n=0, 0, 2, 2) | 0 | 0 | 1 | 2 |
| E. coli (MIC: 2)-Favorable (n=0, 0, 2, 1) | 0 | 0 | 2 | 1 |
| E. coli (MIC: 8)-Favorable (n=0, 0, 2, 4) | 0 | 0 | 2 | 4 |
| K. pneumoniae (MIC: 0.06)-Favorable (n=0,0,2,0) | 0 | 0 | 1 | 0 |
| K. pneumoniae (MIC: 0.12)-Favorable (n=0,1,8,5) | 0 | 0 | 6 | 4 |
| K. pneumoniae (MIC: 0.25)-Favorable (n=0,3,12,6) | 0 | 2 | 7 | 5 |
| K. pneumoniae (MIC: 0.5)-Favorable (n=2,0,24,22) | 1 | 0 | 16 | 19 |
| K. pneumoniae (MIC: 1)-Favorable (n=0,0,16,18) | 0 | 0 | 11 | 16 |
| K. pneumoniae (MIC: 2)-Favorable (n=1, 1, 1, 2) | 1 | 1 | 1 | 1 |
| K. pneumoniae (MIC: 4)-Favorable (n=0, 0, 1, 1) | 0 | 0 | 1 | 0 |
| K. pneumoniae (MIC: 32)-Favorable (n=0, 0, 1, 0) | 0 | 0 | 0 | 0 |
| K. pneumoniae (MIC: >32)-Favorable (n=0,0,0,1) | 0 | 0 | 0 | 0 |
| P. aeruginosa (MIC: 2)-Favorable (n=1, 0, 0, 1) | 1 | 0 | 0 | 1 |
| P. aeruginosa (MIC: 4)-Favorable (n=0, 0, 3, 2) | 0 | 0 | 1 | 1 |
| P. aeruginosa (MIC: 8)-Favorable (n=0, 0, 0, 2) | 0 | 0 | 0 | 2 |
| P. aeruginosa (MIC: 16)-Favorable (n=0, 1, 0, 1) | 0 | 1 | 0 | 0 |
| P. aeruginosa (MIC: 32)-Favorable (n=0, 0, 1, 3) | 0 | 0 | 1 | 3 |
| P. aeruginosa (MIC: >32)-Favorable (n=0,0,1,5) | 0 | 0 | 1 | 4 |

Statistical analyses

No statistical analyses for this end point

Secondary: Per-pathogen microbiological response of Gram-negative pathogen at

TOC by CAZ-AVI MIC in EME at TOC analysis set

| | |
|-----------------|--|
| End point title | Per-pathogen microbiological response of Gram-negative pathogen at TOC by CAZ-AVI MIC in EME at TOC analysis set |
|-----------------|--|

End point description:

Proportion of patients with a favorable per-pathogen microbiological response for pathogens ($\geq 10\%$ of frequency in the combined cIAI and cUTI patients): favourable microbiological response includes: Eradication Absence (or urine quantification $\leq 10^4$ CFU/ml for cUTI patients) of causative pathogen from an appropriately obtained specimen at the site of infection. If the patient was bacteremic at Screening, the bacteremia has also resolved. Presumed eradication where, repeat cultures were not performed/clinically indicated in a patient who had a clinical response of cure (specific to cIAI population).

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

End point timeframe:

6-12 days after last infusion of study therapy

| End point values | cIAI: Best Available Therapy | cIAI: CAZ-AVI + metronidazole | cUTI: Best Available Therapy | cUTI: CAZ-AVI |
|---|------------------------------|-------------------------------|------------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 8 | 124 | 131 |
| Units: Participant | | | | |
| E. coli (MIC: ≤ 0.008)-Favorable (n=0, 0, 1, 1) | 0 | 0 | 1 | 1 |
| E. coli (MIC: 0.03)-Favorable (n=0, 0, 0, 2) | 0 | 0 | 0 | 1 |
| E. coli (MIC: 0.06)-Favorable (n=0, 0, 3, 1) | 0 | 0 | 3 | 1 |
| E. coli (MIC: 0.12)-Favorable (n=2, 1, 18, 18) | 2 | 1 | 10 | 16 |
| E. coli (MIC: 0.25)-Favorable (n=0, 0, 13, 15) | 0 | 0 | 9 | 15 |
| E. coli (MIC: 0.5)-Favorable (n=0, 1, 6, 9) | 0 | 1 | 4 | 9 |
| E. coli (MIC: 1)-Favorable (n=0, 0, 2, 2) | 0 | 0 | 1 | 2 |
| E. coli (MIC: 2)-Favorable (n=0, 0, 2, 1) | 0 | 0 | 2 | 1 |
| E. coli (MIC: 8)-Favorable (n=0, 0, 2, 4) | 0 | 0 | 2 | 4 |
| K. pneumoniae (MIC: 0.06)-Favorable (n=0,0,1,0) | 0 | 0 | 0 | 0 |
| K. pneumoniae (MIC: 0.12)-Favorable (n=0,0,8,5) | 0 | 0 | 6 | 4 |
| K. pneumoniae (MIC: 0.25)-Favorable (n=0,2,11,6) | 0 | 2 | 7 | 5 |
| K. pneumoniae (MIC: 0.5)-Favorable (n=1,0,23,21) | 1 | 0 | 16 | 19 |
| K. pneumoniae (MIC: 1)-Favorable (n=0,0,15,17) | 0 | 0 | 11 | 15 |
| K. pneumoniae (MIC: 2)-Favorable (n=1, 1, 1, 2) | 1 | 1 | 1 | 2 |
| K. pneumoniae (MIC: 4)-Favorable (n=0, 0, 1, 1) | 0 | 0 | 1 | 0 |
| K. pneumoniae (MIC: >32)-Favorable (n=0,0,0,1) | 0 | 0 | 0 | 0 |
| P. aeruginosa (MIC: 2)-Favorable (n=1, 0, 0, 1) | 1 | 0 | 0 | 1 |
| P. aeruginosa (MIC: 4)-Favorable (n=0, 0, 3, 2) | 0 | 0 | 1 | 1 |

| | | | | |
|--|---|---|---|---|
| P. aeruginosa (MIC: 8)-Favorable (n=0, 0, 0, 2) | 0 | 0 | 0 | 2 |
| P. aeruginosa (MIC: 16)-Favorable (n=0, 1, 0, 1) | 0 | 1 | 0 | 0 |
| P. aeruginosa (MIC: 32)-Favorable (n=0, 0, 1, 3) | 0 | 0 | 1 | 3 |
| P. aeruginosa (MIC: >32)-Favorable (n=0,0,1,4) | 0 | 0 | 1 | 4 |

Statistical analyses

No statistical analyses for this end point

Secondary: The reason for treatment change/discontinuation in mMITT analysis set

| | |
|---|---|
| End point title | The reason for treatment change/discontinuation in mMITT analysis set |
| End point description: Proportion of patients in the mMITT analysis set for whom the assigned study treatment was changed, discontinued, or interrupted. | |
| End point type | Secondary |
| End point timeframe: From first infusion to last infusion of study therapy | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|---|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| Treatment Change | 1 | 0 | 8 | 11 |
| Treatment Change - Crcl change | 1 | 0 | 5 | 10 |
| Treatment Change - Other | 0 | 0 | 3 | 1 |
| Treatment discontinuation | 4 | 0 | 3 | 1 |
| Treatment discontinuation - AE | 1 | 0 | 1 | 1 |
| Treatment discontinuation - Other | 3 | 0 | 2 | 0 |
| Treatment interrupted | 0 | 0 | 0 | 1 |
| Treatment interrupted - Change of infusion site | 0 | 0 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: The 28 days all cause mortality rate in mMITT analysis set

| | |
|---|--|
| End point title | The 28 days all cause mortality rate in mMITT analysis set |
| End point description: Proportion of patients with Day 28 all-cause mortality in mMITT analysis set. The death in the cIAI | |

patient were reviewed independently by the SRP Chair.

| | |
|-------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From first infusion to Day 28 | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|---|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 10 | 137 | 144 |
| Units: Participant | | | | |
| All cause mortality | 1 | 0 | 3 | 3 |
| Deaths due to disease progression | 0 | 0 | 0 | 0 |
| Number of patients with any AE with outcome=death | 1 | 0 | 3 | 3 |

Statistical analyses

No statistical analyses for this end point

Secondary: The 28 days all cause mortality rate in EME at TOC analysis set

| | |
|--|---|
| End point title | The 28 days all cause mortality rate in EME at TOC analysis set |
| End point description: | |
| Proportion of patients with Day 28 all-cause mortality in EME at TOC analysis set. The death in the cIAI patient were reviewed independently by the SRP Chair. | |
| End point type | Secondary |
| End point timeframe: | |
| From first infusion to Day 28 | |

| End point values | cIAI:Best Available Therapy | cIAI:CAZ-AVI + metronidazole | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|--|-----------------------------|------------------------------|-----------------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 8 | 124 | 131 |
| Units: Participant | | | | |
| All cause mortality | 0 | 0 | 1 | 1 |
| Deaths due to disease progression | 0 | 0 | 0 | 0 |
| Number of patients with any AE without outcome=death | 0 | 0 | 1 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for ceftazidime (CAZ) within 15 minutes before/ after dose in PK analysis set

| | |
|-----------------|---|
| End point title | Plasma concentrations for ceftazidime (CAZ) within 15 minutes before/ after dose in PK analysis set ^[16] |
|-----------------|---|

End point description:

Blood samples were taken at anytime within 15 minutes prior to or after stopping study drug on Day 3 for ceftazidime and avibactam plasma concentration.

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

End point timeframe:

Anytime within 15 minutes prior to or after stopping study drug

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No treatment comparisons were done in this study. No no statistical analysis section were entered.

| End point values | cIAI:CAZ-AVI + metronidazole | cUTI:CAZ-AVI | | |
|---------------------------------------|------------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 145 | | |
| Units: NG/ML | | | | |
| geometric mean (full range (min-max)) | 23880.3 (2700 to 80900) | 74260.2 (5970 to 1640000) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for avibactam (AVI) within 15 minutes before/ after study dose in PK analysis set

| | |
|-----------------|---|
| End point title | Plasma concentrations for avibactam (AVI) within 15 minutes before/ after study dose in PK analysis set ^[17] |
|-----------------|---|

End point description:

Blood samples were taken at anytime within 15 minutes prior to or after stopping study drug on Day 3 for ceftazidime and avibactam plasma concentration.

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

End point timeframe:

Anytime within 15 minutes prior to or after stopping study drug

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No treatment comparisons were done in this study. No no statistical analysis section were entered.

| End point values | cIAI:CAZ-AVI + metronidazole | cUTI:CAZ-AVI | | |
|---------------------------------------|------------------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 147 | | |
| Units: NG/ML | | | | |
| geometric mean (full range (min-max)) | 3061.3 (286 to 13200) | 10103.8 (504 to 376000) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for ceftazidime (CAZ) between 30 to 90 minutes after dose in PK analysis set

| | |
|-----------------|--|
| End point title | Plasma concentrations for ceftazidime (CAZ) between 30 to 90 minutes after dose in PK analysis set ^[18] |
|-----------------|--|

End point description:

Blood samples were taken at anytime between 30 to 90 minutes after stopping study drug on Day 3 for ceftazidime and avibactam plasma concentration.

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

End point timeframe:

anytime between 30 to 90 minutes after stopping study drug

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No treatment comparisons were done in this study. No no statistical analysis section were entered.

| End point values | cIAI:CAZ-AVI + metronidazole | cUTI:CAZ-AVI | | |
|---------------------------------------|------------------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 141 | | |
| Units: NG/ML | | | | |
| geometric mean (full range (min-max)) | 39465.3 (2620 to 85500) | 56905.9 (14700 to 1910000) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for avibactam (AVI) between 30 to 90 minutes after dose in PK analysis set

| | |
|-----------------|--|
| End point title | Plasma concentrations for avibactam (AVI) between 30 to 90 minutes after dose in PK analysis set ^[19] |
|-----------------|--|

End point description:

Blood samples were taken at anytime between 30 to 90 minutes after stopping study drug on Day 3 for ceftazidime and avibactam plasma concentration.

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

End point timeframe:

anytime between 30 to 90 minutes after stopping study drug

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No treatment comparisons were done in this study. No no statistical analysis section were entered.

| End point values | cIAI:CAZ-AVI + metronidazole | cUTI:CAZ-AVI | | |
|---------------------------------------|------------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 147 | | |
| Units: NG/ML | | | | |
| geometric mean (full range (min-max)) | 6304.1 (285 to 15500) | 8141.2 (773 to 405000) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for ceftazidime (CAZ) between 300 to 360 minutes after dose in PK analysis set

| | |
|-----------------|--|
| End point title | Plasma concentrations for ceftazidime (CAZ) between 300 to 360 minutes after dose in PK analysis set ^[20] |
|-----------------|--|

End point description:

Blood samples were taken at anytime between 300 to 360 minutes after stopping study drug on Day 3 for ceftazidime and avibactam plasma concentration.

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

End point timeframe:

anytime between 300 to 360 minutes after stopping study drug

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No treatment comparisons were done in this study. No no statistical analysis section were entered.

| End point values | cIAI:CAZ-AVI + metronidazole | cUTI:CAZ-AVI | | |
|---------------------------------------|------------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 146 | | |
| Units: NG/ML | | | | |
| geometric mean (full range (min-max)) | 14904.8 (2500 to 58100) | 21442 (2490 to 1600000) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations for avibactam (AVI) between 300 to 360 minutes after dose in PK analysis set

| | |
|-----------------|--|
| End point title | Plasma concentrations for avibactam (AVI) between 300 to 360 minutes after dose in PK analysis set ^[21] |
|-----------------|--|

End point description:

Blood samples were taken at anytime between 300 to 360 minutes after stopping study drug on Day 3 for ceftazidime and avibactam plasma concentration.

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

End point timeframe:

anytime between 300 to 360 minutes after stopping study drug

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No treatment comparisons were done in this study. No no statistical analysis section were entered.

| End point values | cIAI:CAZ-AVI + metronidazole | cUTI:CAZ-AVI | | |
|---------------------------------------|------------------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 12 | 146 | | |
| Units: NG/ML | | | | |
| geometric mean (full range (min-max)) | 1769.3 (277 to 7900) | 2425 (315 to 431000) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non serious AEs and SAEs were from the first infusion of study therapy through the FU visits (cIAI: 28-35 days calendar days from randomization, cUTI: 28-32 calendar days from randomization).

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | cIAI:Best Available Therapy |
|-----------------------|-----------------------------|

Reporting group description:

cIAI: Best Available Therapy Determinated by Investigator

| | |
|-----------------------|-----------------------------|
| Reporting group title | cUTI:Best Available Therapy |
|-----------------------|-----------------------------|

Reporting group description:

cUTI:Best Available Therapy Determinated by Investigator

| | |
|-----------------------|--------------|
| Reporting group title | cUTI:CAZ-AVI |
|-----------------------|--------------|

Reporting group description:

cUTI: CAZ-AVI (2000 mg ceftazidime/500 mg avibactam)

| | |
|-----------------------|------------------------------|
| Reporting group title | cIAI:CAZ-AVI + metronidazole |
|-----------------------|------------------------------|

Reporting group description:

cIAI:CAZ-AVI (2000 mg ceftazidime/500 mg avibactam) plus metronidazole (500 mg)

| Serious adverse events | cIAI:Best Available Therapy | cUTI:Best Available Therapy | cUTI:CAZ-AVI |
|---|-----------------------------|-----------------------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 15 (33.33%) | 5 / 153 (3.27%) | 7 / 152 (4.61%) |
| number of deaths (all causes) | 1 | 3 | 3 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Bladder cancer | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Pancreatic injury | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural fistula | | | |

| | | | |
|--|----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 153 (0.65%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 2 / 153 (1.31%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| Nervous system disorders | | | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 153 (0.65%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hernial eventration | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal perforation | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 153 (0.65%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 153 (0.65%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 153 (0.65%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |

| | | | |
|---|----------------------------------|-----------------------------------|-----------------------------------|
| Infections and infestations Urosepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 15 (0.00%) 0 / 0 0 / 0 | 1 / 153 (0.65%) 0 / 1 0 / 0 | 0 / 152 (0.00%) 0 / 0 0 / 0 |
| Lobar pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 15 (6.67%) 0 / 1 0 / 1 | 0 / 153 (0.00%) 0 / 0 0 / 0 | 0 / 152 (0.00%) 0 / 0 0 / 0 |
| Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 15 (6.67%) 0 / 1 0 / 0 | 0 / 153 (0.00%) 0 / 0 0 / 0 | 0 / 152 (0.00%) 0 / 0 0 / 0 |
| Urinary tract infection enterococcal subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 15 (0.00%) 0 / 0 0 / 0 | 0 / 153 (0.00%) 0 / 0 0 / 0 | 1 / 152 (0.66%) 0 / 1 0 / 0 |
| Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 15 (0.00%) 0 / 0 0 / 0 | 1 / 153 (0.65%) 0 / 1 0 / 0 | 0 / 152 (0.00%) 0 / 0 0 / 0 |

| | | | |
|---|----------------------------------|--|--|
| Serious adverse events | cIAI:CAZ-AVI + metronidazole | | |
| Total subjects affected by serious adverse events subjects affected / exposed number of deaths (all causes) number of deaths resulting from adverse events | 2 / 12 (16.67%) 0 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Bladder cancer subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 12 (0.00%) 0 / 0 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|--|----------------|--|--|
| Pancreatic injury | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post procedural fistula | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Intestinal obstruction | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hernial eventration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nausea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal perforation | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |

| | | | |
|---|----------------|--|--|
| Renal failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lobar pneumonia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | cIAI: Best Available Therapy | cUTI: Best Available Therapy | cUTI: CAZ-AVI |
|---|------------------------------|------------------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 15 (80.00%) | 36 / 153 (23.53%) | 18 / 152 (11.84%) |
| Vascular disorders | | | |

| | | | |
|---|---------------------|----------------------|----------------------|
| Phlebitis subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 2 | 2 / 153 (1.31%) 2 | 1 / 152 (0.66%) 1 |
| General disorders and administration site conditions | | | |
| Catheter site haemorrhage subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Hyperthermia subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 1 / 153 (0.65%) 1 | 0 / 152 (0.00%) 0 |
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 2 / 153 (1.31%) 3 | 4 / 152 (2.63%) 8 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 153 (0.00%) 0 | 1 / 152 (0.66%) 1 |
| Pulmonary fibrosis subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Atelectasis subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Hydrothorax subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Respiratory failure subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Tachypnoea | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Insomnia | | | |
| subjects affected / exposed occurrences (all) | 4 / 15 (26.67%) 4 | 0 / 153 (0.00%) 0 | 2 / 152 (1.32%) 2 |
| Investigations | | | |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Endoscopy gastrointestinal abnormal | | | |
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Weight decreased | | | |
| subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Gastrointestinal stoma complication | | | |
| subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Procedural pain | | | |
| subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 2 / 153 (1.31%) 3 | 0 / 152 (0.00%) 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Arrhythmia supraventricular | | | |
| subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Cardiovascular insufficiency | | | |
| subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |

| | | | |
|--|---------------------|------------------------|----------------------|
| Palpitations subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Supraventricular tachycardia subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Nervous system disorders | | | |
| Hydrocephalus subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Parosmia subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 153 (0.65%) 1 | 1 / 152 (0.66%) 1 |
| Headache subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 11 / 153 (7.19%) 17 | 1 / 152 (0.66%) 1 |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 1 / 152 (0.66%) 1 |
| Ear and labyrinth disorders | | | |
| Tinnitus subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 4 | 4 / 153 (2.61%) 5 | 3 / 152 (1.97%) 3 |
| Constipation subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 2 / 152 (1.32%) 2 |

| | | | |
|--|----------------|-----------------|-----------------|
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 8 / 153 (5.23%) | 3 / 152 (1.97%) |
| occurrences (all) | 0 | 8 | 4 |
| Duodenitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 5 / 153 (3.27%) | 2 / 152 (1.32%) |
| occurrences (all) | 0 | 5 | 2 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 153 (0.65%) | 0 / 152 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Gastritis erosive | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 9 / 153 (5.88%) | 5 / 152 (3.29%) |
| occurrences (all) | 1 | 9 | 5 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 2 / 153 (1.31%) | 4 / 152 (2.63%) |
| occurrences (all) | 1 | 2 | 5 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis contact | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 153 (0.65%) | 0 / 152 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hyperhidrosis | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 153 (0.65%) | 2 / 152 (1.32%) |
| occurrences (all) | 0 | 1 | 2 |
| Rash | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 153 (0.65%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 153 (0.65%) | 0 / 152 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Renal and urinary disorders | | | |
| Nocturia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 153 (0.65%) | 1 / 152 (0.66%) |
| occurrences (all) | 1 | 1 | 1 |
| Back pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 2 / 152 (1.32%) |
| occurrences (all) | 0 | 0 | 2 |
| Neck pain | | | |

| | | | |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 153 (0.00%) 0 | 0 / 152 (0.00%) 0 |
| Infections and infestations | | | |
| Incision site infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Orchitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 153 (0.65%) | 0 / 152 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 153 (0.00%) | 0 / 152 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 153 (0.00%) | 1 / 152 (0.66%) |
| occurrences (all) | 1 | 0 | 1 |

| | | | |
|--|---------------------------------|--|--|
| Non-serious adverse events | cIAI:CAZ-AVI + metronidazole | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 12 (66.67%) | | |
| Vascular disorders | | | |
| Phlebitis | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |
| Catheter site haemorrhage | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperthermia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hydrothorax | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Tachypnoea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |

| | | | |
|---|----------------------|--|--|
| Depression subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Insomnia subjects affected / exposed occurrences (all) | 2 / 12 (16.67%) 2 | | |
| Investigations Electrocardiogram QT prolonged subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Endoscopy gastrointestinal abnormal subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Injury, poisoning and procedural complications Gastrointestinal stoma complication subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Procedural pain subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Arrhythmia supraventricular subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Cardiovascular insufficiency subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Palpitations subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |

| | | | |
|--|----------------------|--|--|
| Supraventricular tachycardia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Nervous system disorders | | | |
| Hydrocephalus subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Parosmia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Dizziness subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Headache subjects affected / exposed occurrences (all) | 2 / 12 (16.67%) 2 | | |
| Paraesthesia subjects affected / exposed occurrences (all) | 2 / 12 (16.67%) 2 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Ear and labyrinth disorders | | | |
| Tinnitus subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Constipation subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 2 / 12 (16.67%) 2 | | |

| | | | |
|--|-----------------|--|--|
| Duodenitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Enteritis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastritis erosive | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Nausea | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | | |
| occurrences (all) | 3 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis contact | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Skin ulcer | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Rash | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |
| Nocturia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Back pain | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | | |
| occurrences (all) | 2 | | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Bone pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | | |
| occurrences (all) | 1 | | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |

| | | | |
|--|---------------------|--|--|
| Incision site infection subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Oral herpes subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Orchitis subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Respiratory tract infection viral subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Metabolic acidosis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Type 2 diabetes mellitus subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |

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