



## Clinical trial results:

### A Phase 3, Randomized, Double-Blind, Double-Dummy, Multicenter, Prospective Study to Assess the Efficacy and Safety of Eravacycline Compared with Meropenem in Complicated Intra-abdominal Infections Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2016-002208-21    |
| Trial protocol           | HU CZ LV EE LT BG |
| Global end of trial date | 19 May 2017       |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 25 December 2021 |
| First version publication date | 25 December 2021 |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | TP-434-025 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02784704 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Tetraphase Pharmaceuticals, Inc.   |
| Sponsor organisation address | 201 Jones Road, Suite 400, Waltham, United States, 02451   |
| Public contact               | Stew Kroll, Tetraphase Pharmaceuticals, Inc., 1 858-207-4264, <a href="mailto:ljpcregulatory@ljpc.com">ljpcregulatory@ljpc.com</a> |
| Scientific contact           | Stew Kroll, Tetraphase Pharmaceuticals, Inc., 1 858-207-4264, <a href="mailto:ljpcregulatory@ljpc.com">ljpcregulatory@ljpc.com</a> |

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                       | 15 July 2017 |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 19 May 2017  |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 19 May 2017  |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that eravacycline is non-inferior to meropenem in clinical response at the test-of-cure (TOC) visit in the all-treated (MITT) and the clinically evaluable (CE) populations

Protection of trial subjects:

This study was conducted in compliance with ICH E6 GCP (consolidated guidelines and the ethical principles of the Declaration of Helsinki), and any additional national or IRB/IED- required procedures

Background therapy: -

Evidence for comparator:

The comparator, meropenem, was chosen because it is approved by the FDA and other regulatory authorities for the treatment of cIAI. It was given at the recommended dose of 1g q8 for a minimum of four-24h dose cycles

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 13 October 2016 |
| 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: 93           |
| Country: Number of subjects enrolled | Czech Republic: 29     |
| Country: Number of subjects enrolled | Estonia: 31            |
| Country: Number of subjects enrolled | Hungary: 30            |
| Country: Number of subjects enrolled | Latvia: 68             |
| Country: Number of subjects enrolled | Lithuania: 40          |
| Country: Number of subjects enrolled | Romania: 57            |
| Country: Number of subjects enrolled | Georgia: 24            |
| Country: Number of subjects enrolled | Russian Federation: 34 |
| Country: Number of subjects enrolled | Ukraine: 82            |
| Country: Number of subjects enrolled | United States: 12      |
| Worldwide total number of subjects   | 500                    |
| EEA total number of subjects         | 348                    |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| 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)                      | 355 |
| From 65 to 84 years                       | 140 |
| 85 years and over                         | 5   |

## Subject disposition

### Recruitment

Recruitment details:

Participants at least 18 years of age with a diagnosis of cIAI were recruited into the study

### Pre-assignment

Screening details:

Screening and baseline were performed after informed consent was obtained and within 48 hours prior to initial dose. Participants were eligible to participate if they met all of the inclusion criteria and none of the exclusion criteria at the Screening visit.

### Period 1

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

Blinding implementation details:

Subjects were assigned to study drug regimens using computerized randomization. Except for the responsible study site pharmacist or designee, and separate unblinded clinical research associates (CRAs) to monitor drug supply and adherence to study drug blinding and randomization procedures, all study staff and participants were blinded to the IV dosing regimens of subjects. The study blind codes were broken after the statistical analysis plan was finalized and the database was locked.

### Arms

|                              |                     |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes                 |
| <b>Arm title</b>             | Eravacycline (MITT) |

Arm description:

Eravacycline IV (MITT) modified intent-to treat population defined as subjects that were randomized and received at least 1 dose of study drug.

|  |                                 |
|--|---------------------------------|
| Arm type                               | Experimental                    |
| Investigational medicinal product name | Eravacycline IV                 |
| Investigational medicinal product code |                                 |
| Other name                             | TP-434                          |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Intravenous use                 |

Dosage and administration details:

Eravacycline was administered intravenously (IV) at a dose of 1.0 milligrams per kilogram (mg/kg) of body weight every 12 hours (q12h) for a minimum of 4 days and a maximum of 14 days.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | Meropenem (MITT) |
|------------------|------------------|

Arm description:

Meropenem IV (MITT) modified intent-to treat population defined as subjects that were randomized and received at least 1 dose of study drug. Please note that one subject randomized to Meropenem did not receive study drug.

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

Dosage and administration details:

Meropenem was administered intravenously (IV) at a dose of 1.0 grams (g) every 8 hours (q8h) for minimum of 4 days and a maximum of 14 days.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Eravacycline (MITT) | Meropenem (MITT) |
|---|---------------------|------------------|
| Started   | 250                 | 249              |
| Completed   | 237                 | 241              |
| Not completed                                       | 13                  | 8                |
| Consent withdrawn by subject                        | 1                   | 2                |
| Adverse event, non-fatal                            | 4                   | 2                |
| noncompliance                                       | 2                   | -                |
| Lost to follow-up                                   | 6                   | 4                |

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Notes:

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

Justification: The number reported in the baseline period differs by 1 subject versus the worldwide number enrolled due to 1 subject being enrolled in the meropenem group who did not receive study drug.

## Baseline characteristics

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Eravacycline (MITT) |
|-----------------------|---------------------|

Reporting group description:

Eravacycline IV (MITT) modified intent-to treat population defined as subjects that were randomized and received at least 1 dose of study drug.

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Meropenem (MITT) |
|-----------------------|------------------|

Reporting group description:

Meropenem IV (MITT) modified intent-to treat population defined as subjects that were randomized and received at least 1 dose of study drug. Please note that one subject randomized to Meropenem did not receive study drug.

| Reporting group values | Eravacycline (MITT) | Meropenem (MITT) | Total |
|------------------------|---------------------|------------------|-------|
| Number of subjects     | 250                 | 249              | 499   |
| Age categorical        |                     |                  |       |
| Units: Subjects        |                     |                  |       |
| Adults (18-64 years)   | 180                 | 174              | 354   |
| From 65-84 years       | 68                  | 72               | 140   |
| 85 years and over      | 2                   | 3                | 5     |
| Age continuous         |                     |                  |       |
| Units: years           |                     |                  |       |
| arithmetic mean        | 52.1                | 52.8             |       |
| standard deviation     | ± 17.69             | ± 18.24          | -     |
| Gender categorical     |                     |                  |       |
| Units: Subjects        |                     |                  |       |
| Female                 | 111                 | 120              | 231   |
| Male                   | 139                 | 129              | 268   |

## End points

### End points reporting groups

|   |                     |
|---|---------------------|
| Reporting group title   | Eravacycline (MITT) |
| Reporting group description:<br>Eravacycline IV (MITT) modified intent-to treat population defined as subjects that were randomized and received at least 1 dose of study drug.   |                     |
| Reporting group title   | Meropenem (MITT)    |
| Reporting group description:<br>Meropenem IV (MITT) modified intent-to treat population defined as subjects that were randomized and received at least 1 dose of study drug. Please note that one subject randomized to Meropenem did not receive study drug. |                     |

### Primary: Clinical Response at the test of cure (TOC) visit in the MITT population

|  |  |
|--|--|
| End point title  | Clinical Response at the test of cure (TOC) visit in the MITT population |
| End point description:<br>This was a co-primary outcome measure for the European Medicines Agency (EMA). Clinical response was classified as cure (complete resolution or significant improvement of signs and symptoms of the index infection such that no additional antibacterial therapy, surgical, or radiological intervention was required), failure (death related to complicated intra-abdominal infection (cIAI), persistence of clinical symptoms of cIAI, unplanned surgical or percutaneous drainage procedures for complication or recurrence of cIAI, post-surgical wound infections requiring systemic antibiotics, or initiation of rescue antibacterial drug therapy for treatment of cIAI), or indeterminate (outcome was neither cure nor failure, or assessment was not available). The number of participants with a clinical response classification of cure, failure, or indeterminate is presented. |  |
| End point type   | Primary  |
| End point timeframe:<br>TOC visit: 25-31 days after the first study dose   |  |

| End point values            | Eravacycline (MITT) | Meropenem (MITT) |  |  |
|-----------------------------|---------------------|------------------|--|--|
| Subject group type          | Reporting group     | Reporting group  |  |  |
| Number of subjects analysed | 250                 | 249              |  |  |
| Units: subjects             |                     |                  |  |  |
| Clinical Cure               | 231                 | 228              |  |  |
| Clinical Failure            | 7                   | 9                |  |  |
| Indeterminate/Missing       | 12                  | 12               |  |  |

### Statistical analyses

|  |  |
|--|--|
| Statistical analysis title   | MITT                                   |
| Statistical analysis description:<br>A 2-sided 95% confidence interval (CI) for the observed difference in primary outcome rates (eravacycline treatment group minus meropenem treatment group) was calculated. If the lower limit of the 95% CI for the difference in clinical cure rates exceeded -12.5%, then the null hypothesis was rejected, and the non-inferiority of eravacycline to meropenem was declared |  |
| Comparison groups  | Eravacycline (MITT) v Meropenem (MITT) |

|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 499                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[1]</sup> |
| P-value                                 | < 0.05                         |
| Method                                  | t-test, 2-sided                |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | 0.8                            |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -4.1                           |
| upper limit                             | 5.8                            |
| Variability estimate                    | Standard deviation             |

Notes:

[1] - pre-specified

### Primary: Clinical Response at the TOC visit in the CE population

|                        |  |
|------------------------|--|
| End point title        | Clinical Response at the TOC visit in the CE population  |
| End point description: | This was a co-primary outcome measure for the European Medicines Agency (EMA). Clinical response was classified as cure (complete resolution or significant improvement of signs and symptoms of the index infection such that no additional antibacterial therapy, surgical, or radiological intervention was required) or failure (death related to complicated intra-abdominal infection (cIAI), persistence of clinical symptoms of cIAI, unplanned surgical or percutaneous drainage procedures for complication or recurrence of cIAI, post-surgical wound infections requiring systemic antibiotics, or initiation of rescue antibacterial drug therapy for treatment of cIAI). The number of participants with a clinical response classification of cure or failure is presented. |
| End point type         | Primary  |
| End point timeframe:   |  |
| TOC visit:             | 25-31 days after the first dose of study drug  |

| End point values            | Eravacycline (MITT) | Meropenem (MITT) |  |  |
|-----------------------------|---------------------|------------------|--|--|
| Subject group type          | Reporting group     | Reporting group  |  |  |
| Number of subjects analysed | 225                 | 231              |  |  |
| Units: subjects             |                     |                  |  |  |
| Clinical Cure               | 218                 | 222              |  |  |
| Clinical Failure            | 7                   | 9                |  |  |

### Statistical analyses

|                                   |  |
|-----------------------------------|--|
| Statistical analysis title        | CE   |
| Statistical analysis description: | A 2-sided 95% confidence interval (CI) for the observed difference in primary outcome rates (eravacycline treatment group minus meropenem treatment group) was calculated. If the lower limit of the 95% CI for the difference in clinical cure rates exceeded -12.5%, then the null hypothesis was rejected, and the non-inferiority of eravacycline to meropenem was declared. |
| Comparison groups                 | Eravacycline (MITT) v Meropenem (MITT)   |



|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 456                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[2]</sup> |
| P-value                                 | < 0.05                         |
| Method                                  | t-test, 2-sided                |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | 0.8                            |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -2.9                           |
| upper limit                             | 4.5                            |
| Variability estimate                    | Standard deviation             |

Notes:

[2] - treatment difference

## Secondary: Clinical Response at the test of cure (TOC) visit in the micro-ITT population

|                 |   |
|-----------------|---|
| End point title | Clinical Response at the test of cure (TOC) visit in the micro-ITT population |
|-----------------|---|

End point description:

This was the primary outcome measure for the United States Food and Drug Administration (FDA). Clinical response was classified as cure (complete resolution or significant improvement of signs and symptoms of the index infection such that no additional antibacterial therapy, surgical, or radiological intervention was required), failure (death related to complicated intra-abdominal infection (cIAI), persistence of clinical symptoms of cIAI, unplanned surgical or percutaneous drainage procedures for complication or recurrence of cIAI, post-surgical wound infections requiring systemic antibiotics, or initiation of rescue antibacterial drug therapy for treatment of cIAI), or indeterminate (outcome was neither cure nor failure, or assessment was not available). The number of participants with a clinical response classification of cure, failure, or indeterminate is presented.

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

End point timeframe:

TOC visit: 25-31 days after the first dose of study drug

| End point values            | Eravacycline (MITT) | Meropenem (MITT) |  |  |
|-----------------------------|---------------------|------------------|--|--|
| Subject group type          | Reporting group     | Reporting group  |  |  |
| Number of subjects analysed | 195                 | 205              |  |  |
| Units: subjects             |                     |                  |  |  |
| Clinical Cure               | 177                 | 187              |  |  |
| Clinical Failure            | 7                   | 7                |  |  |
| Indeterminate/Missing       | 11                  | 11               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from the first dose of study drug through 30 days after the last dose of study drug or the follow-up visit, which occurred 38 to 50 days after the first dose of study drug (whichever was later).

Adverse event reporting additional description:

Eravacycline was administered intravenously (IV) at a dose of 1.0 milligrams per kilogram (mg/kg) of body weight every 12 hours (q12h) for a minimum of 4 days and maximum of 14 days. Meropenem was administered intravenously (IV) at a dose of 1.0 grams (g) every 8 hours (q8h) for a minimum of 4 days and a maximum of 14 days

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 20.0   |

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | Eravacycline |
|-----------------------|--------------|

Reporting group description:

Eravacycline was administered intravenously (IV) at a dose of 1.0 milligrams per kilogram (mg/kg) of body weight every 12 hours (q12h) for a minimum of 4 days and maximum of 14 days.

|                       |           |
|-----------------------|-----------|
| Reporting group title | Meropenem |
|-----------------------|-----------|

Reporting group description:

Meropenem was administered intravenously (IV) at a dose of 1.0 grams (g) every 8 hours (q8h) for a minimum of 4 days and a maximum of 14 days

| Serious adverse events  | Eravacycline     | Meropenem        |  |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events                   |                  |                  |  |
| subjects affected / exposed   | 15 / 250 (6.00%) | 16 / 249 (6.43%) |  |
| number of deaths (all causes)                                       | 4                | 1                |  |
| number of deaths resulting from adverse events                      | 0                | 0                |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                  |  |
| Adenocarcinoma of colon   |                  |                  |  |
| subjects affected / exposed   | 1 / 250 (0.40%)  | 0 / 249 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            |  |
| Neuroendocrine tumour   |                  |                  |  |
| subjects affected / exposed   | 1 / 250 (0.40%)  | 0 / 249 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            |  |
| Vascular disorders  |                  |                  |  |
| Hypotension   |                  |                  |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Pyrexia  |                 |                 |  |
| subjects affected / exposed                          | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Reproductive system and breast disorders             |                 |                 |  |
| Pelvic fluid collection                              |                 |                 |  |
| subjects affected / exposed                          | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders      |                 |                 |  |
| Chronic obstructive pulmonary disorders              |                 |                 |  |
| subjects affected / exposed                          | 1 / 250 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Hydrothorax  |                 |                 |  |
| subjects affected / exposed                          | 1 / 250 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Pulmonary embolism                                   |                 |                 |  |
| subjects affected / exposed                          | 1 / 250 (0.40%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Respiratory failure                                  |                 |                 |  |
| subjects affected / exposed                          | 1 / 250 (0.40%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Injury, poisoning and procedural complications       |                 |                 |  |
| Abdominal wound dehiscence                           |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 250 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Suture related complication                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Wound decomposition                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Wound dehiscence                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 250 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |
| Atrial fibrillation                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac arrest                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Myocardial infarction                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Blood and lymphatic system disorders            |                 |                 |  |
| Splenic haematoma                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Duodenal ulcer                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Duodenal ulcer haemorrhage                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal inflammation                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 250 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ileus   |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Intestinal fistula                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Large intestine perforation                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 250 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Melaena   |                 |                 |  |
| subjects affected / exposed                     | 1 / 250 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pancreatitis acute                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 250 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Cholecystitis                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Renal failure                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ureteric rupture                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 250 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Abdominal abscess                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Peritonitis                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |
| subjects affected / exposed                     | 2 / 250 (0.80%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sepsis  |                 |                 |  |
| subjects affected / exposed                     | 0 / 250 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Dehydration                                     |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 250 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | Eravacycline      | Meropenem       |  |
|---|-------------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                   |                 |  |
| subjects affected / exposed                           | 29 / 250 (11.60%) | 8 / 249 (3.21%) |  |
| General disorders and administration site conditions  |                   |                 |  |
| Infusion site phlebitis                               |                   |                 |  |
| subjects affected / exposed                           | 8 / 250 (3.20%)   | 1 / 249 (0.40%) |  |
| occurrences (all)                                     | 10                | 1               |  |
| Gastrointestinal disorders                            |                   |                 |  |
| Nausea  |                   |                 |  |
| subjects affected / exposed                           | 12 / 250 (4.80%)  | 2 / 249 (0.80%) |  |
| occurrences (all)                                     | 13                | 3               |  |
| Vomiting  |                   |                 |  |
| subjects affected / exposed                           | 9 / 250 (3.60%)   | 5 / 249 (2.01%) |  |
| occurrences (all)                                     | 10                | 6               |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment   |
|---------------|---|
| 20 March 2017 | Amendment number 1 was implemented to documented the following: the increase in study sample size based on the pre-specified, blinded assessment of the proportion of participants who qualified for the micro-ITT population; global administrative changes and clarifications |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

|               |
|---------------|
| None reported |
|---------------|

Notes: