



## Clinical trial results:

### A Phase III, Randomized, Multicenter, Parallel-Group, Double-Blind, Double-Dummy Study in Adolescent and Adult Female Participants Comparing the Efficacy and Safety of Gepotidacin to Nitrofurantoin in the Treatment of Uncomplicated Urinary Tract Infection (Acute Cystitis) Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2018-001801-98          |
| Trial protocol           | GB DE BG GR HU CZ SK RO |
| Global end of trial date | 30 November 2022        |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1           |
| This version publication date  | 14 June 2023 |
| First version publication date | 14 June 2023 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 204989 |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04020341 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                  |
|------------------------------|----------------------------------------------------------------------------------|
| Sponsor organisation name    | GlaxoSmithKline                                                                  |
| Sponsor organisation address | 980 GreatWest Road, Brentford, Middlesex, United Kingdom,                        |
| Public contact               | GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com |

Notes:

#### Paediatric regulatory details

|                                                                      |                     |
|----------------------------------------------------------------------|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-002443-PIP01-18 |
| 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                       | 21 February 2023 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 30 November 2022 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

To assess the combined clinical and microbiological efficacy of gepotidacin compared to nitrofurantoin, at the Test-of-Cure (TOC) Visit, in female participants with acute cystitis in the Microbiological Intent-to-Treat Nitrofurantoin-Susceptible (micro-ITT NTF-S) Population

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment                          | 17 October 2019 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | Yes             |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Bulgaria: 335      |
| Country: Number of subjects enrolled | Czechia: 42        |
| Country: Number of subjects enrolled | Germany: 13        |
| Country: Number of subjects enrolled | Greece: 19         |
| Country: Number of subjects enrolled | Hungary: 34        |
| Country: Number of subjects enrolled | India: 35          |
| Country: Number of subjects enrolled | Mexico: 188        |
| Country: Number of subjects enrolled | Romania: 116       |
| Country: Number of subjects enrolled | Slovakia: 83       |
| Country: Number of subjects enrolled | Spain: 23          |
| Country: Number of subjects enrolled | United Kingdom: 8  |
| Country: Number of subjects enrolled | United States: 635 |
| Worldwide total number of subjects   | 1531               |
| EEA total number of subjects         | 665                |

Notes:

### Subjects enrolled per age group

|                                        |   |
|----------------------------------------|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|                                          |      |
|------------------------------------------|------|
| wk                                       |      |
| Newborns (0-27 days)                     | 0    |
| Infants and toddlers (28 days-23 months) | 0    |
| Children (2-11 years)                    | 0    |
| Adolescents (12-17 years)                | 15   |
| Adults (18-64 years)                     | 1124 |
| From 65 to 84 years                      | 378  |
| 85 years and over                        | 14   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

1680 participants were screened out of which 1531 participants were randomly assigned to the study treatment were included in Intent-to-Treat (ITT) population.

### 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, Subject          |

### Arms

|                              |             |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes         |
| <b>Arm title</b>             | Gepotidacin |

Arm description:

Participants with uncomplicated urinary tract infection (uUTI) (acute cystitis) randomized to receive gepotidacin 1500 milligram (mg) (2\*750 mg, tablets), twice daily (BID), orally on Day 1 to Day 5. The total daily dose of gepotidacin received was 3000 mg. Participants also received 1 capsule of placebo matched with nitrofurantoin BID, orally on Day 1 to Day 5. All doses were administered after food consumption and with water.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Gepotidacin  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Participants with uncomplicated urinary tract infection (acute cystitis) were administered with oral doses of 1500 milligrams (mg) (2\*750 mg) gepotidacin tablet plus nitrofurantoin capsules matching placebo twice daily (BID) for 5 days.

|                  |                |
|------------------|----------------|
| <b>Arm title</b> | Nitrofurantoin |
|------------------|----------------|

Arm description:

Participants with uncomplicated urinary tract infection (acute cystitis) randomized to receive nitrofurantoin 100 mg capsule, BID, orally on Day 1 to Day 5. The total daily dose of nitrofurantoin received was 200 mg. Participants also received 2 tablets of placebo matched with gepotidacin BID, orally on Day 1 to Day 5. All doses were administered after food consumption and with water.

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Nitrofurantoin    |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Tablet            |
| Routes of administration               | Oral use          |

Dosage and administration details:

Participants with uncomplicated urinary tract infection (acute cystitis) were administered with oral doses of 100 mg (25 mg nitrofurantoin macrocrystals and 75 mg nitrofurantoin) nitrofurantoin capsules plus gepotidacin tablet matching placebo BID for 5 days.

| Number of subjects in period 1             | Gepotidacin        | Nitrofurantoin     |
|--------------------------------------------|--------------------|--------------------|
| Started                                    | 767                | 764                |
| Safety Population                          | 766                | 760                |
| Microbiological ITT Population             | 401 <sup>[1]</sup> | 365 <sup>[2]</sup> |
| Micro-ITT NTF-S Population                 | 336 <sup>[3]</sup> | 298 <sup>[4]</sup> |
| Micro-ITT NTF-S (IA Set) Population        | 320 <sup>[5]</sup> | 287 <sup>[6]</sup> |
| Completed                                  | 734                | 736                |
| Not completed                              | 33                 | 28                 |
| Consent withdrawn by subject               | 16                 | 16                 |
| Physician decision                         | -                  | 2                  |
| Adverse event, non-fatal                   | 8                  | 6                  |
| Protocol Deviation                         | -                  | 2                  |
| Participant not able to swallow the tablet | 1                  | -                  |
| Lost to follow-up                          | 8                  | 2                  |

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Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: intermediate milestone is a subset of started population. Hence number of subjects at this milestone are less than started.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: intermediate milestone is a subset of started population. Hence number of subjects at this milestone are less than started.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: intermediate milestone is a subset of started population. Hence number of subjects at this milestone are less than started.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: intermediate milestone is a subset of started population. Hence number of subjects at this milestone are less than started.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: intermediate milestone is a subset of started population. Hence number of subjects at this milestone are less than started.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: intermediate milestone is a subset of started population. Hence number of subjects at this milestone are less than started.

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                           | Gepotidacin    |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                    |                |
| Participants with uncomplicated urinary tract infection (uUTI) (acute cystitis) randomized to receive gepotidacin 1500 milligram (mg) (2*750 mg, tablets), twice daily (BID), orally on Day 1 to Day 5. The total daily dose of gepotidacin received was 3000 mg. Participants also received 1 capsule of placebo matched with nitrofurantoin BID, orally on Day 1 to Day 5. All doses were administered after food consumption and with water. |                |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                           | Nitrofurantoin |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                    |                |
| Participants with uncomplicated urinary tract infection (acute cystitis) randomized to receive nitrofurantoin 100 mg capsule, BID, orally on Day 1 to Day 5. The total daily dose of nitrofurantoin received was 200 mg. Participants also received 2 tablets of placebo matched with gepotidacin BID, orally on Day 1 to Day 5. All doses were administered after food consumption and with water.                                             |                |

| Reporting group values                                                                                                                                                                                                                                              | Gepotidacin | Nitrofurantoin | Total |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|----------------|-------|
| Number of subjects                                                                                                                                                                                                                                                  | 767         | 764            | 1531  |
| Age Categorical                                                                                                                                                                                                                                                     |             |                |       |
| Units: Participants                                                                                                                                                                                                                                                 |             |                |       |
| Less than (<) 18 years                                                                                                                                                                                                                                              | 6           | 9              | 15    |
| More than or equal to (>=) 18 years to 50 years                                                                                                                                                                                                                     | 372         | 369            | 741   |
| More than (>) 50 years                                                                                                                                                                                                                                              | 389         | 386            | 775   |
| Age Continuous                                                                                                                                                                                                                                                      |             |                |       |
| Units: Years                                                                                                                                                                                                                                                        |             |                |       |
| arithmetic mean                                                                                                                                                                                                                                                     | 49.6        | 50.4           |       |
| standard deviation                                                                                                                                                                                                                                                  | ± 17.82     | ± 18.17        | -     |
| Sex/Gender, Customized                                                                                                                                                                                                                                              |             |                |       |
| Units: Participants                                                                                                                                                                                                                                                 |             |                |       |
| Female                                                                                                                                                                                                                                                              | 767         | 764            | 1531  |
| Ethnicity (NIH/OMB)                                                                                                                                                                                                                                                 |             |                |       |
| Units: Subjects                                                                                                                                                                                                                                                     |             |                |       |
| Hispanic or Latino                                                                                                                                                                                                                                                  | 278         | 270            | 548   |
| Not Hispanic or Latino                                                                                                                                                                                                                                              | 489         | 494            | 983   |
| Unknown or Not Reported                                                                                                                                                                                                                                             | 0           | 0              | 0     |
| Race (NIH/OMB)                                                                                                                                                                                                                                                      |             |                |       |
| Units: Subjects                                                                                                                                                                                                                                                     |             |                |       |
| American Indian or Alaska Native                                                                                                                                                                                                                                    | 62          | 75             | 137   |
| Asian                                                                                                                                                                                                                                                               | 23          | 21             | 44    |
| Native Hawaiian or Other Pacific Islander                                                                                                                                                                                                                           | 3           | 1              | 4     |
| Black or African American                                                                                                                                                                                                                                           | 40          | 40             | 80    |
| White                                                                                                                                                                                                                                                               | 627         | 621            | 1248  |
| More than one race                                                                                                                                                                                                                                                  | 12          | 6              | 18    |
| Unknown or Not Reported                                                                                                                                                                                                                                             | 0           | 0              | 0     |
| Baseline Acute Cystitis Recurrence                                                                                                                                                                                                                                  |             |                |       |
| Recurrent infection was defined as a confirmed infection with at least 1 episode within the past 3 months, at least 2 episodes within the past 6 months, or at least 3 episodes within the past 12 months before study entry. Parameter type: Count of Participants |             |                |       |
| Units: Subjects                                                                                                                                                                                                                                                     |             |                |       |

|                                                 |     |     |     |
|-------------------------------------------------|-----|-----|-----|
| Recurrent Infection                             | 312 | 309 | 621 |
| Non-Recurrent Infection                         | 455 | 455 | 910 |
| Age, Customized                                 |     |     |     |
| Units: Subjects                                 |     |     |     |
| Less than (<) 18 years                          | 6   | 9   | 15  |
| More than or equal to (>=) 18 years to 50 years | 372 | 369 | 741 |
| More than (>) 50 years                          | 389 | 386 | 775 |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Gepotidacin    |
| Reporting group description:<br>Participants with uncomplicated urinary tract infection (uUTI) (acute cystitis) randomized to receive gepotidacin 1500 milligram (mg) (2*750 mg, tablets), twice daily (BID), orally on Day 1 to Day 5. The total daily dose of gepotidacin received was 3000 mg. Participants also received 1 capsule of placebo matched with nitrofurantoin BID, orally on Day 1 to Day 5. All doses were administered after food consumption and with water. |                |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Nitrofurantoin |
| Reporting group description:<br>Participants with uncomplicated urinary tract infection (acute cystitis) randomized to receive nitrofurantoin 100 mg capsule, BID, orally on Day 1 to Day 5. The total daily dose of nitrofurantoin received was 200 mg. Participants also received 2 tablets of placebo matched with gepotidacin BID, orally on Day 1 to Day 5. All doses were administered after food consumption and with water.                                             |                |

### Primary: Number of participants with therapeutic response (TR) (combined per participant clinical and microbiological response) at the Test-of-Cure (TOC) visit - Micro-ITT NTF-S ([Interim Analysis] IA Set)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                      |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Number of participants with therapeutic response (TR) (combined per participant clinical and microbiological response) at the Test-of-Cure (TOC) visit - Micro-ITT NTF-S ([Interim Analysis] IA Set) |
| End point description:<br>Therapeutic response (success/failure) is a measure of the overall efficacy response. A therapeutic success referred to participants who had been deemed both a "microbiological success"(reduction of all qualifying bacterial uropathogens [greater than or equal to $\{>= \}10^5$ colony-forming units per milliliter {CFU/mL}] recovered at Baseline to less than ( $<$ ) $10^3$ CFU/mL as observed on quantitative urine culture without the participant receiving other systemic antimicrobials before the TOC Visit) and a "clinical success" (resolution of signs and symptoms of acute cystitis present at Baseline [and no new signs and symptoms] without the participant receiving other systemic antimicrobials before the TOC Visit). Lack of clinical or microbiological success (including missing outcome assessments) was considered as therapeutic failure. |                                                                                                                                                                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Primary                                                                                                                                                                                              |
| End point timeframe:<br>TOC visit (Days 9 to 16)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                      |

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 320             | 287             |  |  |
| Units: Participants         |                 |                 |  |  |
| Therapeutic Success         | 162             | 135             |  |  |
| Therapeutic Failure         | 158             | 152             |  |  |

### Statistical analyses

|                                         |                                         |
|-----------------------------------------|-----------------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 2                  |
| Comparison groups                       | Gepotidacin v Nitrofurantoin            |
| Number of subjects included in analysis | 607                                     |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           |                                         |
| P-value                                 | = 0.1445                                |
| Method                                  | 1-sided p-value for Test of Superiority |
| Parameter estimate                      | Adjusted difference of Percent          |
| Point estimate                          | 4.3                                     |
| Confidence interval                     |                                         |
| level                                   | 95 %                                    |
| sides                                   | 2-sided                                 |
| lower limit                             | -3.6                                    |
| upper limit                             | 12.1                                    |

|                                         |                                |
|-----------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 1         |
| Comparison groups                       | Gepotidacin v Nitrofurantoin   |
| Number of subjects included in analysis | 607                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           |                                |
| Parameter estimate                      | Adjusted Difference in Percent |
| Point estimate                          | 4.3                            |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -3.6                           |
| upper limit                             | 12.1                           |

**Primary: Number of participants with therapeutic response (TR) (combined per participant clinical and microbiological response) at the Test-of-Cure (TOC) visit – Micro-ITT NTF-S population**

|                 |                                                                                                                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of participants with therapeutic response (TR) (combined per participant clinical and microbiological response) at the Test-of-Cure (TOC) visit – Micro-ITT NTF-S population <sup>[1]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

TR at TOC (success/failure) is a measure of the overall efficacy response. A therapeutic success at TOC referred to participant who have been deemed both a microbiological success (reduction of all qualifying bacterial uropathogens recovered at Baseline [BL] to  $<10^3$  colony forming units per milliliter [CFU/mL] without receiving other systemic antimicrobials [AB] before the TOC visit) and a clinical success (resolution of symptoms of acute cystitis present at BL and no new symptoms without receiving other AB before the TOC visit [or AB for uUTI on day of TOC visit]). Lack of clinical or microbiological success (including missing outcome assessments) was considered as therapeutic failure.

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

End point timeframe:

TOC visit (Days 9 to 16)

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: This endpoint was descriptive; hence no statistical analysis to report.

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 336             | 298             |  |  |
| Units: Participants         |                 |                 |  |  |
| Therapeutic Success         | 174             | 140             |  |  |
| Therapeutic Failure         | 162             | 158             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with clinical response at the TOC visit - Micro-ITT NTF-S population

|                 |                                                                                             |
|-----------------|---------------------------------------------------------------------------------------------|
| End point title | Number of participants with clinical response at the TOC visit - Micro-ITT NTF-S population |
|-----------------|---------------------------------------------------------------------------------------------|

End point description:

Clinical response at TOC was categorized as clinical success and clinical failure. Clinical success at TOC was defined as resolution of symptoms of acute cystitis present at BL (and no new symptoms), without receiving any other AB before the TOC visit. Lack of resolution, including receipt of an AB for uUTI at the TOC visit, or a missing outcome assessment was defined as Clinical Failure at TOC.

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

End point timeframe:

TOC visit (Days 9 to 16)

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 336             | 298             |  |  |
| Units: Participants         |                 |                 |  |  |
| Clinical success            | 224             | 196             |  |  |
| Clinical failure            | 112             | 102             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with microbiological response at the TOC visit – Micro-ITT NTF-S population

|                 |                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Number of participants with microbiological response at the TOC visit – Micro-ITT NTF-S population |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

Participant-level microbiological response at TOC was categorized as microbiological success and microbiological failure. Microbiological success at TOC was defined as all baseline qualifying uropathogens (QUP)s had a microbiological outcome of eradication at TOC visit. Microbiological failure was defined as lack of microbiological success, including those participants with UTD outcomes.

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

End point timeframe:  
TOC visit (Days 9 to 16)

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 336             | 298             |  |  |
| Units: Participants         |                 |                 |  |  |
| Microbiological success     | 244             | 199             |  |  |
| Microbiological failure     | 92              | 99              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with clinical outcome at the TOC visit - Micro-ITT NTF-S population

|                 |                                                                                            |
|-----------------|--------------------------------------------------------------------------------------------|
| End point title | Number of participants with clinical outcome at the TOC visit - Micro-ITT NTF-S population |
|-----------------|--------------------------------------------------------------------------------------------|

End point description:

Clinical outcomes at TOC were categorized as clinical resolution, clinical improvement, clinical worsening and unable to determine. Clinical resolution at TOC was defined as resolution of signs and symptoms of acute cystitis present at baseline (BL) (and no symptoms) without receiving any other AB before the TOC visit. Clinical improvement at TOC was defined as improvement (but not complete resolution) in total symptom score (CSS) from BL, without receiving any other AB before the TOC visit. Clinical worsening at TOC was defined as worsening or no change in CSS from BL or received other AB for the current infection (uUTI) before or on the date of the TOC visit. Unable to determine outcome criteria were: BL score is missing (and thus improvement/worsening cannot be determined), TOC assessment is missing, or receipt of other AB not for the current infection before the TOC visit (unless clinical worsening outcome criteria were met).

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

End point timeframe:

TOC visit (Days 9 to 16)

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 336             | 298             |  |  |
| Units: Participants         |                 |                 |  |  |
| Clinical resolution         | 224             | 196             |  |  |
| Clinical improvment         | 82              | 75              |  |  |
| Clinical worsening          | 9               | 16              |  |  |
| Unable to determine         | 21              | 11              |  |  |

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Number of participants with microbiological outcome (MO) at the TOC visit – Micro-ITT NTF-S population**

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|                 |                                                                                                        |
|-----------------|--------------------------------------------------------------------------------------------------------|
| End point title | Number of participants with microbiological outcome (MO) at the TOC visit – Micro-ITT NTF-S population |
|-----------------|--------------------------------------------------------------------------------------------------------|

End point description:

Participant-level MOs at TOC were categorized as microbiological eradication (ME), microbiological persistence (MP), microbiological recurrence (MR) and unable to determine (UTD). ME at TOC was defined as all baseline qualifying uropathogens (QUP) have an outcome of eradication at TOC (i.e.,  $<10^3$  CFU/mL without the participant receiving other systemic antimicrobials before the TOC Visit). MP at TOC was defined as at least 1 QUP has an outcome of persistence ( $\geq 10^3$  CFU/mL) at TOC. MR at TOC was defined as at least 1 QUP had an outcome of recurrence and none have an outcome of persistence at TOC. UTD at TOC was defined as all QUP outcomes are UTD at TOC.

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

End point timeframe:

TOC Visit (Days 9 to 16)

---

| End point values                 | Gepotidacin     | Nitrofurantoin  |  |  |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type               | Reporting group | Reporting group |  |  |
| Number of subjects analysed      | 336             | 298             |  |  |
| Units: Participants              |                 |                 |  |  |
| Microbiological Eradication (ME) | 244             | 199             |  |  |
| Microbiological Persistence (MP) | 15              | 21              |  |  |
| Microbiological Recurrence (MR)  | 36              | 52              |  |  |
| Unable to determine (UTD)        | 41              | 26              |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Number of participants with therapeutic response (TR) (combined per participant clinical and microbiological response) at the follow up visit- Micro-ITT NTF-S population**

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|                 |                                                                                                                                                                           |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of participants with therapeutic response (TR) (combined per participant clinical and microbiological response) at the follow up visit- Micro-ITT NTF-S population |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

TR at FU was categorized as therapeutic success and therapeutic failure. A therapeutic success at FU referred to participants who have been deemed both a microbiological success (reduction of all QUPs recovered at BL to  $<10^3$  CFU/mL, following microbiological eradication at the TOC visit, without receiving other AB before the FU visit) and a clinical success (resolution of signs and symptoms of acute cystitis demonstrated at the TOC visit persist at the FU visit and no new signs and symptoms, without receiving other AB before the FU visit [or AB for uUTI on day of FU visit]). Lack of clinical or microbiological success (including missing outcome assessments) was considered as therapeutic failure.

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

End point timeframe:

FU visit (Days 21 to 31)

---

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 336             | 298             |  |  |
| Units: Participants         |                 |                 |  |  |
| Therapeutic Success         | 117             | 94              |  |  |
| Therapeutic Failure         | 219             | 204             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with clinical outcome at the follow up (FU) visit - Micro-ITT NTF-S population

|                 |                                                                                                       |
|-----------------|-------------------------------------------------------------------------------------------------------|
| End point title | Number of participants with clinical outcome at the follow up (FU) visit - Micro-ITT NTF-S population |
|-----------------|-------------------------------------------------------------------------------------------------------|

End point description:

Clinical outcomes at FU were categorized as SCR, DCR, CI, CW, CR and (UTD. SCR at FU was resolution of symptoms of acute cystitis demonstrated at the TOC persist at the FU (and no symptoms), without receiving other AB before the FU. DCR at FU was resolution of symptoms of acute cystitis present at BL after clinical failure at TOC without receiving AB before FU. CI at FU was improvement in CSS from BL, but not complete resolution without receiving AB before FU. CW at FU was worsening or no change in CSS at FU compared to BL after clinical failure at TOC or receiving other AB for the current infection (uUTI) before or on the date of the FU. CR at FU was symptoms of acute cystitis reoccur at FU after clinical success at TOC. Unable to determine outcome criteria at FU were BL score missing, FU assessment missing or received other AB not for the current infection (uUTI) prior to the assessment (unless CS or CR outcome criteria were met).

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

End point timeframe:

FU visit (Days 21 to 31)

| End point values                    | Gepotidacin     | Nitrofurantoin  |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 336             | 298             |  |  |
| Units: Participants                 |                 |                 |  |  |
| Sustained clinical resolution (SCR) | 184             | 162             |  |  |
| Delayed clinical resolution (DCR)   | 61              | 44              |  |  |
| Clinical improvement (CI)           | 28              | 27              |  |  |
| Clinical worsening (CW)             | 12              | 23              |  |  |
| Clinical recurrence (CR)            | 11              | 11              |  |  |
| Unable to determine (UTD)           | 40              | 31              |  |  |

## Statistical analyses

**Secondary: Number of participants with microbiological outcome (MO) at the follow up (FU) visit – Micro-ITT NTF-S population**

|                 |                                                                                                                   |
|-----------------|-------------------------------------------------------------------------------------------------------------------|
| End point title | Number of participants with microbiological outcome (MO) at the follow up (FU) visit – Micro-ITT NTF-S population |
|-----------------|-------------------------------------------------------------------------------------------------------------------|

## End point description:

Participant-level MOs at FU were categorized as sustained microbiological eradication (SME), microbiological recurrence (MR), microbiological persistence (MP), delayed microbiological eradication (DME) and unable to determine (UTD). SME at FU was defined as all baseline QUPs had an outcome of sustained eradication at FU (i.e.,  $<10^3$  CFU/mL without the participant receiving other systemic antimicrobials before the FU Visit). MR at FU was defined as at least one QUP had an outcome of recurrence ( $\geq 10^3$  CFU/mL) and none had an outcome of persistence at FU. MP at FU was defined as at least one QUP had an outcome of persistence at FU. DME at FU was defined as at least one QUP had an outcome of delayed eradication and none had an outcome of persistence or recurrence at FU. UTD at FU was defined as all QUP outcomes were unable to determine at FU.

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

## End point timeframe:

FU visit (Days 21 to 31)

| End point values                            | Gepotidacin     | Nitrofurantoin  |  |  |
|---------------------------------------------|-----------------|-----------------|--|--|
| Subject group type                          | Reporting group | Reporting group |  |  |
| Number of subjects analysed                 | 336             | 298             |  |  |
| Units: Participants                         |                 |                 |  |  |
| Sustained microbiological eradication (SME) | 174             | 136             |  |  |
| Microbiological persistence (MP)            | 32              | 38              |  |  |
| Microbiological recurrence (MR)             | 36              | 35              |  |  |
| Delayed microbiological eradication (DME)   | 34              | 31              |  |  |
| Unable to determine (UTD)                   | 60              | 58              |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of participants with clinical response at the follow up (FU) visit – Micro-ITT NTF-S population**

|                 |                                                                                                        |
|-----------------|--------------------------------------------------------------------------------------------------------|
| End point title | Number of participants with clinical response at the follow up (FU) visit – Micro-ITT NTF-S population |
|-----------------|--------------------------------------------------------------------------------------------------------|

## End point description:

Clinical response at FU was categorized as clinical success and clinical failure. Clinical success at FU was defined as resolution of symptoms of acute cystitis demonstrated at TOC persist at the FU visit (and no new symptoms), without receiving other AB before the FU visit. Lack of sustained clinical resolution or a missing outcome assessment was defined as clinical failure.

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

## End point timeframe:

FU visit (Days 21 to 31)

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 336             | 298             |  |  |
| Units: Participants         |                 |                 |  |  |
| Clinical success            | 184             | 162             |  |  |
| Clinical failure            | 152             | 136             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with clinical outcome at the TOC visit - Intent-to-Treat (ITT) population

|                 |                                                                                                  |
|-----------------|--------------------------------------------------------------------------------------------------|
| End point title | Number of participants with clinical outcome at the TOC visit - Intent-to-Treat (ITT) population |
|-----------------|--------------------------------------------------------------------------------------------------|

End point description:

Clinical outcomes at TOC were categorized as clinical resolution, clinical improvement, clinical worsening and unable to determine. Clinical resolution at TOC was defined as resolution symptoms of acute cystitis present at baseline (BL) (and no symptoms) without receiving any other AB before the TOC visit. Clinical improvement at TOC was defined as improvement (but not complete resolution) in CSS from BL, without receiving any other AB before the TOC visit. Clinical worsening at TOC was defined as worsening or no change in CSS from BL or received other AB for the current infection (uUTI) before or on the date of the TOC visit. Unable to determine outcome criteria were: BL score is missing (and thus improvement/worsening cannot be determined), TOC assessment is missing, or receipt of other AB not for the current infection before the TOC visit (unless clinical worsening outcome criteria were met).

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

End point timeframe:

TOC visit (Days 9 to 16)

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 767             | 764             |  |  |
| Units: Participants         |                 |                 |  |  |
| Clinical resolution         | 497             | 484             |  |  |
| Clinical improvement        | 194             | 206             |  |  |
| Clinical worsening          | 26              | 37              |  |  |
| Unable to determine         | 50              | 37              |  |  |

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Number of participants with microbiological response at the follow up (FU) visit – Micro-ITT NTF-S population**

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|                 |                                                                                                               |
|-----------------|---------------------------------------------------------------------------------------------------------------|
| End point title | Number of participants with microbiological response at the follow up (FU) visit – Micro-ITT NTF-S population |
|-----------------|---------------------------------------------------------------------------------------------------------------|

End point description:

Participant- level microbiological response at FU was categorized as microbiological success and microbiological failure. Microbiological success at FU was defined as all baseline QUPs had a microbiological outcome of sustained eradication at FU visit. Microbiological failure at FU was defined as not meeting criteria of microbiological success including those participants with UTD outcome.

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

End point timeframe:

FU visit (Days 21 to 31)

---

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 336             | 298             |  |  |
| Units: Participants         |                 |                 |  |  |
| Microbiological Success     | 174             | 136             |  |  |
| Microbiological Failure     | 162             | 162             |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Number of participants with clinical outcome at the follow up (FU) visit - Intent-to-Treat (ITT) population**

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|                 |                                                                                                             |
|-----------------|-------------------------------------------------------------------------------------------------------------|
| End point title | Number of participants with clinical outcome at the follow up (FU) visit - Intent-to-Treat (ITT) population |
|-----------------|-------------------------------------------------------------------------------------------------------------|

End point description:

Clinical outcomes at FU were categorized as SCR, DCR, CI, CW, CR and (UTD. SCR at FU was resolution of symptoms of acute cystitis demonstrated at the TOC persist at the FU (and no symptoms), without receiving other AB before the FU. DCR at FU was resolution of symptoms of acute cystitis present at BL after clinical failure at TOC without receiving AB before FU. CI at FU was improvement in CSS from BL, but not complete resolution without receiving AB before FU. CW at FU was worsening or no change in CSS at FU compared to BL after clinical failure at TOC or receiving other AB for the current infection (uUTI) before or on the date of the FU. CR at FU was symptoms of acute cystitis reoccur at FU after clinical success at TOC. Unable to determine outcome criteria at FU were BL score missing, FU assessment missing or received other AB not for the current infection (uUTI) prior to the assessment (unless CS or CR outcome criteria were met).

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

End point timeframe:

FU visit (Days 21 to 31)

---

| End point values                    | Gepotidacin     | Nitrofurantoin  |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 767             | 764             |  |  |
| Units: Participants                 |                 |                 |  |  |
| Sustained clinical resolution (SCR) | 421             | 404             |  |  |
| Delayed clinical resolution (DCR)   | 130             | 127             |  |  |
| Clinical improvement (CI)           | 75              | 71              |  |  |
| Clinical worsening (CW)             | 29              | 48              |  |  |
| Clinical recurrence (CR)            | 25              | 30              |  |  |
| Unable to determine (UTD)           | 87              | 84              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with clinical response at the TOC visit - Intent-to-Treat (ITT) population

|                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                   |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                   | Number of participants with clinical response at the TOC visit - Intent-to-Treat (ITT) population |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                   |
| Clinical response at TOC was categorized as clinical success and clinical failure. Clinical success at TOC was defined as resolution of signs and symptoms of acute cystitis present at BL (and no new symptoms), without receiving any other AB before the TOC visit. Lack of resolution, including receipt of an AB for uUTI at the TOC visit, or a missing outcome assessment was defined as Clinical Failure. |                                                                                                   |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                    | Secondary                                                                                         |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                   |
| TOC visit (Days 9 to 16)                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                   |

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 767             | 764             |  |  |
| Units: Participants         |                 |                 |  |  |
| Clinical success            | 497             | 484             |  |  |
| Clinical failure            | 270             | 280             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with clinical response at the follow up (FU) visit - Intent-to-Treat (ITT) population

|                                                                                                              |                                                                                                              |
|--------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| End point title                                                                                              | Number of participants with clinical response at the follow up (FU) visit - Intent-to-Treat (ITT) population |
| End point description:                                                                                       |                                                                                                              |
| Clinical response at FU was categorized as clinical success and clinical failure. Clinical success at FU was |                                                                                                              |

defined as resolution of symptoms of acute cystitis demonstrated at TOC persist at the FU visit (and no new symptoms), without receiving other AB before the FU visit. Lack of sustained clinical resolution or a missing outcome assessment was defined as clinical failure.

|                          |           |
|--------------------------|-----------|
| End point type           | Secondary |
| End point timeframe:     |           |
| FU visit (Days 21 to 31) |           |

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 767             | 764             |  |  |
| Units: Participants         |                 |                 |  |  |
| Clinical success            | 421             | 404             |  |  |
| Clinical failure            | 346             | 360             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma concentration of gepotidacin

|                 |                                                    |
|-----------------|----------------------------------------------------|
| End point title | Plasma concentration of gepotidacin <sup>[2]</sup> |
|-----------------|----------------------------------------------------|

End point description:

Blood samples were collected for plasma concentration of gepotidacin. Pharmacokinetic (PK) Population included all randomized participants who received at least 1 dose of study treatment and had at least 1 non missing plasma or urine PK concentration. Only those participants with data available at specified time points have been analyzed.

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

End point timeframe:

Baseline (Day 1) 0-2 hour (h) and >2h post-dose; On-therapy (Day 2), morning (am) pre-dose, 0-6h, 6-8h, 8-10h, 10-12h post-dose, 0-2h, >2h evening (pm) post-dose; On-therapy (Day 3 to 5), 0-6h, 6-8h, 8-10h, 10-12h post-dose

Notes:

[2] - 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: This endpoint is only analyzed for gepotidacin arm.

| End point values                       | Gepotidacin     |  |  |  |
|----------------------------------------|-----------------|--|--|--|
| Subject group type                     | Reporting group |  |  |  |
| Number of subjects analysed            | 495             |  |  |  |
| Units: Microgram/millilitre (ug/mL)    |                 |  |  |  |
| arithmetic mean (standard deviation)   |                 |  |  |  |
| Baseline Day 1, 0-2hour (h) post-dose  | 8.52 (± 84.21)  |  |  |  |
| Baseline Day 1, >2h post-dose          | 2.96 (± 1.865)  |  |  |  |
| On-Therapy Day 2, am, pre-dose         | 3.48 (± 21.58)  |  |  |  |
| On-Therapy Day 2, 0-6h, am, post-dose  | 4.20 (± 4.210)  |  |  |  |
| On-Therapy Day 2, 6-8h, am, post-dose  | 1.22 (± 0.4729) |  |  |  |
| On-Therapy Day 2, 8-10h, am, post-dose | 1.10 (± 1.103)  |  |  |  |

|                                         |                      |  |  |  |
|-----------------------------------------|----------------------|--|--|--|
| On-Therapy Day 2, 10-12h, am, post-dose | 1.26 ( $\pm$ 1.358)  |  |  |  |
| On-Therapy Day 2, 0-2h, pm post-dose    | 2.56 ( $\pm$ 2.717)  |  |  |  |
| On-Therapy Day 2, >2h, pm, post-dose    | 2.61 ( $\pm$ 2.579)  |  |  |  |
| On-Therapy Day 3 to 5, 0-6h post-dose   | 4.10 ( $\pm$ 3.955)  |  |  |  |
| On-Therapy Day 3 to 5, 6-8h post-dose   | 2.54 ( $\pm$ 3.006)  |  |  |  |
| On-Therapy Day 3 to 5, 8-10h post-dose  | 1.08 ( $\pm$ 0.9247) |  |  |  |
| On-Therapy Day 3 to 5, 10-12h post-dose | 1.17 ( $\pm$ 1.688)  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Urine concentration of gepotidacin

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | Urine concentration of gepotidacin <sup>[3]</sup> |
|-----------------|---------------------------------------------------|

End point description:

Urine samples were collected from participants. Pharmacokinetic (PK) Population included all randomized participants who received at least 1 dose of study treatment and had at least 1 non missing plasma or urine PK concentration. Only those participants with data available at specified time points have been analyzed.

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

End point timeframe:

Baseline (Day 1) 0-2 hour (h) and >2h post-dose; On-therapy (Day 2), morning (am) pre-dose, 0-6h, 6-8h, 8-10h, 10-12h post-dose, 0-2h, >2h evening (pm) post-dose; On-therapy (Day 3 to 5), 0-6h, 6-8h, 8-10h, 10-12h post-dose

Notes:

[3] - 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: This endpoint is only analyzed for gepotidacin arm.

| End point values                        | Gepotidacin        |  |  |  |
|-----------------------------------------|--------------------|--|--|--|
| Subject group type                      | Reporting group    |  |  |  |
| Number of subjects analysed             | 490                |  |  |  |
| Units: ug/mL                            |                    |  |  |  |
| arithmetic mean (standard deviation)    |                    |  |  |  |
| Baseline Day 1, 0-2hour (h) post-dose   | 317 ( $\pm$ 680.3) |  |  |  |
| Baseline Day 1, >2h post-dose           | 857 ( $\pm$ 1539)  |  |  |  |
| On-Therapy Day 2, am, pre-dose          | 391 ( $\pm$ 402.5) |  |  |  |
| On-Therapy Day 2, 0-6h, am, post-dose   | 781 ( $\pm$ 1449)  |  |  |  |
| On-Therapy Day 2, 6-8h, am, post-dose   | 363 ( $\pm$ 443.7) |  |  |  |
| On-Therapy Day 2, 8-10h, am, post-dose  | 326 ( $\pm$ 274.4) |  |  |  |
| On-Therapy Day 2, 10-12h, am, post-dose | 287 ( $\pm$ 423.2) |  |  |  |
| On-Therapy Day 2, 0-2h, pm post-dose    | 156 ( $\pm$ 216.1) |  |  |  |
| On-Therapy Day 2, >2h, pm, post-dose    | 624 ( $\pm$ 0)     |  |  |  |
| On-Therapy Day 3 to 5, 0-6h post-dose   | 651 ( $\pm$ 1313)  |  |  |  |
| On-Therapy Day 3 to 5, 6-8h post-dose   | 259 ( $\pm$ 164.9) |  |  |  |
| On-Therapy Day 3 to 5, 8-10h post-dose  | 522 ( $\pm$ 663.1) |  |  |  |

|                                         |                    |  |  |  |
|-----------------------------------------|--------------------|--|--|--|
| On-Therapy Day 3 to 5, 10-12h post-dose | 370 ( $\pm$ 498.8) |  |  |  |
|-----------------------------------------|--------------------|--|--|--|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with treatment-emergent adverse events (TEAEs)

|                 |                                                                       |
|-----------------|-----------------------------------------------------------------------|
| End point title | Number of participants with treatment-emergent adverse events (TEAEs) |
|-----------------|-----------------------------------------------------------------------|

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

From the time of first dose (Day 1) through the final follow-up visit (Day 21-31)

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 766             | 760             |  |  |
| Units: Participants         | 266             | 165             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with serious adverse events (SAEs)

|                 |                                                           |
|-----------------|-----------------------------------------------------------|
| End point title | Number of participants with serious adverse events (SAEs) |
|-----------------|-----------------------------------------------------------|

End point description:

An SAE is defined as any untoward medical occurrence that, at any dose may result in death or is life-threatening or requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity or is a congenital anomaly/birth defect or any other situation according to medical or scientific judgment or is associated with liver injury and impaired liver function. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

From the time of first dose (Day 1) through the final follow-up visit (Day 21-31)

| End point values            | Gepotidacin     | Nitrofurantoin  |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 766             | 760             |  |  |
| Units: Participants         | 2               | 3               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in hematology parameters - neutrophil count, lymphocyte count, monocyte count, eosinophil count, basophil count and platelet count at On Therapy and Test of Cure Visit

|                 |                                                                                                                                                                                              |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline in hematology parameters - neutrophil count, lymphocyte count, monocyte count, eosinophil count, basophil count and platelet count at On Therapy and Test of Cure Visit |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected for the analysis of hematology parameters: neutrophil count, lymphocyte count, monocyte count, eosinophil count, basophil count and platelet count. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)

| End point values                                      | Gepotidacin       | Nitrofurantoin    |  |  |
|-------------------------------------------------------|-------------------|-------------------|--|--|
| Subject group type                                    | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed                           | 725               | 704               |  |  |
| Units: Giga cells per Liter (10 <sup>9</sup> cells/L) |                   |                   |  |  |
| arithmetic mean (standard deviation)                  |                   |                   |  |  |
| Basophils, Baseline                                   | 0.053 (± 0.217)   | 0.055 (± 0.0256)  |  |  |
| Basophils, On-Therapy                                 | -0.001 (± 0.187)  | 0.000 (± 0.0204)  |  |  |
| Basophils, Test of Cure                               | 0.002 (± 0.0204)  | 0.001 (± 0.0244)  |  |  |
| Eosinophils, Baseline                                 | 0.152 (± 0.1137)  | 0.154 (± 0.1338)  |  |  |
| Eosinophils, On-Therapy                               | 0.013 (± 0.0680)  | 0.017 (± 0.0691)  |  |  |
| Eosinophils, Test of Cure                             | 0.024 (± 0.0770)  | 0.022 (± 0.0865)  |  |  |
| Lymphocytes, Baseline                                 | 2.074 (± 0.6603)  | 2.133 (± 2.0797)  |  |  |
| Lymphocytes, On-Therapy                               | 0.009 (± 0.4233)  | -0.026 (± 0.5333) |  |  |
| Lymphocytes, Test of Cure                             | -0.003 (± 0.5106) | 0.067 (± 0.6268)  |  |  |
| Monocytes, Baseline                                   | 0.528 (± 0.1808)  | 0.529 (± 0.1906)  |  |  |

|                           |                   |                   |  |  |
|---------------------------|-------------------|-------------------|--|--|
| Monocytes, On-Therapy     | -0.022 (± 0.1445) | -0.018 (± 0.1400) |  |  |
| Monocytes, Test of Cure   | -0.022 (± 0.1528) | -0.010 (± 0.1678) |  |  |
| Neutrophils, Baseline     | 4.715 (± 1.9781)  | 4.640 (± 1.8018)  |  |  |
| Neutrophils, On-Therapy   | -0.540 (± 1.5771) | -0.519 (± 1.4975) |  |  |
| Neutrophils, Test of Cure | -0.703 (± 1.7653) | -0.470 (± 1.7541) |  |  |
| Platelets, Baseline       | 278.0 (± 70.32)   | 279.0 (± 73.76)   |  |  |
| Platelets, On-Therapy     | 2.4 (± 24.46)     | 2.6 (± 29.94)     |  |  |
| Platelets, Test of Cure   | 3.0 (± 39.74)     | 8.6 (± 47.92)     |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in hematology parameter-hemoglobin level at On Therapy and Test of Cure Visit

|                 |                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Change from baseline in hematology parameter-hemoglobin level at On Therapy and Test of Cure Visit |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected for the analysis of hemoglobin level. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)

| End point values                     | Gepotidacin     | Nitrofurantoin  |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 726             | 704             |  |  |
| Units: Gram per Liter (g/L)          |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Hemoglobin, Baseline                 | 132.2 (± 13.13) | 131.7 (± 14.33) |  |  |
| Hemoglobin, On-Therapy               | -0.1 (± 5.27)   | -0.4 (± 6.39)   |  |  |
| Hemoglobin, Test of Cure             | -0.9 (± 6.63)   | -1.6 (± 7.27)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in hematology parameter- hematocrit level at On Therapy and Test of Cure Visit

|                                                                                                                                                                                                                                                                                     |                                                                                                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                     | Change from baseline in hematology parameter- hematocrit level at On Therapy and Test of Cure Visit |
| End point description:<br>Blood samples were collected for the analysis of hematocrit level. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment. |                                                                                                     |
| End point type                                                                                                                                                                                                                                                                      | Secondary                                                                                           |
| End point timeframe:<br>Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)                                                                                                                                                                    |                                                                                                     |

| End point values                     | Gepotidacin         | Nitrofurantoin      |  |  |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type                   | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed          | 726                 | 704                 |  |  |
| Units: Percentage of hematocrit      |                     |                     |  |  |
| arithmetic mean (standard deviation) |                     |                     |  |  |
| Hematocrit, Baseline                 | 0.4302 (± 0.04292)  | 0.4282 (± 0.4584)   |  |  |
| Hematocrit, On-Therapy               | 0.0003 (± 0.02238)  | -0.0007 (± 0.02431) |  |  |
| Hematocrit, Test of Cure             | -0.0023 (± 0.02689) | -0.0055 (± 0.02757) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in hematology parameter- erythrocytes count at On Therapy and Test of Cure Visit

|                                                                                                                                                                                                                                                                                       |                                                                                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                       | Change from baseline in hematology parameter- erythrocytes count at On Therapy and Test of Cure Visit |
| End point description:<br>Blood samples were collected for the analysis of erythrocytes count. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment. |                                                                                                       |
| End point type                                                                                                                                                                                                                                                                        | Secondary                                                                                             |
| End point timeframe:<br>Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)                                                                                                                                                                      |                                                                                                       |

| End point values                                       | Gepotidacin      | Nitrofurantoin   |  |  |
|--------------------------------------------------------|------------------|------------------|--|--|
| Subject group type                                     | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed                            | 726              | 704              |  |  |
| Units: Tera cells per Liter (10 <sup>12</sup> cells/L) |                  |                  |  |  |
| arithmetic mean (standard deviation)                   |                  |                  |  |  |
| Erythrocytes, Baseline                                 | 4.538 (± 0.4315) | 4.515 (± 0.4324) |  |  |

|                            |                   |                   |  |  |
|----------------------------|-------------------|-------------------|--|--|
| Erythrocytes, On-Therapy   | -0.005 (± 0.1900) | -0.011 (± 0.2247) |  |  |
| Erythrocytes, Test of Cure | -0.033 (± 0.2377) | -0.048 (± 0.2528) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in hematology parameter - mean corpuscular hemoglobin (MCH) at On Therapy and Test of Cure Visit

|                 |                                                                                                                       |
|-----------------|-----------------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline in hematology parameter - mean corpuscular hemoglobin (MCH) at On Therapy and Test of Cure Visit |
|-----------------|-----------------------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected for the analysis of MCH. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)

| End point values                     | Gepotidacin     | Nitrofurantoin  |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 726             | 704             |  |  |
| Units: Picogram (pg)                 |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| MCH, Baseline                        | 29.20 (± 2.392) | 29.24 (± 2.499) |  |  |
| MCH, On-Therapy                      | 0.02 (± 0.500)  | -0.03 (± 0.536) |  |  |
| MCH, Test of Cure                    | 0.02 (± 0.596)  | -0.05 (± 0.644) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in hematology parameter - mean corpuscular volume (MCV) at On Therapy and Test of Cure Visit

|                 |                                                                                                                   |
|-----------------|-------------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline in hematology parameter - mean corpuscular volume (MCV) at On Therapy and Test of Cure Visit |
|-----------------|-------------------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected for the analysis of MCV. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)

| End point values                     | Gepotidacin     | Nitrofurantoin   |  |  |
|--------------------------------------|-----------------|------------------|--|--|
| Subject group type                   | Reporting group | Reporting group  |  |  |
| Number of subjects analysed          | 726             | 704              |  |  |
| Units: Femtoliter (fL)               |                 |                  |  |  |
| arithmetic mean (standard deviation) |                 |                  |  |  |
| MCV, Baseline                        | 95.02 (± 7.057) | 95.03 (± 7.438)  |  |  |
| MCV, On-Therapy                      | 0.17 (± 3.269)  | 0.07 (± 3.248)   |  |  |
| MCV, Test of Cure                    | 0.17 (± 3.511)  | -0.019 (± 3.689) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in clinical chemistry parameters - Serum urea nitrogen, glucose, calcium, chloride, sodium, magnesium, phosphate, and potassium levels at On Therapy and Test of Cure Visit

|                 |                                                                                                                                                                                                  |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in clinical chemistry parameters - Serum urea nitrogen, glucose, calcium, chloride, sodium, magnesium, phosphate, and potassium levels at On Therapy and Test of Cure Visit |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected for the analysis of clinical chemistry parameters. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)

| End point values                     | Gepotidacin       | Nitrofurantoin    |  |  |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed          | 751               | 741               |  |  |
| Units: millimoles per liter (mmol/L) |                   |                   |  |  |
| arithmetic mean (standard deviation) |                   |                   |  |  |
| Serum Calcium, Baseline              | 2.357 (± 0.1118)  | 2.374 (± 0.1154)  |  |  |
| Serum Calcium, On-Therapy            | -0.009 (± 0.0914) | -0.012 (± 0.0992) |  |  |
| Serum Calcium, Test of Cure          | -0.016 (± 0.0981) | -0.016 (± 0.1017) |  |  |
| Serum Chloride, Baseline             | 101.6 (± 3.23)    | 101.3 (± 3.08)    |  |  |
| Serum Chloride, On-Therapy           | 0.2 (± 2.59)      | 0.0 (± 2.49)      |  |  |

|                                   |                   |                   |  |  |
|-----------------------------------|-------------------|-------------------|--|--|
| Serum Chloride, Test of Cure      | 0.4 (± 2.88)      | 0.2 (± 2.67)      |  |  |
| Serum Glucose, Baseline           | 5.778 (± 2.3665)  | 5.689 (± 1.9348)  |  |  |
| Serum Glucose, On-Therapy         | 0.199 (± 1.4728)  | 0.397 (± 1.5986)  |  |  |
| Serum Glucose, Test of Cure       | 0.156 (± 1.5893)  | 0.290 (± 1.5996)  |  |  |
| Serum Magnesium, Baseline         | 0.836 (± 0.0760)  | 0.831 (± 0.0781)  |  |  |
| Serum Magnesium, On-Therapy       | -0.006 (± 0.0634) | -0.015 (± 0.0604) |  |  |
| Serum Magnesium, Test of Cure     | -0.008 (± 0.0626) | -0.014 (± 0.0616) |  |  |
| Serum Phosphate, Baseline         | 1.138 (± 0.1641)  | 1.133 (± 0.1750)  |  |  |
| Serum Phosphate, On-Therapy       | 0.005 (± 0.1642)  | -0.012 (± 0.1826) |  |  |
| Serum Phosphate, Test of Cure     | 0.009 (± 0.1857)  | 0.008 (± 0.1908)  |  |  |
| Serum Potassium, Baseline         | 4.32 (± 0.441)    | 4.33 (± 0.447)    |  |  |
| Serum Potassium, On-Therapy       | 0.00 (± 0.443)    | -0.01 (± 0.495)   |  |  |
| Serum Potassium, Test of Cure     | 0.00 (± 0.488)    | 0.01 (± 0.495)    |  |  |
| Serum Sodium, Baseline            | 139.5 (± 2.69)    | 139.2 (± 2.64)    |  |  |
| Serum Sodium, On-Therapy          | -0.1 (± 2.41)     | -0.2 (± 2.54)     |  |  |
| Serum Sodium, Test of Cure        | 0.0 (± 2.68)      | -0.1 (± 2.64)     |  |  |
| Serum Urea Nitrogen, Baseline     | 4.855 (± 1.8877)  | 4.912 (± 2.1175)  |  |  |
| Serum Urea Nitrogen, On-Therapy   | -0.039 (± 1.1285) | -0.045 (± 1.1848) |  |  |
| Serum Urea Nitrogen, Test of Cure | 0.031 (± 1.3613)  | 0.054 (± 1.5544)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in clinical chemistry parameters - Total bilirubin, direct bilirubin and creatinine levels at On Therapy and Test of Cure Visit

|                 |                                                                                                                                                      |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in clinical chemistry parameters - Total bilirubin, direct bilirubin and creatinine levels at On Therapy and Test of Cure Visit |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected for the analysis of clinical chemistry parameters. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

Baseline, On-Therapy (Days 2 to 4), and Test of cure (Days 10 to 13)

| End point values                     | Gepotidacin     | Nitrofurantoin  |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 750             | 740             |  |  |
| Units: micromoles per Liter (umol/L) |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Serum direct bilirubin, Baseline     | 4.71 (± 1.534)  | 4.78 (± 1.462)  |  |  |
| Serum direct bilirubin, On-Therapy   | -0.26 (± 1.443) | -0.16 (± 1.276) |  |  |
| Serum direct bilirubin, Test of cure | -0.24 (± 1.577) | -0.08 (± 1.534) |  |  |
| Serum Creatinine, Baseline           | 59.5 (± 20.67)  | 59.3 (± 20.17)  |  |  |
| Serum Creatinine, On-Therapy         | 2.8 (± 13.51)   | 2.3 (± 23.79)   |  |  |
| Serum Creatinine, Test of Cure       | 0.9 (± 16.98)   | 2.2 (± 29.46)   |  |  |
| Serum total bilirubin, Baseline      | 6.72 (± 3.914)  | 6.77 (± 3.909)  |  |  |
| Serum total bilirubin, On-Therapy    | -0.10 (± 2.718) | -0.15 (± 2.655) |  |  |
| Serum total bilirubin, Test of Cure  | -0.15 (± 2.904) | -0.16 (± 3.107) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in clinical chemistry parameters - albumin and total protein levels at On Therapy and Test of Cure Visit

|                 |                                                                                                                               |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in clinical chemistry parameters - albumin and total protein levels at On Therapy and Test of Cure Visit |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected for the analysis of clinical chemistry parameters. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

Baseline, On-Therapy (Days 2 to 4), and Test of cure (Days 10 to 13)

| End point values                     | Gepotidacin     | Nitrofurantoin  |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 752             | 760             |  |  |
| Units: gram per Liter (g/L)          |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Serum Albumin, Baseline              | 45.2 (± 3.07)   | 45.4 (± 2.91)   |  |  |
| Serum Albumin, On-Therapy            | 0.0 (± 2.21)    | -0.3 (± 2.06)   |  |  |
| Serum Albumin, Test of Cure          | -0.5 (± 2.42)   | -0.5 (± 2.50)   |  |  |
| Serum Protein, Baseline              | 71.6 (± 4.73)   | 71.8 (± 4.72)   |  |  |
| Serum Protein, On-Therapy            | 0.0 (± 3.70)    | -0.4 (± 3.46)   |  |  |
| Serum Protein, Test of Cure          | -0.9 (± 4.02)   | -1.0 (± 3.76)   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in clinical chemistry parameters - Aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) levels at On Therapy and Test of Cure Visit

|                 |                                                                                                                                                                                                     |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in clinical chemistry parameters - Aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) levels at On Therapy and Test of Cure Visit |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Blood samples were collected for the analysis of clinical chemistry parameters. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

Baseline, On-Therapy (Days 2 to 4), and Test of cure (Days 10 to 13)

| End point values                     | Gepotidacin     | Nitrofurantoin  |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 749             | 739             |  |  |
| Units: Units per Liter (U/L)         |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Serum ALP, Baseline                  | 79.0 (± 27.98)  | 78.4 (± 30.89)  |  |  |
| Serum ALP, On-Therapy                | -0.5 (± 6.91)   | 0.1 (± 7.24)    |  |  |
| Serum ALP, Test of Cure              | -1.5 (± 9.43)   | 0.0 (± 12.65)   |  |  |
| Serum AST, Baseline                  | 20.1 (± 9.40)   | 21.5 (± 16.55)  |  |  |
| Serum AST, On-Therapy                | 0.5 (± 5.97)    | 0.1 (± 5.33)    |  |  |
| Serum AST, Test of Cure              | 1.1 (± 7.21)    | 1.6 (± 38.77)   |  |  |
| Serum ALT, Baseline                  | 18.9 (± 13.55)  | 20.0 (± 17.84)  |  |  |
| Serum ALT, On-Therapy                | 0.8 (± 5.17)    | 0.2 (± 5.43)    |  |  |
| Serum ALT, Test of Cure              | 1.0 (± 8.93)    | 1.2 (± 23.91)   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with urinalysis dipstick results at Baseline, On Therapy and Test of Cure visit

|                 |                                                                                                        |
|-----------------|--------------------------------------------------------------------------------------------------------|
| End point title | Number of participants with urinalysis dipstick results at Baseline, On Therapy and Test of Cure visit |
|-----------------|--------------------------------------------------------------------------------------------------------|

End point description:

Urine samples were collected for urinalysis: Urine Glucose (GLU), Urine Protein (PRO), Urine Occult Blood (BLO), Urine Ketones (KET), Urine Nitrite (NIT) and Urine Leukocyte Esterase (LEU). Baseline is defined as the latest pre-dose assessment with a non-missing value. The dipstick test gives results in a semi-quantitative manner, and results can be read as Negative, Trace, Small, Moderate, Large, Positive, 50 milligram per deciliter (mg/dL), 150 mg/dL,  $\geq 500$  mg/dL, 30 mg/dL, 100 mg/dL, 200 mg/dL, 5 mg/dL, 20 mg/dL,  $\geq 80$  mg/dL indicating concentrations in the urine sample. In the category (GLU, Baseline, Negative), GLU indicates parameter, Baseline is the visit and Negative indicates the concentration in the urine sample.

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

End point timeframe:

Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)

| End point values                    | Gepotidacin     | Nitrofurantoin  |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 756             | 752             |  |  |
| Units: Participants                 |                 |                 |  |  |
| GLU, Baseline, Negative             | 703             | 717             |  |  |
| GLU, Baseline, 50 mg/dL             | 15              | 5               |  |  |
| GLU, Baseline, 150 mg/dL            | 4               | 3               |  |  |
| GLU, Baseline, $\geq 500$ mg/dL     | 21              | 15              |  |  |
| GLU, On-Therapy, Negative           | 681             | 680             |  |  |
| GLU, On-Therapy, 50 mg/dL           | 11              | 6               |  |  |
| GLU, On-Therapy, 150 mg/dL          | 7               | 4               |  |  |
| GLU, On-Therapy, $\geq 500$ mg/dL   | 22              | 21              |  |  |
| GLU, Test of Cure, Negative         | 672             | 672             |  |  |
| GLU, Test of Cure, 50 mg/dL         | 6               | 4               |  |  |
| GLU, Test of Cure, 150 mg/dL        | 2               | 4               |  |  |
| GLU, Test of Cure, $\geq 500$ mg/dL | 21              | 20              |  |  |
| PRO, Baseline, Negative             | 501             | 501             |  |  |
| PRO, Baseline, 30 mg/dL             | 179             | 160             |  |  |
| PRO, Baseline, 100 mg/dL            | 60              | 72              |  |  |
| PRO, Baseline, $\geq 500$ mg/dL     | 3               | 6               |  |  |
| PRO, On-Therapy, Negative           | 546             | 587             |  |  |
| PRO, On-Therapy, 30 mg/dL           | 133             | 102             |  |  |
| PRO, On-Therapy, 100 mg/dL          | 40              | 20              |  |  |
| PRO, On-Therapy, $\geq 500$ mg/dL   | 2               | 2               |  |  |
| PRO, Test of Cure, Negative         | 602             | 591             |  |  |
| PRO, Test of Cure, 30 mg/dL         | 77              | 89              |  |  |
| PRO, Test of Cure, 100 mg/dL        | 21              | 15              |  |  |
| PRO, Test of Cure, $\geq 500$ mg/dL | 1               | 5               |  |  |
| BLO, Baseline, Negative             | 310             | 297             |  |  |
| BLO, Baseline, Positive             | 2               | 0               |  |  |
| BLO, Baseline, Small                | 248             | 266             |  |  |
| BLO, Baseline, Moderate             | 118             | 107             |  |  |
| BLO, Baseline, Large                | 72              | 75              |  |  |
| BLO, On-Therapy, Negative           | 531             | 475             |  |  |
| BLO, On-Therapy, Small              | 123             | 167             |  |  |
| BLO, On-Therapy, Moderate           | 38              | 40              |  |  |
| BLO, On-Therapy, Large              | 29              | 29              |  |  |

|                               |     |     |  |  |
|-------------------------------|-----|-----|--|--|
| BLO, Test of Cure, Negative   | 503 | 510 |  |  |
| BLO, Test of Cure, Small      | 124 | 114 |  |  |
| BLO, Test of Cure, Moderate   | 46  | 50  |  |  |
| BLO, Test of Cure, Large      | 28  | 26  |  |  |
| KET, Baseline, Negative       | 724 | 726 |  |  |
| KET, Baseline, 5 mg/dL        | 14  | 8   |  |  |
| KET, Baseline, 20 mg/dL       | 4   | 5   |  |  |
| KET, Baseline, >=80 mg/dL     | 1   | 1   |  |  |
| KET, On-Therapy, Negative     | 704 | 688 |  |  |
| KET, On-Therapy, 5 mg/dL      | 10  | 20  |  |  |
| KET, On-Therapy, 20 mg/dL     | 6   | 2   |  |  |
| KET, On-Therapy, >=80 mg/dL   | 1   | 1   |  |  |
| KET, Test of Cure, Negative   | 683 | 688 |  |  |
| KET, Test of Cure, 5 mg/dL    | 13  | 11  |  |  |
| KET, Test of Cure, >=80 mg/dL | 5   | 1   |  |  |
| NIT, Baseline, Negative       | 466 | 458 |  |  |
| NIT, Baseline, Positive       | 286 | 291 |  |  |
| NIT, On-Therapy, Negative     | 655 | 647 |  |  |
| NIT, On-Therapy, Positive     | 66  | 64  |  |  |
| NIT, Test of Cure, Negative   | 662 | 639 |  |  |
| NIT, Test of Cure, Positive   | 39  | 61  |  |  |
| LEU, Baseline, Negative       | 186 | 169 |  |  |
| LEU, Baseline, Trace          | 80  | 77  |  |  |
| LEU, Baseline, Small          | 89  | 74  |  |  |
| LEU, Baseline, Moderate       | 109 | 116 |  |  |
| LEU, Baseline, Large          | 292 | 314 |  |  |
| LEU, Baseline, Positive       | 0   | 2   |  |  |
| LEU, On-Therapy, Negative     | 429 | 387 |  |  |
| LEU, On-Therapy, Trace        | 82  | 86  |  |  |
| LEU, On-Therapy, Small        | 48  | 69  |  |  |
| LEU, On-Therapy, Moderate     | 57  | 63  |  |  |
| LEU, On-Therapy, Large        | 105 | 106 |  |  |
| LEU, Test of Cure, Negative   | 506 | 442 |  |  |
| LEU, Test of Cure, Trace      | 60  | 73  |  |  |
| LEU, Test of Cure, Small      | 38  | 54  |  |  |
| LEU, Test of Cure, Moderate   | 38  | 50  |  |  |
| LEU, Test of Cure, Large      | 59  | 81  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Absolute mean values of urine specific gravity at Baseline, On Therapy and Test of Cure visit

|                 |                                                                                               |
|-----------------|-----------------------------------------------------------------------------------------------|
| End point title | Absolute mean values of urine specific gravity at Baseline, On Therapy and Test of Cure visit |
|-----------------|-----------------------------------------------------------------------------------------------|

End point description:

Urine samples were collected from participants to assess urine specific gravity. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

|                                                                                          |           |
|------------------------------------------------------------------------------------------|-----------|
| End point type                                                                           | Secondary |
| End point timeframe:                                                                     |           |
| Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16) |           |

| End point values                     | Gepotidacin        | Nitrofurantoin     |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 742                | 740                |  |  |
| Units: Ratio                         |                    |                    |  |  |
| arithmetic mean (standard deviation) |                    |                    |  |  |
| Urine Specific Gravity, Baseline     | 1.0168 (± 0.00639) | 1.0166 (± 0.00636) |  |  |
| Urine Specific Gravity, On-Therapy   | 1.0175 (± 0.00663) | 1.0166 (± 0.00636) |  |  |
| Urine Specific Gravity, Test of Cure | 1.0179 (± 0.00700) | 1.0179 (± 0.00701) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Absolute mean values of urine potential of hydrogen (pH) at Baseline, On Therapy and Test of Cure visit

|                                                                                                                                                                                                                                                                  |                                                                                                         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                  | Absolute mean values of urine potential of hydrogen (pH) at Baseline, On Therapy and Test of Cure visit |
| End point description:                                                                                                                                                                                                                                           |                                                                                                         |
| Urine samples were collected from participants to assess urine pH levels. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment. |                                                                                                         |
| End point type                                                                                                                                                                                                                                                   | Secondary                                                                                               |
| End point timeframe:                                                                                                                                                                                                                                             |                                                                                                         |
| Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)                                                                                                                                                                         |                                                                                                         |

| End point values                     | Gepotidacin     | Nitrofurantoin  |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 733             | 760             |  |  |
| Units: pH                            |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Urine pH, Baseline                   | 5.6 (± 0.76)    | 5.7 (± 0.79)    |  |  |
| Urine pH, On-Therapy                 | 5.6 (± 0.68)    | 5.6 (± 0.73)    |  |  |
| Urine pH, Test of Cure               | 5.6 (± 0.68)    | 5.6 (± 0.70)    |  |  |

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Change from baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at On-Therapy and Test of Cure Visit**

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|                 |                                                                                                                               |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at On-Therapy and Test of Cure Visit |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------|

End point description:

SBP and DBP were measured in a semi-supine position after 5 minutes rest. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)

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| End point values                     | Gepotidacin     | Nitrofurantoin  |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 766             | 760             |  |  |
| Units: Millimeters of mercury (mmHg) |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| SBP, Baseline                        | 123.1 (± 13.23) | 123.4 (± 12.61) |  |  |
| SBP, On-Therapy                      | -0.8 (± 9.20)   | -1.4 (± 9.64)   |  |  |
| SBP, Test of Cure                    | -0.9 (± 10.44)  | -1.2 (± 10.86)  |  |  |
| DBP, Baseline                        | 76.5 (± 8.36)   | 76.7 (± 8.25)   |  |  |
| DBP, On-Therapy                      | -0.2 (± 7.48)   | -0.7 (± 7.33)   |  |  |
| DBP, Test of Cure                    | -0.5 (± 7.80)   | -1.2 (± 8.28)   |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Change from baseline in pulse rate at On Therapy and Test of Cure Visit**

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|                 |                                                                         |
|-----------------|-------------------------------------------------------------------------|
| End point title | Change from baseline in pulse rate at On Therapy and Test of Cure Visit |
|-----------------|-------------------------------------------------------------------------|

End point description:

Pulse rate was measured in a semi-supine position after 5 minutes rest. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)

---

| End point values                     | Gepotidacin     | Nitrofurantoin  |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 766             | 760             |  |  |
| Units: beats per minute (bpm)        |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Pulse rate, Baseline                 | 73.5 (± 9.84)   | 73.3 (± 9.91)   |  |  |
| Pulse rate, On-Therapy               | 1.4 (± 8.39)    | 1.7 (± 8.80)    |  |  |
| Pulse rate, Test of Cure             | 1.2 (± 9.63)    | 1.0 (± 10.18)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in body temperature at On Therapy and Test of Cure Visit

|                 |                                                                               |
|-----------------|-------------------------------------------------------------------------------|
| End point title | Change from Baseline in body temperature at On Therapy and Test of Cure Visit |
|-----------------|-------------------------------------------------------------------------------|

End point description:

Temperature was measured in a semi-supine position after 5 minutes rest. Baseline is defined as the latest pre-dose assessment with a non-missing value. Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

End point timeframe:

Baseline (on or before Day 1), On-Therapy (Days 2 to 5), and Test of cure (Days 9 to 16)

| End point values                     | Gepotidacin     | Nitrofurantoin  |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 766             | 760             |  |  |
| Units: celsius                       |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Temperature, Baseline                | 36.62 (± 0.372) | 36.62 (± 0.406) |  |  |
| Temperature, On-Therapy              | -0.04 (± 0.300) | -0.04 (± 0.379) |  |  |
| Temperature, Test of Cure            | -0.04 (± 0.330) | -0.07 (± 0.400) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All cause mortality, non-serious adverse events (Non-SAEs) and serious adverse events (SAEs) were collected from the time of first dose (Day 1) through the final follow-up visit (Day 21-31).

Adverse event reporting additional description:

Safety population included all randomized participants who receive at least 1 dose of study treatment.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | Nitrofurantoin |
|-----------------------|----------------|

Reporting group description:

Participants with uncomplicated urinary tract infection (acute cystitis) randomized to receive nitrofurantoin 100 mg capsule, BID, orally on Day 1 to Day 5. The total daily dose of nitrofurantoin received was 200 mg. Participants also received 2 tablets of placebo matched with gepotidacin BID, orally on Day 1 to Day 5. All doses were administered after food consumption and with water.

|                       |             |
|-----------------------|-------------|
| Reporting group title | Gepotidacin |
|-----------------------|-------------|

Reporting group description:

Participants with uncomplicated urinary tract infection (uUTI) (acute cystitis) randomized to receive gepotidacin 1500 milligram (mg) (2\*750 mg, tablets), twice daily (BID), orally on Day 1 to Day 5. The total daily dose of gepotidacin received was 3000 mg. Participants also received 1 capsule of placebo matched with nitrofurantoin BID, orally on Day 1 to Day 5. All doses were administered after food consumption and with water.

| Serious adverse events                            | Nitrofurantoin  | Gepotidacin     |  |
|---------------------------------------------------|-----------------|-----------------|--|
| Total subjects affected by serious adverse events |                 |                 |  |
| subjects affected / exposed                       | 3 / 760 (0.39%) | 2 / 766 (0.26%) |  |
| number of deaths (all causes)                     | 0               | 0               |  |
| number of deaths resulting from adverse events    |                 |                 |  |
| Nervous system disorders                          |                 |                 |  |
| Sciatica                                          |                 |                 |  |
| subjects affected / exposed                       | 1 / 760 (0.13%) | 0 / 766 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0           |  |
| Dysarthria                                        |                 |                 |  |
| subjects affected / exposed                       | 0 / 760 (0.00%) | 1 / 766 (0.13%) |  |
| occurrences causally related to treatment / all   | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0           |  |
| Lumbar radiculopathy                              |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 760 (0.13%) | 0 / 766 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Blood and lymphatic system disorders</b>     |                 |                 |  |
| Lymphadenopathy                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 760 (0.13%) | 0 / 766 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Gastrointestinal disorders</b>               |                 |                 |  |
| Enterovesical fistula                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 760 (0.00%) | 1 / 766 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Infections and infestations</b>              |                 |                 |  |
| Dengue fever                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 760 (0.13%) | 0 / 766 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Metabolism and nutrition disorders</b>       |                 |                 |  |
| Food intolerance                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 760 (0.13%) | 0 / 766 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                            | Nitrofurantoin    | Gepotidacin        |  |
|--------------------------------------------------------------|-------------------|--------------------|--|
| <b>Total subjects affected by non-serious adverse events</b> |                   |                    |  |
| subjects affected / exposed                                  | 94 / 760 (12.37%) | 207 / 766 (27.02%) |  |
| <b>Investigations</b>                                        |                   |                    |  |
| Aspartate aminotransferase increased                         |                   |                    |  |
| subjects affected / exposed                                  | 5 / 760 (0.66%)   | 8 / 766 (1.04%)    |  |
| occurrences (all)                                            | 6                 | 8                  |  |
| <b>Nervous system disorders</b>                              |                   |                    |  |

|                                                                             |                        |                           |  |
|-----------------------------------------------------------------------------|------------------------|---------------------------|--|
| Headache<br>subjects affected / exposed<br>occurrences (all)                | 18 / 760 (2.37%)<br>18 | 17 / 766 (2.22%)<br>17    |  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)               | 8 / 760 (1.05%)<br>8   | 11 / 766 (1.44%)<br>11    |  |
| Gastrointestinal disorders                                                  |                        |                           |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)               | 27 / 760 (3.55%)<br>27 | 111 / 766 (14.49%)<br>116 |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                  | 29 / 760 (3.82%)<br>29 | 81 / 766 (10.57%)<br>84   |  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)    | 8 / 760 (1.05%)<br>8   | 20 / 766 (2.61%)<br>20    |  |
| Flatulence<br>subjects affected / exposed<br>occurrences (all)              | 4 / 760 (0.53%)<br>4   | 15 / 766 (1.96%)<br>15    |  |
| Faeces soft<br>subjects affected / exposed<br>occurrences (all)             | 4 / 760 (0.53%)<br>4   | 14 / 766 (1.83%)<br>14    |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                | 3 / 760 (0.39%)<br>3   | 10 / 766 (1.31%)<br>10    |  |
| Infections and infestations                                                 |                        |                           |  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 5 / 760 (0.66%)<br>5   | 8 / 766 (1.04%)<br>9      |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 06 May 2021      | Clarifications that the primary analysis population will be "micro-ITT NTF-S (IA Set)" if the study is stopped early for success (and inclusion of corresponding outputs). Clarifications that <18 years and ≥18 to 50 years strata will be combined for use as an analysis covariate to ensure participants with valid data are not excluded.                                                                                                                                                                |
| 03 November 2021 | Updates to the IA recommendation framework to include a supplementary analysis performed on a supplementary analysis population defined as the primary analysis population excluding participants from investigators/sites which have had a corrective and preventative action (CAPA) put in place requiring that a supplementary analysis excluding data from these sites be performed. This population will be labeled micro-ITT NTF-S (CAPA) population and will be performed on the IA Set if applicable. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported