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)	EMEA-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 cystitisin 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 which1531 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
Arm title	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.

Arm title	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 [1]	365 [2]
Micro-ITT NTF-S Population	336 [3]	298 [4]
Micro-ITT NTF-S (IA Set) Population	320 [5]	287 [6]
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

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:

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.

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:

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:

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

Statistical analysis title	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

Statistical analysis title	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[1]

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 outcome (MO) at the TOC visit – Micro-ITT NTF-S population

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 (≥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		

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

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 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

No statistical analyses for this end point

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

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 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 (≥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 microbiological response at the follow up (FU) visit – Micro-ITT NTF-S population

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		

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

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

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[2]

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

Statistical analyses

No statistical analyses for this end point

Secondary: Urine concentration of gepotidacin

End point title	Urine concentration of gepotidacin[3]

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 (± 680.3)			
Baseline Day 1, >2h post-dose	857 (± 1539)			
On-Therapy Day 2, am, pre-dose	391 (± 402.5)			
On-Therapy Day 2, 0-6h, am, post-dose	781 (± 1449)			
On-Therapy Day 2, 6-8h, am, post-dose	363 (± 443.7)			
On-Therapy Day 2, 8-10h, am, post-dose	326 (± 274.4)			
On-Therapy Day 2, 10-12h, am, post-dose	287 (± 423.2)			
On-Therapy Day 2, 0-2h, pm post-dose	156 (± 216.1)			
On-Therapy Day 2, >2h, pm, post-dose	624 (± 0)			
On-Therapy Day 3 to 5, 0-6h post-dose	651 (± 1313)			
On-Therapy Day 3 to 5, 6-8h post-dose	259 (± 164.9)			
On-Therapy Day 3 to 5, 8-10h post-dose	522 (± 663.1)			

On-Therapy Day 3 to 5, 10-12h post-dose	370 (± 498.8)			

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: 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: 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 (10^9 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:

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:

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:

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:

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 (10^12 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 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 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 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 (± 0.992)		
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, >=500 mg/dL, 30 mg/dL, 100 mg/dL, 200 mg/dL, 5 mg/dL, 20 mg/dL, >=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, >= 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, >= 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, >= 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, >=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, >=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, >=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 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

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

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)

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)		

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

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

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

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	
Blood and lymphatic system disorders			
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	
Gastrointestinal disorders			
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	
Infections and infestations			
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	
Metabolism and nutrition disorders			
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 %

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

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

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported