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	2020-000553-27
Trial protocol	BG PL
Global end of trial date	01 December 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	212390

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04187144
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 GreatWest Road, Brentford,Middlesex, United Kingdom, TW8 9GS
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	27 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 December 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The study was conducted to evaluate the therapeutic response (combined per participant microbiological and clinical response) of oral gepotidacin compared to oral nitrofurantoin for treatment of uncomplicated UTI (acute cystitis) in adolescent and adult female participants.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 April 2020
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	Australia: 19
Country: Number of subjects enrolled	Bulgaria: 356
Country: Number of subjects enrolled	India: 63
Country: Number of subjects enrolled	Poland: 42
Country: Number of subjects enrolled	United States: 1095
Country: Number of subjects enrolled	Korea, Republic of: 30
Worldwide total number of subjects	1605
EEA total number of subjects	398

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	11

Adults (18-64 years)	1253
From 65 to 84 years	326
85 years and over	15

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

1731 unique participants were screened, of these 1605 unique participants were enrolled. This includes one participant that was enrolled twice in error.

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	Subject, Investigator

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	Capsule
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	805	800
Safety Population	804	798
Microbiological ITT (microITT)Population	331 [1]	324 [2]
Micro-ITT NTF-S Population	292 [3]	275 [4]
Micro-ITT NTF-S (IA Set) Population	277 [5]	264 [6]
Completed	748	759
Not completed	57	41
Consent withdrawn by subject	20	18
Physician decision	5	3
Adverse event, non-fatal	19	4
Protocol Deviation	1	4
ScreenFailure - CreatinineClearance/BodyMassIndex	-	1
Lost to follow-up	12	11

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	805	800	1605
Age Categorical Units: Participants			
Less than (<) 18 years	8	3	11
More than or equal to (>=) 18 years to 50 years	427	430	857
More than (>) 50 years	370	367	737
Age Continuous Units: Years			
arithmetic mean	48.2	48.4	
standard deviation	± 17.84	± 17.72	-
Sex/Gender, Customized Units: Participants			
Female	805	800	1605
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	246	232	478
Not Hispanic or Latino	559	568	1127
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	1	3
Asian	51	65	116
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	74	62	136
White	674	668	1342
More than one race	2	4	6
Unknown or Not Reported	1	0	1
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.			
Units: Subjects			

Recurrent Infection	334	338	672
Non-Recurrent Infection	471	462	933

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 (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 (IA Set)

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 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. Micro-ITT NTF-S) (Interim Analysis [IA] Set) population included participants in the micro ITT NTF-S who per the interim analysis data had the opportunity to reach their Test of Cure (TOC) visit, or had not yet reached their TOC visit, but were already known to be failures.

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	277	264		
Units: Participants				
Therapeutic Success	162	115		
Therapeutic Failure	115	149		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Nitrofurantoin v Gepotidacin
Number of subjects included in analysis	541
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Adjusted Difference in Percent
Point estimate	14.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.4
upper limit	22.8

Notes:

[1] - The difference in success rate between treatment groups (gepotidacin – nitrofurantoin) was calculated using Miettinen-Nurminen Summary Score Method adjusted for age group and acute cystitis recurrence strata combinations. Criteria for non-inferiority is if the Z-statistic for non-inferiority is greater than the 2.098 Z-statistic boundary.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The difference in success rate between treatment groups (gepotidacin – nitrofurantoin) was calculated using Miettinen-Nurminen Summary Score Method adjusted for age group and acute cystitis recurrence strata combinations. Criteria for superiority is if the one-sided p-value is less than the 0.018 p-value boundary

Comparison groups	Gepotidacin v Nitrofurantoin
Number of subjects included in analysis	541
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	1-sided p-value for Test of Superiority
Parameter estimate	p-value Boundary for Superiority
Point estimate	14.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.4
upper limit	22.8

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[2]

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:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is only descriptive endpoint.

End point values	Gepotidacin	Nitrofurantoin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	275		
Units: Participants				
Therapeutic Success	172	121		
Therapeutic Failure	120	154		

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	292	275		
Units: Participants				
Clinical Resolution	199	175		
Clinical Improvement (CI)	51	68		
Clinical Worsening (CW)	20	17		
Unable to Determine	22	15		

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	292	275		
Units: Participants				
Clinical Success	199	175		
Clinical Failure	93	100		

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	292	275		
Units: Participants				
Microbiological Eradication (ME)	213	158		
Microbiological Persistence (MP)	13	31		
Microbiological Recurrence (MR)	19	52		
Unable to Determine (UTD)	47	34		

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	292	275		
Units: Participants				
Microbiological Success	213	158		
Microbiological Failure	79	117		

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 (FU) 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 (FU) 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	292	275		
Units: Participants				
Therapeutic Success	126	95		
Therapeutic Failure	166	180		

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	292	275		
Units: Participants				
Sustained Clinical Resolution (SCR)	168	154		
Delayed Clinical Resolution (DCR)	34	35		
Clinical Improvement (CI)	15	19		
Clinical Worsening (CW)	26	32		

Clinical Recurrence (CR)	8	7		
Unable to Determine (UTD)	41	28		

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	292	275		
Units: Participants				
Sustained Microbiological Eradication (SME)	154	119		
Microbiological Persistence (MP)	19	44		
Microbiological Recurrence (MR)	29	23		
Delayed Microbiological Eradication (DME)	20	28		
Unable to Determine (UTD)	70	61		

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	292	275		
Units: Participants				
Microbiological Success	154	119		
Microbiological Failure	138	156		

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	292	275		
Units: Participants				
Clinical Success	168	154		
Clinical Failure	124	121		

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	805	800		
Units: Participants				
Clinical Success	549	517		
Clinical Failure	256	283		

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	805	800		
Units: Participants				
Clinical Resolution	549	517		
Clinical Improvement	153	199		
Clinical Worsening	36	39		
Unable to Determine	67	45		

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	805	800		
Units: Participants				
Clinical Success	478	443		
Clinical Failure	327	357		

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 Sustained Clinical Response (SCR), Delayed Clinical Response (DCR), CI, CW, Clinical Recurrence (CR) and UTD. SCR at FU was resolution of symptoms of acute cystitis demonstrated at 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. UTD outcome criteria at FU were BL score missing, FU assessment missing or received other AB not for current infection (uUTI) prior to 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	805	800		
Units: Participants				
Sustained Clinical Resolution (SCR)	478	443		
Delayed Clinical Resolution (DCR)	108	116		
Clinical Improvement (CI)	40	52		
Clinical Worsening (CW)	51	65		
Clinical Recurrence (CR)	25	28		
Unable to Determine (UTD)	103	96		

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	804	798		
Units: Participants	285	200		

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	804	798		
Units: Participants	5	5		

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	736	737		
Units: Giga cells per Liter (10^9 cells/L)				
arithmetic mean (standard deviation)				
Eosinophils, Baseline	0.161 (± 0.1350)	0.163 (± 0.1331)		
Eosinophils, On-Therapy	0.006 (± 0.0841)	0.013 (± 0.0814)		
Eosinophils, Test of Cure	0.015 (± 0.0906)	0.018 (± 0.1081)		
Basophils, Baseline	0.054 (± 0.0227)	0.053 (± 0.0228)		
Basophils, On-Therapy	-0.001 (± 0.0195)	0.001 (± 0.0194)		
Basophils, Test of Cure	0.000 (± 0.0209)	0.001 (± 0.0183)		
Lymphocytes, Baseline	2.091 (± 0.6954)	2.121 (± 0.7122)		
Lymphocytes, On-Therapy	-0.018 (± 0.4523)	-0.076 (± 0.5051)		
Lymphocytes, Test of Cure	-0.010 (± 0.5292)	0.059 (± 0.5839)		
Monocytes, Baseline	0.529 (± 0.1803)	0.525 (± 0.1790)		
Monocytes, On-Therapy	-0.020 (± 0.1487)	0.003 (± 0.1711)		
Monocytes, Test of Cure	-0.029 (± 0.1731)	-0.012 (± 0.1778)		
Neutrophils, Baseline	4.582 (± 1.8893)	4.755 (± 1.8821)		
Neutrophils, On-Therapy	-0.490 (± 1.6201)	-0.453 (± 1.7453)		
Neutrophils, Test of Cure	-0.534 (± 2.0207)	-0.494 (± 1.9072)		
Platelets, Baseline	280.3 (± 68.46)	287.2 (± 73.51)		
Platelets, On-Therapy	-1.1 (± 33.03)	-2.5 (± 36.67)		
Platelets, Test of Cure	6.8 (± 42.12)	5.5 (± 58.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in hematology parameter: hemoglobin level

End point title	Change from baseline in hematology parameter: hemoglobin level

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	739	737		
Units: Gram per Liter (g/L)				
arithmetic mean (standard deviation)				
Baseline	132.5 (± 13.25)	131.7 (± 14.28)		
On-Therapy	-1.5 (± 6.74)	-1.9 (± 6.82)		
Test of Cure	-1.3 (± 7.44)	-1.4 (± 8.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in hematology parameter: hematocrit level

End point title	Change from baseline in hematology parameter: hematocrit level

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	739	737		
Units: Percentage of hematocrit				
arithmetic mean (standard deviation)				
Baseline	0.4314 (± 0.04146)	0.4292 (± 0.04348)		
On-Therapy	-0.0033 (± 0.02832)	-0.0041 (± 0.02715)		
Test of Cure	-0.0045 (± 0.02806)	-0.0029 (± 0.03194)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in hematology parameter: erythrocytes (RBC) count

End point title	Change from baseline in hematology parameter: erythrocytes (RBC) count

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	739	737		
Units: Tera cells per Liter (10^12 cells/L)				
arithmetic mean (standard deviation)				
Baseline	4.539 (± 0.4211)	4.539 (± 0.4379)		
On-Therapy	-0.046 (± 0.2309)	-0.060 (± 0.2513)		
Test of Cure	-0.038 (± 0.2634)	-0.049 (± 0.3052)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in hematology parameter: mean corpuscular hemoglobin (MCH)

End point title	Change from baseline in hematology parameter: mean corpuscular hemoglobin (MCH)

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	739	737		
Units: Picogram (pg)				
arithmetic mean (standard deviation)				
Baseline	29.28 (± 2.537)	29.09 (± 2.644)		
On-Therapy	-0.02 (± 0.795)	-0.02 (± 0.820)		
Test of Cure	-0.04 (± 0.780)	0.02 (± 0.917)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in hematology parameter: mean corpuscular volume (MCV)

End point title	Change from baseline in hematology parameter: mean corpuscular volume (MCV)

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	739	737		
Units: Femtolitre (fL)				
arithmetic mean (standard deviation)				
Baseline	95.30 (± 7.191)	94.82 (± 7.511)		
On-Therapy	0.26 (± 4.287)	0.35 (± 4.303)		
Test of Cure	-0.15 (± 4.049)	0.39 (± 4.730)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in clinical chemistry parameters: serum blood urea nitrogen (BUN), glucose non-fasting, calcium, chloride, sodium, magnesium, phosphate, and potassium levels

End point title	Change from baseline in clinical chemistry parameters: serum blood urea nitrogen (BUN), glucose non-fasting, calcium, chloride, sodium, magnesium, phosphate, and potassium levels

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	781	777		
Units: millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
Serum Urea Nitrogen, Baseline	4.742 (± 2.1107)	4.724 (± 1.8645)		
Serum Urea Nitrogen, On- Therapy	-0.056 (± 1.4269)	-0.018 (± 1.1663)		
Serum Urea Nitrogen, Test of Cure	0.022 (± 1.4000)	0.131 (± 1.4826)		
Serum Calcium, Baseline	2.363 (± 0.1196)	2.362 (± 0.1083)		
Serum Calcium, On-Therapy	-0.010 (± 0.0950)	-0.018 (± 0.0944)		
Serum Calcium, Test of Cure	-0.014 (± 0.1070)	-0.016 (± 0.0981)		
Serum Chloride, Baseline	101.0 (± 3.27)	100.9 (± 3.27)		
Serum Chloride, On-Therapy	0.3 (± 2.80)	0.1 (± 2.85)		
Serum Chloride, Test of Cure	0.4 (± 2.93)	0.4 (± 3.02)		
Serum Glucose, Baseline	5.590 (± 1.9980)	5.719 (± 2.1915)		
Serum Glucose, On-Therapy	0.230 (± 1.5120)	0.328 (± 1.9380)		
Serum Glucose, Test of Cure	0.215 (± 1.4412)	0.266 (± 1.6667)		
Serum Magnesium, Baseline	0.839 (± 0.0749)	0.835 (± 0.0802)		
Serum Magnesium, On-Therapy	-0.001 (± 0.0635)	-0.015 (± 0.0616)		
Serum Magnesium, Test of Cure	-0.011 (± 0.0674)	-0.015 (± 0.0689)		
Serum Potassium, Baseline	4.32 (± 0.414)	4.27 (± 0.415)		
Serum Potassium, On-Therapy	-0.04 (± 0.417)	-0.03 (± 0.428)		
Serum Potassium, Test of Cure	-0.03 (± 0.438)	0.00 (± 0.461)		
Serum Phosphate, Baseline	1.141 (± 0.1828)	1.139 (± 0.1725)		
Serum Phosphate, On-Therapy	-0.005 (± 0.1782)	-0.027 (± 0.1836)		
Serum Phosphate, Test of Cure	0.002 (± 0.1851)	-0.004 (± 0.1939)		
Serum Sodium, Baseline	138.8 (± 2.64)	138.8 (± 2.76)		

Serum Sodium, On-Therapy	0.0 (± 2.64)	-0.2 (± 2.64)		
Serum Sodium, Test of Cure	0.2 (± 2.91)	0.1 (± 2.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in clinical chemistry parameters: total bilirubin, direct bilirubin and creatinine levels

End point title	Change from baseline in clinical chemistry parameters: total bilirubin, direct bilirubin and creatinine levels

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	779	776		
Units: micromoles per Liter (umol/L)				
arithmetic mean (standard deviation)				
Serum Direct Bilirubin, Baseline	4.61 (± 1.669)	4.47 (± 1.128)		
Serum Direct Bilirubin, On- Therapy	-0.18 (± 1.192)	-0.18 (± 1.114)		
Serum Direct Bilirubin, Test of Cure	-0.19 (± 1.059)	0.15 (± 1.288)		
Serum Total Bilirubin, Baseline	6.57 (± 3.940)	6.56 (± 3.518)		
Serum Total Bilirubin, On-Therapy	-0.28 (± 2.510)	-0.42 (± 2.672)		
Serum Total Bilirubin, Test of Cure	-0.01 (± 2.976)	-0.29 (± 3.230)		
Serum Creatinine, Baseline	58.8 (± 30.59)	58.1 (± 17.22)		
Serum Creatinine, On-Therapy	0.8 (± 30.31)	0.3 (± 10.31)		
Serum Creatinine, Test of Cure	1.7 (± 14.00)	1.5 (± 13.40)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in clinical chemistry parameters: albumin and total protein levels

End point title	Change from baseline in clinical chemistry parameters: albumin

	and total protein levels

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	781	777		
Units: gram per Liter (g/L)				
arithmetic mean (standard deviation)				
Serum Albumin, Baseline	45.2 (± 3.33)	45.2 (± 3.11)		
Serum Albumin, On-Therapy	-0.4 (± 2.38)	-0.8 (± 2.56)		
Serum Albumin, Test of Cure	-0.5 (± 2.65)	-0.6 (± 2.84)		
Serum Protein, Baseline	71.5 (± 5.12)	71.6 (± 4.72)		
Serum Protein, On-Therapy	-0.7 (± 3.71)	-1.2 (± 3.89)		
Serum Protein, Test of Cure	-1.0 (± 4.19)	-1.1 (± 4.32)		

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

End point title	Change from baseline in clinical chemistry parameters: aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) levels

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	777	774		
Units: Units per Liter (U/L)				
arithmetic mean (standard deviation)				
Serum ALT, Baseline	20.3 (± 20.34)	19.5 (± 14.66)		

Serum ALT, On-Therapy	0.2 (± 10.8)	-0.1 (± 7.9)		
Serum ALT, Test of Cure	0.4 (± 15.81)	-0.2 (± 9.93)		
Serum AST, Baseline	21.0 (± 13.72)	20.2 (± 10.48)		
Serum AST, On-Therapy	0.1 (± 9.83)	0.0 (± 7.90)		
Serum AST, Test of Cure	0.9 (± 9.89)	-0.5 (± 8.29)		
Serum ALP, Baseline	81.4 (± 29.96)	81.7 (± 28.99)		
Serum ALP, On- Therapy	-0.5 (± 9.61)	-0.1 (± 12.91)		
Serum ALP, Test of Cure	-1.0 (± 12.00)	-0.4 (± 15.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with urinalysis dipstick results

End point title	Number of participants with urinalysis dipstick results

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	789	783		
Units: Participants				
GLU, Baseline, Negative	751	738		
GLU, Baseline, 50 mg/dL	4	5		
GLU, Baseline, 150 mg/dL	3	4		
GLU, Baseline, >= 500 mg/dL	21	26		
GLU, On-Therapy, Negative	700	697		
GLU, On-Therapy, 50 mg/dL	7	7		
GLU, On-Therapy, 150 mg/dL	1	5		
GLU, On-Therapy, >= 500 mg/dL	23	28		
GLU, Test of Cure, Negative	686	693		
GLU, Test of Cure, 50 mg/dL	9	10		
GLU, Test of Cure, 150 mg/dL	12	4		
GLU, Test of Cure, >= 500 mg/dL	12	20		
PRO, Baseline, Negative	524	529		
PRO, Baseline, 30 mg/dL	171	149		
PRO, Baseline, 100 mg/dL	78	85		
PRO, Baseline, >=500 mg/dL	5	6		

PRO, On-Therapy, Negative	575	631		
PRO, On-Therapy, 30 mg/dL	110	83		
PRO, On-Therapy, 100 mg/dL	43	19		
PRO, On-Therapy, >=500 mg/dL	3	4		
PRO, Test of Cure, Negative	605	605		
PRO, Test of Cure, 30 mg/dL	88	88		
PRO, Test of Cure, 100 mg/dL	25	34		
PRO, Test of Cure, >=500 mg/dL	1	0		
BLO, Baseline, Positive	0	2		
BLO, Baseline, Negative	345	348		
BLO, Baseline, Trace	2	0		
BLO, Baseline, Small	229	217		
BLO, Baseline, Moderate	128	129		
BLO, Baseline, Large	80	81		
BLO, On-Therapy, Negative	560	520		
BLO, On-Therapy, Small	116	161		
BLO, On-Therapy, Moderate	23	30		
BLO, On-Therapy, Large	32	26		
BLO, Test of Cure, Negative	517	511		
BLO, Test of Cure, Small	128	139		
BLO, Test of Cure, Moderate	49	45		
BLO, Test of Cure, Large	25	32		
KET, Baseline, Negative	754	748		
KET, Baseline, 5 mg/dL	14	18		
KET, Baseline, 20 mg/dL	11	7		
KET, On-Therapy, Negative	712	699		
KET, On-Therapy, 5 mg/dL	14	22		
KET, On-Therapy, 20 mg/dL	5	15		
KET, On-Therapy, >=80 mg/dL	0	1		
KET, Test of Cure, Negative	706	700		
KET, Test of Cure, 5 mg/dL	7	20		
KET, Test of Cure, 20 mg/dL	6	7		
NIT, Baseline, Negative	552	531		
NIT, Baseline, Positive	237	252		
NIT, On-Therapy, Negative	694	697		
NIT, On-Therapy, Positive	37	40		
NIT, Test of Cure, Negative	697	669		
NIT, Test of Cure, Positive	22	58		
LEU, Baseline, Negative	245	232		
LEU, Baseline, Trace	96	91		
LEU, Baseline, Small	75	80		
LEU, Baseline, Moderate	120	116		
LEU, Baseline, Large	251	262		
LEU, Baseline, Missing	2	1		
LEU, On-Therapy, Negative	510	475		
LEU, On-Therapy, Trace	79	82		
LEU, On-Therapy, Small	50	49		
LEU, On-Therapy, Moderate	34	57		
LEU, On-Therapy, Large	58	74		
LEU, Test of Cure, Negative	526	494		
LEU, Test of Cure, Trace	61	49		
LEU, Test of Cure, Small	43	48		

LEU, Test of Cure, Moderate	35	59		
LEU, Test of Cure, Large	54	77		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute mean values of urine potential of hydrogen (pH)

End point title	Absolute mean values of urine potential of hydrogen (pH)

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	763	764		
Units: pH				
arithmetic mean (standard deviation)				
pH, Baseline	5.7 (± 0.8)	5.7 (± 0.79)		
pH, On-Therapy	5.6 (± 0.66)	5.6 (± 0.69)		
pH, Test of Cure	5.6 (± 0.69)	5.7 (± 0.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute mean values of urine specific gravity

End point title	Absolute mean values of urine specific gravity

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	779	773		
Units: Ratio				
arithmetic mean (standard deviation)				
Baseline	1.0172 (± 0.00693)	1.0174 (± 0.00686)		
On-Therapy	1.0176 (± 0.00716)	1.0167 (± 0.00696)		
Test of Cure	1.0179 (± 0.00712)	1.0179 (± 0.00719)		

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	804	798		
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP, Baseline	122 (± 13.33)	122.7 (± 13.98)		
SBP, On-Therapy	-1.1 (± 10.14)	-1.1 (± 10.72)		
SBP, Test of Cure	-0.4 (± 11.67)	-1.8 (± 12.19)		
DBP, Baseline	76.9 (± 8.17)	77 (± 9)		
DBP, On-Therapy	-0.5 (± 7.30)	-0.6 (± 7.73)		
DBP, Test of Cure	-0.1 (± 7.98)	-1.3 (± 8.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in body temperature

End point title	Change from baseline in body temperature

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	804	798		
Units: Celsius				
arithmetic mean (standard deviation)				
Temperature, Baseline	36.61 (± 0.346)	36.63 (± 0.317)		
Temperature, On-Therapy	-0.01 (± 0.334)	-0.01 (± 0.372)		
Temperature, Test of Cure	-0.01 (± 0.349)	-0.04 (± 0.351)		

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	804	798		
Units: beats per minute (bpm)				
arithmetic mean (standard deviation)				
Pulse rate, Baseline	73.2 (± 9.64)	73.7 (± 10.32)		
Pulse rate, On-Therapy	0.9 (± 8.24)	1.3 (± 8.66)		
Pulse rate, Test of Cure	1.8 (± 9.74)	1.7 (± 9.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with maximum change from baseline in electrocardiograms (ECG) parameter: QT interval corrected for heart rate according to Bazett's formula (QTcB) at Worst-case Post-baseline

End point title	Number of participants with maximum change from baseline in electrocardiograms (ECG) parameter: QT interval corrected for heart rate according to Bazett's formula (QTcB) at Worst-case Post-baseline

End point description:

Triplicate 12-lead ECGs (over an approximate 5- to 10-minute period) were performed using an ECG machine. Baseline is defined as the latest pre-dose assessment with a non-missing value. The row titles <=450, >450 to <=480, >480 to <=500 millisecond (msec) are the values at baseline. The category titles <= 30, 31-60, >60 msec are the maximum change from baseline values. The maximum change from baseline value category was determined by comparing the baseline value category to the worst-case post-baseline value category for each participant, which considered unscheduled and out of visit window assessments. Data of number of participants with any change at worst-case post-baseline (maximum grade increase post-baseline) is presented. Safety population included all randomized participants who receive at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Day 31

End point values	Gepotidacin	Nitrofurantoin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	791	784		
Units: Participants				
<= 450 msec|<=30 msec	675	700		
>450 to <=480 msec|<=30 msec	40	37		
>480 to <=500 msec|<=30 msec	0	1		
<= 450 msec|31-60 msec	23	12		
>450 to <=480 msec|31-60 msec	2	0		
>480 to <=500 msec|31-60 msec	0	0		
<= 450 msec|>60 msec	1	0		
>450 to <=480 msec|>60 msec	0	0		
>480 to <=500 msec|>60 msec	0	0		
<= 450 msec|Missing	47	31		
>450 to <=480 msec|Missing	3	3		
>480 to <=500 msec|Missing	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Maximum Change from Baseline in Electrocardiograms (ECG) parameter- QT interval corrected for heart rate according to Fridericia's formula (QTcF) at Worst-case Post-baseline

End point title	Number of Participants with Maximum Change from Baseline in Electrocardiograms (ECG) parameter- QT interval corrected for heart rate according to Fridericia's formula (QTcF) at Worst-case Post-baseline

End point description:

Triplicate 12-lead ECGs (over an approximate 5- to 10-minute period) were performed using an ECG machine. Baseline is defined as the latest pre-dose assessment with a non-missing value. The row titles <=450 msec, >450 msec to <=480 msec are the values at baseline. The category titles <= 30, 31-60, >60 msec are the maximum change from baseline values. The maximum change from baseline value category was determined by comparing the baseline value category to the worst-case post-baseline value category for each participant, which considered unscheduled and out of visit window assessments. Data of number of participants with any change at worst-case post-baseline (maximum grade increase post-baseline) is presented. Safety population included all randomized participants who receive at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Day 31

End point values	Gepotidacin	Nitrofurantoin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	791	784		
Units: Participants				
<= 450|<=30 msec	721	742		
>450 to <=480|<=30 msec	8	4		
<= 450|31-60 msec	12	4		
>450 to <=480|31-60 msec	0	0		
<= 450|>60 msec	0	0		
>450 to <=480|>60 msec	0	0		
<= 450|Missing	50	33		
>450 to <=480|Missing	0	1		

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	25.1
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 (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	5 / 798 (0.63%)	5 / 804 (0.62%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Cardiac disorders			
Atrial fribrillation			
subjects affected / exposed	0 / 798 (0.00%)	1 / 804 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 798 (0.13%)	0 / 804 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 798 (0.00%)	1 / 804 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 798 (0.00%)	1 / 804 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 798 (0.13%)	0 / 804 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 798 (0.00%)	2 / 804 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	2 / 798 (0.25%)	0 / 804 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 798 (0.13%)	0 / 804 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Nitrofurantoin	Gepotidacin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	119 / 798 (14.91%)	235 / 804 (29.23%)	
Nervous system disorders			
Headache			
subjects affected / exposed	22 / 798 (2.76%)	21 / 804 (2.61%)	
occurrences (all)	27	23	

Dizziness			
subjects affected / exposed	11 / 798 (1.38%)	18 / 804 (2.24%)	
occurrences (all)	12	18	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 798 (1.00%)	3 / 804 (0.37%)	
occurrences (all)	8	3	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	24 / 798 (3.01%)	147 / 804 (18.28%)	
occurrences (all)	25	166	
Nausea			
subjects affected / exposed	35 / 798 (4.39%)	65 / 804 (8.08%)	
occurrences (all)	36	66	
Flatulence			
subjects affected / exposed	4 / 798 (0.50%)	28 / 804 (3.48%)	
occurrences (all)	4	29	
Faeces soft			
subjects affected / exposed	4 / 798 (0.50%)	23 / 804 (2.86%)	
occurrences (all)	4	30	
Vomiting			
subjects affected / exposed	7 / 798 (0.88%)	18 / 804 (2.24%)	
occurrences (all)	7	18	
Abdominal pain			
subjects affected / exposed	7 / 798 (0.88%)	12 / 804 (1.49%)	
occurrences (all)	8	12	
Abdominal discomfort			
subjects affected / exposed	4 / 798 (0.50%)	9 / 804 (1.12%)	
occurrences (all)	5	9	
Infections and infestations			
Fungal infection			
subjects affected / exposed	10 / 798 (1.25%)	9 / 804 (1.12%)	
occurrences (all)	10	9	
Urinary tract infection			
subjects affected / exposed	15 / 798 (1.88%)	11 / 804 (1.37%)	
occurrences (all)	15	11	

COVID-19 subjects affected / exposed occurrences (all)	5 / 798 (0.63%) 6	9 / 804 (1.12%) 9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2019	This global amendment added details for an interim analysis to be conducted and managed by an Independent Data Monitoring Committee and sample size impact on the primary analysis population.
14 April 2021	This global amendment added a secondary objective to assess clinical response in the primary analysis population also also increased the planned total enrollment population.
03 November 2021	This global amendment provided clarification on Inclusion Criteria 3 and 4, including no requirement for contraception use or abstinence within 14 days of study entry in women of childbearing potential (WOCBP) with a negative high sensitivity urine pregnancy test result at Baseline (Day 1), expanded the On therapy Visit window, allowed flexible options for pregnancy testing and dose administration for the On-therapy Visit, and further defined the optimum window for pregnancy testing while participants were receiving study treatment. The amendment also included additional minor administrative edits.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported