Clinical trial results:
A Phase III, Randomized, Multicenter, Open-Label Study in Adolescent and Adult Participants Comparing the Efficacy and Safety of Gepotidacin to Ceftriaxone Plus Azithromycin in the Treatment of Uncomplicated Urogenital Gonorrhea Caused by Neisseria gonorrhoeae

Summary

EudraCT number	2018-001780-23
Trial protocol	GB DE
Global end of trial date	10 October 2023

Results information

Result version number	v1 (current)
This version publication date	17 May 2024
First version publication date	17 May 2024

Trial information

Trial identification

Sponsor protocol code	BTZ116577

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04010539
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West 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-PIP02-18
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	14 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 October 2023
Global end of trial reached?	Yes
Global end of trial date	10 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1)To evaluate the efficacy of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin to treat participants with uncomplicated urogenital gonorrhea caused by Neisseria gonorrhoeae (NG)
(2)To evaluate the efficacy of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin to treat participants with rectal gonorrhea caused by NG
(3) To evaluate the efficacy of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin to treat participants with pharyngeal gonorrhea caused by NG
(4) To evaluate the safety and tolerability of oral gepotidacin compared to IM ceftriaxone plus oral azithromycin

Protection of trial subjects:

Not Applicable

Background therapy:

Not Applicable

Evidence for comparator: -

Actual start date of recruitment	21 October 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 105
Country: Number of subjects enrolled	Germany: 139
Country: Number of subjects enrolled	Mexico: 15
Country: Number of subjects enrolled	United Kingdom: 98
Country: Number of subjects enrolled	United States: 85
Country: Number of subjects enrolled	Spain: 186
Worldwide total number of subjects	628
EEA total number of subjects	325

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)	2
Adults (18-64 years)	623
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

None

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Gepotidacin

Arm description:

Participants with uncomplicated urogenital gonorrhea (GC) were randomized to receive first dose of 3000 milligram (mg) (4*750 mg, tablets) gepotidacin orally on Day 1. Participants self-administered second dose of 3000 mg (4*750 mg, tablets) gepotidacin orally 10-12 hours after first dose. All doses were to be 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 urogenital gonorrhea (GC) were randomized to receive first dose of 3000 milligram (mg) (4*750 mg, tablets) gepotidacin orally on Day 1. Participants self-administered second dose of 3000 mg (4*750 mg, tablets) gepotidacin orally 10-12 hours after first dose. All doses were to be administered after food consumption and with water.

Arm title	Ceftriaxone plus azithromycin

Arm description:

Participants with uncomplicated urogenital gonorrhea (GC) were randomized to receive single dose of 500 mg Ceftriaxone as intramuscular sterile powder reconstituted with appropriate diluent plus single oral dose of 1 gram (g) Azithromycin (2*500 mg, tablets) on Day 1. Azithromycin was to be administered after food consumption and with water.

Arm type	Active comparator
Investigational medicinal product name	Ceftriaxone plus azithromycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Powder for injection
Routes of administration	Oral use, Intramuscular use

Dosage and administration details:

Participants with uncomplicated urogenital gonorrhea (GC) were randomized to receive single dose of 500 mg Ceftriaxone as intramuscular sterile powder reconstituted with appropriate diluent plus single oral dose of 1 gram (g) Azithromycin (2*500 mg, tablets) on Day 1. Azithromycin was to be administered after food consumption and with water.

Number of subjects in period 1	Gepotidacin	Ceftriaxone plus azithromycin
Started	314	314
Safety population	309	313
Microbiological ITT(Micro-ITT)population	202 [1]	204 [2]
Micro-ITT Rectal population	26 [3]	15 [4]
Micro-ITT Pharyngeal population	18 [5]	17 [6]
Completed	294	295
Not completed	20	19
Consent withdrawn by subject	4	1
Physician decision	-	2
Adverse event, non-fatal	3	-
Protocol Deviation	-	1
Randomized in Error/ Mistake	2	-
Participant Did Not Receive IP	-	1
Lost to follow-up	10	14
Eligibility Criteria Unable to Evaluate	1	-

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 milestones are a subset of started population. Hence number of participants at the milestones 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 milestones are a subset of started population. Hence number of participants at the milestones 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 milestones are a subset of started population. Hence number of participants at the milestones 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 milestones are a subset of started population. Hence number of participants at the milestones 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 milestones are a subset of started population. Hence number of participants at the milestones 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 milestones are a subset of started population. Hence number of participants at the milestones are less than started.

Baseline characteristics

Reporting groups	
Reporting group title	Gepotidacin
Reporting group description:	
Participants with uncomplicated urogenital gonorrhea (GC) were randomized to receive first dose of 3000 milligram (mg) (4*750 mg, tablets) gepotidacin orally on Day 1. Participants self-administered second dose of 3000 mg (4*750 mg, tablets) gepotidacin orally 10-12 hours after first dose. All doses were to be administered after food consumption and with water.	
Reporting group title	Ceftriaxone plus azithromycin
Reporting group description:	
Participants with uncomplicated urogenital gonorrhea (GC) were randomized to receive single dose of 500 mg Ceftriaxone as intramuscular sterile powder reconstituted with appropriate diluent plus single oral dose of 1 gram (g) Azithromycin (2*500 mg, tablets) on Day 1. Azithromycin was to be administered after food consumption and with water.	

Reporting group values	Gepotidacin	Ceftriaxone plus azithromycin	Total
Number of subjects	314	314	628
Age categorical Units: Participants			
12-84 years	314	314	628
Age Continuous Units: Years			
arithmetic mean	33.9	33.7	
standard deviation	± 10.42	± 10.70	-
Sex: Female, Male Units: Participants			
Female	35	34	69
Male	279	280	559
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	9	10	19
Asian	12	17	29
Native Hawaiian or Other Pacific Islander	7	2	9
Black or African American	49	39	88
White	231	241	472
More than one race	6	5	11
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Gepotidacin

Reporting group description:

Participants with uncomplicated urogenital gonorrhea (GC) were randomized to receive first dose of 3000 milligram (mg) (4*750 mg, tablets) gepotidacin orally on Day 1. Participants self-administered second dose of 3000 mg (4*750 mg, tablets) gepotidacin orally 10-12 hours after first dose. All doses were to be administered after food consumption and with water.

Reporting group title	Ceftriaxone plus azithromycin

Reporting group description:

Participants with uncomplicated urogenital gonorrhea (GC) were randomized to receive single dose of 500 mg Ceftriaxone as intramuscular sterile powder reconstituted with appropriate diluent plus single oral dose of 1 gram (g) Azithromycin (2*500 mg, tablets) on Day 1. Azithromycin was to be administered after food consumption and with water.

Primary: Number of Participants with Culture-Confirmed Bacterial Eradication of Neisseria Gonorrhoeae (NG) From the Urogenital Site at the Test-Of-Cure (TOC) Visit (Day 4 to 8) - Micro-ITT population

End point title	Number of Participants with Culture-Confirmed Bacterial Eradication of Neisseria Gonorrhoeae (NG) From the Urogenital Site at the Test-Of-Cure (TOC) Visit (Day 4 to 8) - Micro-ITT population

End point description:

Urogenital specimens obtained for bacteriological culture at Baseline and TOC visits were compared to determine microbiological outcome. Microbiological Success: Culture-confirmed elimination of baseline NG from a bacteriology sample taken at TOC visit without participant receiving other systemic antimicrobials before this visit. Microbiological Failure categorized as Bacterial Persistence (BP): Culture-confirmed persistence of baseline NG pathogen from a bacteriology sample taken at TOC visit without the participant receiving other systemic antimicrobials before this visit. Unable To Determine (UTD): Inability to determine TOC NG pathogen outcome (e.g no bacteriological sample taken for culture, sample lost, visit did not occur etc) or participant received other systemic antimicrobials before the TOC visit.

End point type	Primary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	204		
Units: Participants				
Microbiological success	187	186		
Microbiological failure, BP	0	0		
Microbiological failure, UTD	15	18		

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The difference in microbiological success rates between treatment groups (Gepotidacin - Ceftriaxone plus azithromycin) was calculated using the Miettinen-Nurminen Summary Score Method adjusted for sex and sexual orientation combination. Superiority was declared if the lower limit of the 2-sided 95% confidence interval for the difference was above 0.0%.

Comparison groups	Gepotidacin v Ceftriaxone plus azithromycin
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5072
Method	1-sided p-value for TestOfSuperiority
Parameter estimate	Adjusted Difference in Percent
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	5.5

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The difference in microbiological success rates between treatment groups (Gepotidacin - Ceftriaxone plus azithromycin) was calculated using the Miettinen-Nurminen Summary Score Method adjusted for sex and sexual orientation combination. Non-inferiority was declared if the lower limit of the 2-sided 95% confidence interval for the difference was above -10.0%.

Comparison groups	Gepotidacin v Ceftriaxone plus azithromycin
Number of subjects included in analysis	406
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Adjusted Difference in Percent
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	5.5

Secondary: Number of Participants with Culture-Confirmed Bacterial Eradication of NG From the Rectal Site at the TOC visit - Micro-ITT rectal population

End point title	Number of Participants with Culture-Confirmed Bacterial Eradication of NG From the Rectal Site at the TOC visit - Micro-ITT rectal population

End point description:

Urogenital specimens obtained for bacteriological culture at Baseline and TOC visits were compared to determine microbiological outcome. Microbiological Success: Culture-confirmed elimination of baseline NG from a bacteriology sample taken at the TOC visit without participant receiving other systemic antimicrobials before this visit. Microbiological Failure categorized as BP: Culture-confirmed persistence of baseline NG pathogen from a bacteriology sample taken at the TOC visit without the participant receiving other systemic antimicrobials before this visit. UTD: Inability to determine the TOC NG

pathogen outcome (e.g., no bacteriological sample taken for culture, sample lost, visit did not occur etc.) or participant received other systemic antimicrobials before the TOC visit. Micro-ITT Rectal population: participants who met the definition of the Micro-ITT and have confirmed NG isolated that is ceftriaxone susceptible from baseline culture of their rectal specimen.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	15		
Units: Participants				
Microbiological success	26	12		
Microbiological failure, BP	0	0		
Microbiological failure, UTD	0	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any treatment-emergent adverse events (TEAEs) and any serious adverse events (SAEs) - Safety population

End point title	Number of participants with any treatment-emergent adverse events (TEAEs) and any serious adverse events (SAEs) - Safety population

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 treatment, whether or not considered related to the study treatment. A TEAE is an event that emerges during treatment having been absent pretreatment or worsens relative to the pretreatment state. An SAE is defined as any untoward medical occurrence that, at any dose, results in death; was life threatening; required hospitalization or prolongation of existing hospitalization; resulted in disability/incapacity; was a congenital anomaly/birth defect.

End point type	Secondary

End point timeframe:

Up to 21 days

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309	313		
Units: Participants				
Any TEAEs	230	104		
Any SAEs	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Culture-Confirmed Bacterial Eradication of NG from the Pharyngeal Site at the TOC visit - Micro-ITT pharyngeal population

End point title	Number of Participants with Culture-Confirmed Bacterial Eradication of NG from the Pharyngeal Site at the TOC visit - Micro-ITT pharyngeal population

End point description:

Urogenital specimens obtained for bacteriological culture at Baseline and TOC visits were compared to determine microbiological outcome. Microbiological Success: Culture-confirmed elimination of baseline NG from a bacteriology sample taken at the TOC visit without participant receiving other systemic antimicrobials before this visit. Microbiological Failure categorized as BP: Culture-confirmed persistence of baseline NG pathogen from a bacteriology sample taken at the TOC visit without the participant receiving other systemic antimicrobials before this visit. UTD: Inability to determine the TOC NG pathogen outcome (e.g., no bacteriological sample taken for culture, sample lost, visit did not occur etc.) or participant received other systemic antimicrobials before the TOC visit. Micro-ITT Pharyngeal population:participants who met the definition of the Micro-ITT Population and have confirmed NG isolated that is ceftriaxone susceptible from baseline culture of their pharyngeal specimen

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	17		
Units: Participants				
Microbiological success	14	16		
Microbiological failure, BP	2	0		
Microbiological failure, UTD	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (CFB) in Hematology Parameters: Basophils, Eosinophil, Leukocytes, Neutrophils, Platelets, Lymphocytes, Monocytes, Neutrophils and Nucleated Erythrocytes - Safety population

End point title	Change from Baseline (CFB) in Hematology Parameters: Basophils, Eosinophil, Leukocytes, Neutrophils, Platelets, Lymphocytes, Monocytes, Neutrophils and Nucleated Erythrocytes - Safety population

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters: basophils, eosinophil, leukocytes, neutrophils, platelets, lymphocytes, monocytes, neutrophils and nucleated erythrocytes. Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	293		
Units: Giga cells per liter (10^9 cells/L)				
arithmetic mean (standard deviation)				
Basophils, Baseline (Day 1)	0.044 (± 0.0196)	0.045 (± 0.0222)		
Basophils, CFB to TOC	0.001 (± 0.0167)	0.000 (± 0.0152)		
Eosinophils, Baseline (Day 1)	0.154 (± 0.2117)	0.160 (± 0.1384)		
Eosinophils, CFB to TOC	0.009 (± 0.1289)	0.018 (± 0.0827)		
Leukocytes, Baseline (Day 1)	7.143 (± 2.2808)	7.507 (± 2.2045)		
Leukocytes, CFB to TOC	-0.811 (± 1.8536)	-1.267 (± 1.9362)		
Neutrophils, Baseline (Day 1)	4.443 (± 1.9621)	4.774 (± 1.9355)		
Neutrophils, CFB to TOC	-1.062 (± 1.7309)	-1.473 (± 1.8860)		
Platelets, Baseline (Day 1)	260.3 (± 61.79)	268.4 (± 69.26)		
Platelets, CFB to TOC	10.2 (± 32.14)	9.7 (± 34.94)		
Lymphocytes, Baseline (Day 1)	1.934 (± 0.5941)	1.948 (± 0.6321)		
Lymphocytes, CFB to TOC	0.277 (± 0.5205)	0.245 (± 0.5511)		
Monocytes, Baseline (Day 1)	0.559 (± 0.2209)	0.572 (± 0.1877)		
Monocytes, CFB to TOC	-0.034 (± 0.1917)	-0.053 (± 0.1782)		
Nucleated Erythrocytes, Baseline (Day 1)	0.002 (± 0.0047)	0.001 (± 0.0038)		
Nucleated Erythrocytes, CFB to TOC	0.000 (± 0.0070)	0.001 (± 0.0059)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hematology Parameters: Mean Corpuscular

Hemoglobin Concentration (MCHC) and Hemoglobin (Hb) - Safety population

End point title	Change from Baseline in Hematology Parameters: Mean Corpuscular Hemoglobin Concentration (MCHC) and Hemoglobin (Hb) - Safety population

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters: mean corpuscular hemoglobin concentration and hemoglobin. Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	293		
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
MCHC, Baseline (Day 1)	318.5 (± 16.27)	318.8 (± 16.12)		
MCHC, CFB to TOC	2.4 (± 10.67)	0.3 (± 11.27)		
Hb, Baseline (Day 1)	149.1 (± 12.83)	149.2 (± 12.58)		
Hb, CFB to TOC	0.00 (± 6.70)	0.6 (± 6.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hematology Parameter: Hematocrit - Safety population

End point title	Change from Baseline in Hematology Parameter: Hematocrit - Safety population

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameter: hematocrit. Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	293		
Units: Percentage				
arithmetic mean (standard deviation)				
Baseline (Day 1)	0.4691 (± 0.04205)	0.4687 (± 0.04104)		
CFB to TOC	-0.0038 (± 0.02526)	0.0012 (± 0.02666)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hematology Parameter: Erythrocytes - Safety population

End point title	Change from Baseline in Hematology Parameter: Erythrocytes - Safety population

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameter: red blood cell (RBC) count. Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	293		
Units: Trillion cells per liter (10^12 cells/L)				
arithmetic mean (standard deviation)				
Baseline (Day 1)	4.911 (± 0.4722)	4.926 (± 0.4601)		
CFB to TOC	0.003 (± 0.2261)	0.019 (± 0.2332)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hematology Parameter: Mean Corpuscular Volume (MCV) - Safety population

End point title	Change from Baseline in Hematology Parameter: Mean

	Corpuscular Volume (MCV) - Safety population

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameter: mean corpuscular volume (MCV). Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	293		
Units: Femtoliters (fL)				
arithmetic mean (standard deviation)				
Baseline (Day 1)	95.79 (± 6.266)	95.43 (± 6.760)		
CFB to TOC	-0.85 (± 3.104)	-0.12 (± 3.084)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Hematology Parameter: Mean Corpuscular Hemoglobin (MCH) - Safety population

End point title	Change from Baseline in Hematology Parameter: Mean Corpuscular Hemoglobin (MCH) - Safety population

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameter: mean corpuscular hemoglobin (MCH). Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	293		
Units: Picograms (pg)				
arithmetic mean (standard deviation)				
Baseline (Day 1)	30.46 (± 1.978)	30.38 (± 1.987)		
CFB to TOC	-0.03 (± 0.451)	0.00 (± 0.594)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Chemistry Parameters: Urea Nitrogen (UN), Glucose, Calcium, Chloride, Sodium, Magnesium and Potassium - Safety population

End point title	Change from Baseline in Clinical Chemistry Parameters: Urea Nitrogen (UN), Glucose, Calcium, Chloride, Sodium, Magnesium and Potassium - Safety population

End point description:

Blood samples were collected for the assessment of change from baseline in clinincal chemistry parameters: urea nitrogen (UN), glucose, calcium, chloride, sodium, magnesium and potassium. Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	306		
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
UN, Baseline (Day 1)	4.793 (± 1.4293)	4.800 (± 1.4669)		
UN, CFB to TOC	0.190 (± 1.1640)	0.282 (± 1.1920)		
Glucose, Baseline	5.049 (± 1.0557)	5.090 (± 1.1183)		
Glucose, CFB to TOC	0.227 (± 0.9425)	0.064 (± 0.9684)		
Calcium, Baseline (Day 1)	2.387 (± 0.0986)	2.387 (± 0.0954)		
Calcium, CFB to TOC	-0.009 (± 0.0852)	-0.015 (± 0.0871)		
Chloride, Baseline (Day 1)	101.7 (± 2.26)	101.7 (± 2.30)		
Chloride, CFB to TOC	0.7 (± 2.57)	0.5 (± 2.40)		
Sodium, Baseline (Day 1)	139.6 (± 2.11)	139.6 (± 2.02)		
Sodium, CFB to TOC	0.2 (± 2.19)	0.1 (± 2.44)		
Magnesium, Baseline (Day 1)	0.854 (± 0.0612)	0.855 (± 0.0637)		
Magnesium, CFB to TOC	-0.003 (± 0.0604)	-0.004 (± 0.0584)		
Potassium, Baseline (Day 1)	4.29 (± 0.323)	4.30 (± 0.332)		

Potassium, CFB to TOC	-0.04 (± 0.336)	-0.03 (± 0.345)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Chemistry Parameters: Bilirubin, Direct Bilirubin and Creatinine - Safety population

End point title	Change from Baseline in Clinical Chemistry Parameters: Bilirubin, Direct Bilirubin and Creatinine - Safety population

End point description:

Blood samples were collected for the assessment of change from baseline in clinical chemistry parameters: bilirubin, direct bilirubin and creatinine levels. Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	303	305		
Units: Micromoles per liter (umol/L)				
arithmetic mean (standard deviation)				
Bilirubin, Baseline (Day 1)	8.54 (± 5.861)	7.71 (± 4.806)		
Bilirubin, CFB to TOC	-0.05 (± 5.025)	-0.14 (± 3.914)		
Direct Bilirubin, Baseline (Day 1)	3.83 (± 1.248)	3.76 (± 1.210)		
Direct Bilirubin, CFB to TOC	-0.02 (± 0.897)	0.01 (± 0.876)		
Creatinine, Baseline (Day 1)	75.9 (± 34.12)	75.0 (± 20.63)		
Creatinine, CFB to TOC	-0.2 (± 34.08)	2.6 (± 9.52)		

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) - Safety population

End point title	Change from Baseline in Clinical Chemistry Parameters: Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT) and Alkaline Phosphatase (ALP) - Safety population

End point description:

Blood samples were collected for the assessment of change from baseline in clinincal chemistry parameters: aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP). Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	303	305		
Units: International units per Liter (IU/L)				
arithmetic mean (standard deviation)				
AST, Baseline (Day 1)	24.4 (± 15.30)	24.2 (± 16.29)		
AST, CFB to TOC	2.8 (± 19.51)	0.9 (± 13.25)		
ALT, Baseline (Day 1)	23.7 (± 18.78)	23.7 (± 14.35)		
ALT, CFB to TOC	1.4 (± 12.59)	1.1 (± 7.64)		
ALP, Baseline (Day 1)	76.0 (± 20.86)	77.1 (± 26.53)		
ALP, CFB to TOC	-0.4 (± 7.73)	-1.5 (± 7.80)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Clinical Chemistry Parameters: Albumin and Protein - Safety population

End point title	Change from Baseline in Clinical Chemistry Parameters: Albumin and Protein - Safety population

End point description:

Blood samples were collected for the assessment of change from baseline in clinical chemistry parameters: albumin and protein. Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	305	306		
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				

Albumin, Baseline (Day 1)	46.9 (± 3.12)	46.8 (± 3.19)		
Albumin, CFB to TOC	-0.3 (± 2.35)	-0.3 (± 2.67)		
Protein, Baseline (Day 1)	73.1 (± 4.80)	73.3 (± 4.85)		
Protein, CFB to TOC	-0.5 (± 3.86)	-0.5 (± 4.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Urinalysis Dipstick Results - Safety population

End point title	Number of Participants with Urinalysis Dipstick Results - Safety population

End point description:

Urine samples were collected for urinalysis: Glucose, Protein, Occult Blood and Ketones. The dipstick test gives results in a semi-quantitative manner, and results can be read as Negative, Small, Moderate, Large, Positive, 5 milligram per deciliter (mg/dL), 20 mg/dL, 30 mg/dL 50 mg/dL, 100 mg/dL, 150 mg/dL and >=500 mg/dL indicating concentrations in the urine sample. In the row title (Glucose, Baseline, Negative), Glucose indicates parameter, Baseline is the visit and Negative indicates the concentration in the urine sample. Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	307		
Units: Participants				
Glucose, Baseline (Day 1), Negative	296	305		
Glucose, Baseline (Day 1), 150 mg/dL	0	0		
Glucose, Baseline (Day 1), >=500 mg/dL	3	2		
Glucose, TOC, Negative	284	283		
Glucose, TOC, 150 mg/dL	1	1		
Glucose, TOC, >=500 mg/dL	2	1		
Ketones, Baseline (Day 1), Negative	288	300		
Ketones, Baseline (Day 1), 5 mg/dL	10	7		
Ketones, Baseline (Day 1), 20 mg/dL	1	0		
Ketones, TOC, Negative	279	279		
Ketones, TOC, 5 mg/dL	7	6		
Ketones, TOC, 20 mg/dL	1	0		
Occult Blood, Baseline (Day 1), Negative	202	192		
Occult Blood, Baseline (Day 1), Small	77	91		
Occult Blood, Baseline (Day 1), Moderate	18	19		
Occult Blood, Baseline (Day 1), Large	2	5		
Occult Blood, TOC, Negative	251	252		

Occult Blood, TOC, Small	30	24		
Occult Blood, TOC, Moderate	3	6		
Occult Blood, TOC, Large	3	3		
Protein, Baseline (Day 1), Negative	212	210		
Protein, Baseline (Day 1), 30 mg/dL	79	83		
Protein, Baseline (Day 1), 100 mg/dL	8	13		
Protein, Baseline (Day 1), >=500 mg/dL	0	1		
Protein, TOC, Negative	239	244		
Protein, TOC, 30 mg/dL	46	37		
Protein, TOC, 100 mg/dL	2	4		
Protein, TOC, >=500 mg/dL	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Signs: Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) - Safety population

End point title	Change from Baseline in Vital Signs: Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) - Safety population

End point description:

SBP and DBP were measured in a semi-supine position after 5 minutes rest. Baseline (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	307	313		
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP, Baseline (Day 1)	123.9 (± 13.69)	125.1 (± 14.41)		
SBP, CFB to TOC	-0.4 (± 12.61)	-0.5 (± 12.86)		
DBP, Baseline (Day 1)	76.7 (± 10.77)	77.2 (± 10.50)		
DBP, CFB to TOC	0.1 (± 9.10)	-0.9 (± 9.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values in Potential of Hydrogen (pH) of Urine - Safety population

End point title	Absolute Values in Potential of Hydrogen (pH) of Urine - Safety population

End point description:

Urine samples were collected from participants to assess urine pH. Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	307		
Units: pH				
arithmetic mean (standard deviation)				
Baseline (Day 1)	5.6 (± 0.69)	5.6 (± 0.70)		
TOC	5.5 (± 0.64)	5.4 (± 0.62)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Values in Specific Gravity of Urine - Safety population

End point title	Absolute Values in Specific Gravity of Urine - Safety population

End point description:

Urine samples were collected from participants to assess urine specific gravity. Baseline (Day 1) was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	307		
Units: Ratio				
arithmetic mean (standard deviation)				
Baseline (Day 1)	1.0211 (± 0.00750)	1.0207 (± 0.00747)		
TOC	1.0211 (± 0.00720)	1.0216 (± 0.00748)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Sign: Pulse Rate - Safety population

End point title	Change from Baseline in Vital Sign: Pulse Rate - Safety population

End point description:

Pulse rate was measured in a semi-supine position after 5 minutes rest. Baseline (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	308	313		
Units: Beats per minute				
arithmetic mean (standard deviation)				
Baseline (Day 1)	73.0 (± 12.24)	72.8 (± 12.20)		
CFB to TOC	2.2 (± 12.44)	2.4 (± 12.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Vital Sign: Temperature - Safety population

End point title	Change from Baseline in Vital Sign: Temperature - Safety population

End point description:

Temperature was measured after 5 minutes rest. Baseline (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and TOC visit (Day 4 to 8)

End point values	Gepotidacin	Ceftriaxone plus azithromycin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	306	313		
Units: Celsius (C)				
arithmetic mean (standard deviation)				
Baseline (Day 1)	36.45 (± 0.395)	36.44 (± 0.457)		
CFB to TOC	-0.03 (± 0.381)	-0.06 (± 0.485)		

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 Day 1 through the final follow-up visit (up to 21Days)

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Ceftriaxone plus azithromycin

Reporting group description:

Participants with uncomplicated urogenital gonorrhea (GC) were randomized to receive single dose of 500 mg Ceftriaxone as intramuscular sterile powder reconstituted with appropriate diluent plus single oral dose of 1 gram (g) Azithromycin (2*500 mg, tablets) on Day 1. Azithromycin was to be administered after food consumption and with water.

Reporting group title	Gepotidacin

Reporting group description:

Participants with uncomplicated urogenital gonorrhea (GC) were randomized to receive first dose of 3000 milligram (mg) (4*750 mg, tablets) gepotidacin orally on Day 1. Participants self-administered second dose of 3000 mg (4*750 mg, tablets) gepotidacin orally 10-12 hours after first dose. All doses were to be administered after food consumption and with water.

Serious adverse events	Ceftriaxone plus azithromycin	Gepotidacin	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 313 (0.00%)	1 / 309 (0.32%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 313 (0.00%)	1 / 309 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ceftriaxone plus azithromycin	Gepotidacin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	81 / 313 (25.88%)	230 / 309 (74.43%)	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 313 (2.56%)	10 / 309 (3.24%)	
occurrences (all)	8	10	
Dizziness			
subjects affected / exposed	2 / 313 (0.64%)	16 / 309 (5.18%)	
occurrences (all)	2	19	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 313 (0.00%)	8 / 309 (2.59%)	
occurrences (all)	0	9	
Injection site pain			
subjects affected / exposed	5 / 313 (1.60%)	0 / 309 (0.00%)	
occurrences (all)	5	0	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 313 (0.00%)	6 / 309 (1.94%)	
occurrences (all)	0	6	
Gastrointestinal disorders			
Flatulence			
subjects affected / exposed	1 / 313 (0.32%)	20 / 309 (6.47%)	
occurrences (all)	1	20	
Vomiting			
subjects affected / exposed	2 / 313 (0.64%)	20 / 309 (6.47%)	
occurrences (all)	2	21	
Nausea			
subjects affected / exposed	9 / 313 (2.88%)	73 / 309 (23.62%)	
occurrences (all)	9	80	
Diarrhoea			
subjects affected / exposed	30 / 313 (9.58%)	151 / 309 (48.87%)	
occurrences (all)	30	167	
Abdominal distension			

subjects affected / exposed	2 / 313 (0.64%)	5 / 309 (1.62%)	
occurrences (all)	2	5	
Faeces soft			
subjects affected / exposed	1 / 313 (0.32%)	16 / 309 (5.18%)	
occurrences (all)	1	16	
Abdominal Pain			
subjects affected / exposed	3 / 313 (0.96%)	16 / 309 (5.18%)	
occurrences (all)	4	17	
Abdominal discomfort			
subjects affected / exposed	2 / 313 (0.64%)	4 / 309 (1.29%)	
occurrences (all)	2	4	
Abdominal pain upper			
subjects affected / exposed	1 / 313 (0.32%)	6 / 309 (1.94%)	
occurrences (all)	1	6	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 313 (0.00%)	7 / 309 (2.27%)	
occurrences (all)	0	8	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 313 (1.28%)	0 / 309 (0.00%)	
occurrences (all)	4	0	
Proctitis chlamydial			
subjects affected / exposed	1 / 313 (0.32%)	4 / 309 (1.29%)	
occurrences (all)	1	4	
Urethritis chlamydial			
subjects affected / exposed	0 / 313 (0.00%)	6 / 309 (1.94%)	
occurrences (all)	0	6	
Chlamydial infection			
subjects affected / exposed	10 / 313 (3.19%)	12 / 309 (3.88%)	
occurrences (all)	10	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported