



Clinical trial results:

A Phase II, Randomized, Multicenter, Dose-Ranging Study in Adult Subjects Evaluating the Efficacy, Safety, and Tolerability of Single Doses of GSK2140944 in the Treatment of Uncomplicated Urogenital Gonorrhea Caused by Neisseria Gonorrhoeae

Summary

EudraCT number	2015-005120-26
Trial protocol	GB
Global end of trial date	02 August 2016

Results information

Result version number	v2 (current)
This version publication date	16 June 2017
First version publication date	02 March 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	116576
-----------------------	--------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 November 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the effectiveness of single oral doses of GSK2140944 to treat adult subjects with uncomplicated urogenital gonorrhea caused by *N. gonorrhoeae*

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2015
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	United Kingdom: 2
Country: Number of subjects enrolled	United States: 104
Worldwide total number of subjects	106
EEA total number of subjects	2

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)	0
Adults (18-64 years)	105
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a phase II, randomized, multicenter, open-label, dose ranging study evaluating the efficacy, safety and tolerability of gepotidacin therapy in participants with uncomplicated urogenital gonorrhea. The study duration was approximately 1 week with 2 planned study visits: Baseline (Day 1, pre-dose) and Test-of-Cure (TOC) (Day 4 to 8) visit.

Pre-assignment

Screening details:

A total of 106 participants (par.) were randomized to receive GSK2140944 1500 milligrams (mg) or GSK2140944 3000 mg, of which 105 participants received any dose of study treatment and 1 par. was unable to swallow the capsule; therefore, did not receive study drug.

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	GSK2140944 1500 mg

Arm description:

Participants were randomized to receive oral dose of GSK2140944 1500 mg (3 immediate-release capsules of 500 mg each) with food and 240 milliliters (mL) of water. Additional 100 mL of water was given to assist in swallowing a large number of capsules. Participants who tested positive for chlamydia trachomatis at the Baseline visit, received a single 1 gram dose of azithromycin or local standard of care at the TOC visit.

Arm type	Experimental
Investigational medicinal product name	GSK2140944 1500 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

GSK2140944 1500 mg (3 immediate-release capsules of 500 mg each), orally dosed with food and 240 mL of water, additionally 100 mL of water was given to assist in swallowing a large number of capsules.

Arm title	GSK2140944 3000 mg
------------------	--------------------

Arm description:

Participants were randomized to receive oral dose of GSK2140944 3000 mg (6 immediate-release capsules of 500 mg each) with food and 240 mL of water. Additional 100 mL of water was given to assist in swallowing a large number of capsules. Participants who tested positive for chlamydia trachomatis at the Baseline visit, received a single 1 gram dose of azithromycin or local standard of care at the TOC visit.

Arm type	Experimental
Investigational medicinal product name	GSK2140944 3000 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

GSK2140944 3000 mg (6 immediate-release capsules of 500 mg each), orally dosed with food and 240 mL of water, additionally 100 mL of water was given to assist in swallowing a large number of capsules.

Number of subjects in period 1	GSK2140944 1500 mg	GSK2140944 3000 mg
Started	53	53
Completed	52	53
Not completed	1	0
Could not swallow pills	1	-

Baseline characteristics

Reporting groups

Reporting group title	GSK2140944 1500 mg
-----------------------	--------------------

Reporting group description:

Participants were randomized to receive oral dose of GSK2140944 1500 mg (3 immediate-release capsules of 500 mg each) with food and 240 milliliters (mL) of water. Additional 100 mL of water was given to assist in swallowing a large number of capsules. Participants who tested positive for chlamydia trachomatis at the Baseline visit, received a single 1 gram dose of azithromycin or local standard of care at the TOC visit.

Reporting group title	GSK2140944 3000 mg
-----------------------	--------------------

Reporting group description:

Participants were randomized to receive oral dose of GSK2140944 3000 mg (6 immediate-release capsules of 500 mg each) with food and 240 mL of water. Additional 100 mL of water was given to assist in swallowing a large number of capsules. Participants who tested positive for chlamydia trachomatis at the Baseline visit, received a single 1 gram dose of azithromycin or local standard of care at the TOC visit.

Reporting group values	GSK2140944 1500 mg	GSK2140944 3000 mg	Total
Number of subjects	53	53	106
Age categorical			
Units: Subjects			

Age continuous			
----------------	--	--	--

Age continuous description

Units: years			
arithmetic mean	34.1	32.4	
standard deviation	± 11.45	± 11.33	-

Gender categorical			
--------------------	--	--	--

Gender categorical description

Units: Subjects			
Female	3	2	5
Male	50	51	101

Race/Ethnicity, Customized			
Units: Subjects			

African American/African Heritage (Heri.)	22	25	47
American Indian or Alaska Native	1	1	2
Central/South Asian Heritage	0	1	1
Japanese/East Asian Heri. /South East Asian Heri.	1	0	1
Native Hawaiian or other Pacific Islander	0	1	1
White	24	21	45
White & African American/African Heritage	0	1	1
Unknown	5	3	8

End points

End points reporting groups

Reporting group title	GSK2140944 1500 mg
-----------------------	--------------------

Reporting group description:

Participants were randomized to receive oral dose of GSK2140944 1500 mg (3 immediate-release capsules of 500 mg each) with food and 240 milliliters (mL) of water. Additional 100 mL of water was given to assist in swallowing a large number of capsules. Participants who tested positive for chlamydia trachomatis at the Baseline visit, received a single 1 gram dose of azithromycin or local standard of care at the TOC visit.

Reporting group title	GSK2140944 3000 mg
-----------------------	--------------------

Reporting group description:

Participants were randomized to receive oral dose of GSK2140944 3000 mg (6 immediate-release capsules of 500 mg each) with food and 240 mL of water. Additional 100 mL of water was given to assist in swallowing a large number of capsules. Participants who tested positive for chlamydia trachomatis at the Baseline visit, received a single 1 gram dose of azithromycin or local standard of care at the TOC visit.

Primary: Number of participants with culture-confirmed bacterial eradication of urogenital neisseria gonorrhoeae at the Test-of-Cure visit

End point title	Number of participants with culture-confirmed bacterial eradication of urogenital neisseria gonorrhoeae at the Test-of-Cure visit
-----------------	---

End point description:

Pre-treatment urogenital, pharyngeal, and rectal swab specimens were obtained for bacteriological culture for neisseria (N.) gonorrhoeae at the Baseline visit. Test- of-Cure was defined by infection site (that is urogenital and, as appropriate, rectal and/or pharyngeal) as culture confirmed bacterial eradication of N. gonorrhoeae observed 3 to 7 days post-treatment. Pre-treatment urogenital specimens were obtained for nucleic acid amplification test (NAAT) assay to detect the presence of N. gonorrhoeae and chlamydia trachomatis at the Baseline visit. Only participants who had a pre-therapy N. gonorrhoeae isolate recovered from their urogenital specimen were evaluated. Microbiologically evaluable (ME) Population comprised of all randomized participants who had N. gonorrhoeae isolated from Baseline cultures of urogenital swab specimens, received any dose of gepotidacin, and returned for their TOC visit.

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

End point timeframe:

Baseline (Day 1, pre-dose) and Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30 ^[1]	39 ^[2]		
Units: Participants	29	37		

Notes:

[1] - ME Population

[2] - ME Population

Statistical analyses

Statistical analysis title	Statistical analysis 2
----------------------------	------------------------

Statistical analysis description:

GSK2140944 3000 mg

Comparison groups	GSK2140944 1500 mg v GSK2140944 3000 mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Microbio Response Urogenital Gonorrhea
Point estimate	95
Confidence interval	
level	95 %
sides	1-sided
lower limit	84.7

Statistical analysis title	Statistical analysis 1
Statistical analysis description: GSK2140944 1500 mg	
Comparison groups	GSK2140944 1500 mg v GSK2140944 3000 mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Microbio Response Urogenital Gonorrhea
Point estimate	97
Confidence interval	
level	95 %
sides	1-sided
lower limit	85.1

Secondary: Number of participants with any adverse event (AE) or serious adverse event (SAE)

End point title	Number of participants with any adverse event (AE) or serious adverse event (SAE)
-----------------	---

End point description:

An AE is any untoward medical occurrence in a clinical investigation participants, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment or all events of possible drug-induced liver injury with hyperbilirubinaemia (defined as alanine aminotransferase [ALT] ≥ 3 times upper limit of normal [ULN] and bilirubin ≥ 2 times ULN [>35 percent direct] [or ALT ≥ 3 times ULN and international normalization ratio INR >1.5 , if INR is measured]).

Safety Population: comprised of all randomized participants who received any dose of study medication.

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

End point timeframe:

From start of the study treatment until Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[3]	53 ^[4]		
Units: Participants				
Any SAE	0	0		
Any AE	27	34		

Notes:

[3] - Safety Population

[4] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in systolic and diastolic blood pressure (BP) at the indicated time points

End point title	Change from Baseline in systolic and diastolic blood pressure (BP) at the indicated time points
-----------------	---

End point description:

BP was measured in semi-supine position after 5 minutes rest. It was recorded at Baseline visit, 2 hour post-dose visit for participants enrolled under original protocol, 0.5 hour post-dose for participants enrolled under protocol amendment 1 and up to TOC visit (Day 4 to 8). Vital sign measurements were obtained prior to any scheduled blood collection visit on the same assessment day. Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as TOC visit value minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

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

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[5]	53 ^[6]		
Units: Millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)				
Systolic BP, Day 1, 2 hr post-dose, n=47, 48	0.4 (± 11.61)	1.3 (± 11.97)		
Systolic BP, Day 4 to 8, n=52, 53	-2.8 (± 13.11)	0.5 (± 11.73)		
Diastolic BP, Day 1, 2 hr post-dose, n=47, 48	0.1 (± 7.61)	-0.9 (± 8.4)		
Diastolic BP, Day 4 to 8, n=52, 53	-2.3 (± 8.73)	-2.2 (± 9.86)		

Notes:

[5] - Safety Population

[6] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in pulse rate at the indicated time points

End point title	Change from Baseline in pulse rate at the indicated time points
-----------------	---

End point description:

Pulse rate was measured in semi-supine position after 5 minutes rest. It was recorded at Baseline visit, 2 hour post-dose visit for participants enrolled under original protocol, 0.5 hour post-dose for participants enrolled under protocol amendment 1 and up to TOC visit (Day 4 to 8). Vital sign measurements were obtained prior to any scheduled blood collection visit on the same assessment day. Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as TOC visit value minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

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

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[7]	53 ^[8]		
Units: Beats per minute				
arithmetic mean (standard deviation)				
Pulse rate Day 1, 2 hr post-dose, n=47, 48	-0.3 (± 12.2)	-1.4 (± 8.72)		
Pulse rate, Day 4 to 8, n=52, 53	1.1 (± 11.92)	2.2 (± 14.12)		

Notes:

[7] - Safety Population

[8] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in temperature at the indicated time points

End point title	Change from Baseline in temperature at the indicated time points
-----------------	--

End point description:

Temperature was measured in semi-supine position after 5 minutes rest. It was recorded at Baseline visit, 2 hour post-dose visit for participants enrolled under original protocol, 0.5 hour post-dose for participants enrolled under protocol amendment 1 and up to TOC visit (Day 4 to 8). Vital sign measurements were obtained prior to any scheduled blood collection visit on the same assessment day. Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as TOC visit value minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

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

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[9]	53 ^[10]		
Units: Celsius				
arithmetic mean (standard deviation)				

Temperature, Day 1, 2 hr post-dose, n=47, 48	-0.126 ($\pm$ 0.4327)	-0.052 ($\pm$ 0.3664)		
Temperature, Day 4 to 8, n=52, 53	-0.121 ($\pm$ 0.4953)	-0.088 ($\pm$ 0.3742)		

Notes:

[9] - Safety Population

[10] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in respiratory rate at the indicated time points

End point title	Change from Baseline in respiratory rate at the indicated time points
-----------------	---

End point description:

Respiratory rate was measured in semi-supine position after 5 minutes rest. It was recorded at Baseline visit, 2 hour post-dose visit for participants enrolled under original protocol, 0.5 hour post-dose for participants enrolled under protocol amendment 1 and up to TOC visit (Day 4 to 8). Vital sign measurements was obtained prior to any scheduled blood collection visit on the same assessment day. Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as TOC Visit value minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

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

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[11]	53 ^[12]		
Units: Breaths per minute				
arithmetic mean (standard deviation)				
Respiratory rate, Day 1, 2 hr post-dose, n=47, 48	-0.1 ($\pm$ 1.39)	-0.3 ($\pm$ 1.51)		
Respiratory rate, Day 4 to 8, n=52, 53	0.1 ($\pm$ 1.66)	-0.1 ($\pm$ 1.61)		

Notes:

[11] - Safety Population

[12] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal electrocardiogram (ECG) findings

End point title	Number of participants with abnormal electrocardiogram (ECG) findings
-----------------	---

End point description:

A single 12-lead ECGs were obtained at the Baseline, 2 hour post-dose, and at the TOC (Day 4 to 8) visit using an ECG machine that automatically calculates the heart rate and measures PR, QRS, QT, and corrected QT (QTc) intervals. ECG was obtained prior to any vital sign measurements or blood draws scheduled on the same assessment day. For participants enrolled under protocol amendment 1, ECG was measured at Baseline visit Day 1 (pre-dose) only. ECG assessments were presented as abnormal-clinically significant (CS) and abnormal-not clinically significant (NCS) at the indicated time points. Only

those participants available at the specified time points were analyzed (represented by n=X , X in the category titles).

End point type	Secondary
End point timeframe:	
Baseline visit and up to Day 8	

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[13]	53 ^[14]		
Units: Participants				
Abnormal-NCS, pre-dose Day 1, n=52, 53	14	12		
Abnormal-CS, pre-dose Day 1, n=52, 53	0	0		
Abnormal-NCS, Day 1, 2 hr post, n=37, 36	8	9		
Abnormal-CS, Day 1, 2 hr post, n=37, 36	0	0		
Abnormal-NCS, Day 4 to 8, n=37, 35	7	11		
Abnormal-CS, Day 4 to 8, n=37, 35	0	0		

Notes:

[13] - Safety Population

[14] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal physical examination finding

End point title	Number of participants with abnormal physical examination finding
-----------------	---

End point description:

Physical examination of respiratory, cardiovascular, abdomen, gastrointestinal, urogenital systems, pharyngeal and rectal examinations with collections of microbiology specimen was performed at the Baseline and TOC (Day 4 to 8) visit. Baseline was defined as the study assessment on Day 1 (pre-dose). Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary
End point timeframe:	
Baseline visit and Test-of-Cure visit (Day 4 to 8)	

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[15]	53 ^[16]		
Units: Participants				
Abdomen, Baseline, n=50, 53	2	0		
Abdomen, TOC, n=51, 52	0	0		
Cardiovascular, Baseline, n=52, 53	1	1		
Cardiovascular, TOC, n=51, 53	0	0		

Gastrointestinal, Baseline, n=49, 52	1	0		
Gastrointestinal, TOC, n=50, 51	2	0		
Pharyngeal, Baseline, n=51, 51	1	4		
Pharyngeal, TOC, n=51, 52	0	0		
Rectal examination, Baseline, n=46,46	2	4		
Rectal examination, TOC, n=41,42	1	2		
Respiratory, Baseline, n=52, 53	1	0		
Respiratory, TOC, n=52, 53	0	0		
Urogenital, Baseline, n=52, 53	49	47		
Urogenital, TOC, n=52, 51	5	6		

Notes:

[15] - Safety Population

[16] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hemoglobin, protein and albumin at Test-of-Cure visit (Day 4 to 8)

End point title	Change from Baseline in hemoglobin, protein and albumin at Test-of-Cure visit (Day 4 to 8)
-----------------	--

End point description:

Blood samples were collected at Baseline Day 1 (pre-dose) and at TOC visit (Day 4 to 8) to evaluate hemoglobin, total protein and albumin. Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as value obtained at TOC visit minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

Baseline visit and Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[17]	53 ^[18]		
Units: Gram (G)/Liter (L)				
arithmetic mean (standard deviation)				
Hemoglobin, n=46, 53	-3 (± 6.89)	-3.9 (± 8.79)		
Albumin, n=52, 53	-0.5 (± 2.1)	-0.8 (± 2.51)		
Protein, n=52, 53	-1.1 (± 3.62)	-2 (± 4.01)		

Notes:

[17] - Safety Population

[18] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematocrit at Test-of-Cure visit (Day 4 to 8)

End point title	Change from Baseline in hematocrit at Test-of-Cure visit (Day
-----------------	---

End point description:

Blood samples were collected at Baseline Day 1 (pre-dose) and at TOC visit (Day 4 to 8) to evaluate hematocrit. Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as value obtained at TOC visit minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type Secondary

End point timeframe:

Baseline visit and Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46 ^[19]	53 ^[20]		
Units: Proportion of Blood				
arithmetic mean (standard deviation)	-0.0117 (± 0.02213)	-0.0155 (± 0.03166)		

Notes:

[19] - Safety Population

[20] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lymphocyte, monocyte, neutrophil basophil, eosinophil, leukocyte and platelet count at Test-of-Cure visit (Day 4 to 8)

End point title	Change from Baseline in lymphocyte, monocyte, neutrophil basophil, eosinophil, leukocyte and platelet count at Test-of-Cure visit (Day 4 to 8)
-----------------	--

End point description:

Blood samples were collected at Baseline Day 1 (pre-dose) and at TOC visit (Day 4 to 8) to evaluate neutrophil, lymphocyte, basophil, eosinophil, monocyte, leukocyte and platelet count. Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as value obtained at TOC visit minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type Secondary

End point timeframe:

Baseline visit and Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[21]	53 ^[22]		
Units: 10 ⁹ cells/L				
arithmetic mean (standard deviation)				
Lymphocytes, n=46, 52	0.141 (± 0.5437)	0.053 (± 0.6846)		
Monocytes, n=46, 52	-0.013 (± 0.1339)	0.026 (± 0.1377)		

Neutrophils , n=46, 52	-0.834 (± 1.7564)	-0.598 (± 1.9185)		
Platelets, n=45, 53	6.4 (± 35.63)	-5.8 (± 26.41)		
Basophils, n=46, 52	-0.001 (± 0.0146)	0.002 (± 0.0155)		
Eosinophils, n=46, 52	0.023 (± 0.1147)	0.027 (± 0.1187)		
Leukocytes, n=46, 52	-0.69 (± 1.692)	-0.49 (± 1.947)		

Notes:

[21] - Safety Population

[22] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in bilirubin, direct bilirubin and creatinine at Test-of-Cure visit (Day 4 to 8)

End point title	Change from Baseline in bilirubin, direct bilirubin and creatinine at Test-of-Cure visit (Day 4 to 8)
-----------------	---

End point description:

Blood samples were collected at Baseline Day 1 (pre-dose) and at TOC visit (Day 4 to 8) to evaluate bilirubin, direct bilirubin and creatinine. Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as value obtained at TOC visit minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

Baseline visit and Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[23]	53 ^[24]		
Units: Micromole (UMOL)/ L				
arithmetic mean (standard deviation)				
Bilirubin, n=52, 53	-1.4 (± 5.42)	0.4 (± 4.01)		
Direct bilirubin, n=52, 53	-0.2 (± 1.11)	0.2 (± 1.45)		
Creatinine, n=52, 53	1.38 (± 9.989)	2.01 (± 7.737)		

Notes:

[23] - Safety Population

[24] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase at Test-of-Cure visit (Day 4 to 8)

End point title	Change from Baseline in alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase at Test-of-Cure visit (Day 4 to 8)
-----------------	--

End point description:

Blood samples were collected at Baseline Day 1.(pre-dose) and at TOC visit (Day 4 to 8) to evaluate alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase. Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as value obtained at TOC visit minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

Baseline visit and Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[25]	53 ^[26]		
Units: International units (IU)/ L				
arithmetic mean (standard deviation)				
Alanine Aminotransferase, n=52, 53	1.2 (± 7.24)	1.8 (± 8.41)		
Aspartate Aminotransferase, n=52, 53	2 (± 7.69)	2.5 (± 8.69)		
Alkaline Phosphatase, n=52, 53	-1.8 (± 6.73)	-2.2 (± 6.26)		

Notes:

[25] - Safety Population

[26] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in chloride, calcium, glucose, potassium, sodium and urea at Test-of-Cure visit (Day 4 to 8)

End point title	Change from Baseline in chloride, calcium, glucose, potassium, sodium and urea at Test-of-Cure visit (Day 4 to 8)
-----------------	---

End point description:

Blood samples were collected at Baseline Day 1.(pre-dose) and at TOC visit (Day 4 to 8) to evaluate chloride, calcium, glucose, potassium, sodium and urea (blood urea nitrogen). Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as value obtained at TOC visit minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

Baseline visit and Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[27]	53 ^[28]		
Units: Millimole (MMOL)/L				
arithmetic mean (standard deviation)				
Chloride, n=52, 53	0.7 (± 2.02)	0.3 (± 1.92)		
Calcium, n=52, 53	-0.017 (± 0.0869)	-0.047 (± 0.0874)		

Glucose, n=52, 53	-0.18 (± 1.184)	-0.02 (± 0.959)		
Potassium, n=52, 53	0.04 (± 0.359)	-0.01 (± 0.355)		
Sodium, n=52, 53	0.1 (± 2.28)	-0.1 (± 1.95)		
Urea, n=52, 53	0.07 (± 1.098)	0.04 (± 1.228)		

Notes:

[27] - Safety Population

[28] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in erythrocytes at Test-of-Cure visit (Day 4 to 8)

End point title	Change from Baseline in erythrocytes at Test-of-Cure visit (Day 4 to 8)
-----------------	---

End point description:

Blood samples were collected at Baseline Day 1 (pre-dose) and at TOC visit (Day 4 to 8) to evaluate erythrocytes (red blood cell count). Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as value obtained at TOC visit minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

Baseline visit and Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46 ^[29]	53 ^[30]		
Units: 10 ¹² /L				
arithmetic mean (standard deviation)	-0.1 (± 0.227)	-0.15 (± 0.338)		

Notes:

[29] - Safety Population

[30] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in erythrocytes mean corpuscular hemoglobin at Test-of-Cure visit (Day 4 to 8)

End point title	Change from Baseline in erythrocytes mean corpuscular hemoglobin at Test-of-Cure visit (Day 4 to 8)
-----------------	---

End point description:

Blood samples were collected at Baseline Day 1 (pre-dose) and at TOC visit (Day 4 to 8) to evaluate erythrocytes mean corpuscular hemoglobin. Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as value obtained at TOC Visit minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

Baseline visit and Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46 ^[31]	53 ^[32]		
Units: Picograms				
arithmetic mean (standard deviation)	0.08 (± 0.457)	0.12 (± 0.461)		

Notes:

[31] - Safety Population

[32] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in erythrocytes mean corpuscular volume at Test-of-Cure visit (Day 4 to 8)

End point title	Change from Baseline in erythrocytes mean corpuscular volume at Test-of-Cure visit (Day 4 to 8)
-----------------	---

End point description:

Blood samples were collected at Baseline Day 1 (pre-dose) and at TOC visit (Day 4 to 8) to evaluate erythrocytes mean corpuscular volume. Baseline was defined as the study assessment on Day 1 (pre-dose). Change from Baseline was calculated as value obtained at TOC Visit minus value at Baseline. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

Baseline visit and Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46 ^[33]	53 ^[34]		
Units: Femtoliters				
arithmetic mean (standard deviation)	-0.3 (± 1.85)	-0.2 (± 1.71)		

Notes:

[33] - Safety Population

[34] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal urinalysis dipstick results

End point title	Number of participants with abnormal urinalysis dipstick results
-----------------	--

End point description:

Dipstick urinalysis was done for glucose, ketones, occult blood, protein, potential hydrogen (pH) and

specific gravity at Baseline visit Day 1 (pre-dose) and Test-of-Cure visit (Day 4 to 8). Results were presented as negative (normal) or other findings reported only if observed under microscopic examination trace, 1+, 2+, 3+, 4+ and 5+ glucose, ketones, occult blood and protein. pH results were categorized as per their pH values. Baseline was defined as the study assessment on Day 1 (pre-dose). Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

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

End point timeframe:

Baseline visit and Test-of-Cure visit (Day 4 to 8)

End point values	GSK2140944 1500 mg	GSK2140944 3000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52 ^[35]	53 ^[36]		
Units: Participants				
Glucose, pre-dose, Day 1, negative, n=50, 53	48	53		
Glucose, pre-dose, Day 1, trace, n=50, 53	1	0		
Glucose, pre-dose, Day 1, 1+, n=50, 53	0	0		
Glucose, pre-dose, Day 1, 2+, n=50, 53	0	0		
Glucose, pre-dose, Day 1, 3+, n=50, 53	1	0		
Glucose, pre-dose, Day 1, 4+, n=50, 53	0	0		
Glucose, pre-dose, Day 1, 5+, n=50, 53	0	0		
Glucose, Day 4 to 8, negative, n=48, 53	47	53		
Glucose, Day 4 to 8, trace, n=48, 53	0	0		
Glucose, Day 4 to 8, 1+, n=48, 53	0	0		
Glucose, Day 4 to 8, 2+, n=48, 53	0	0		
Glucose, Day 4 to 8, 3+, n=48, 53	1	0		
Glucose, Day 4 to 8, 4+, n=48, 53	0	0		
Glucose, Day 4 to 8, 5+, n=48, 53	0	0		
Ketones, pre-dose, Day 1, negative, n=50, 53	48	49		
Ketones, pre-dose, Day 1, trace, n=50, 53	2	3		
Ketones, pre-dose, Day 1, 1+, n=50, 53	0	1		
Ketones, pre-dose, Day 1, 2+, n=50, 53	0	0		
Ketones, pre-dose, Day 1, 3+, n=50, 53	0	0		
Ketones, pre-dose, Day 1, 4+, n=50, 53	0	0		
Ketones, pre-dose, Day 1, 5+, n=50, 53	0	0		
Ketones, Day 4 to 8, negative, n=48, 53	45	48		
Ketones, Day 4 to 8, trace, n=48, 53	3	4		
Ketones, Day 4 to 8, 1+, n=48, 53	0	1		
Ketones, Day 4 to 8, 2+, n=48, 53	0	0		
Ketones, Day 4 to 8, 3+, n=48, 53	0	0		
Ketones, Day 4 to 8, 4+, n=48, 53	0	0		
Ketones, Day 4 to 8, 5+, n=48, 53	0	0		
Occult blood, pre-dose, Day 1, negative, n=50, 53	35	42		
Occult blood, pre-dose, Day 1, trace, n=50, 53	6	4		
Occult blood, pre-dose, Day 1, 1+, n=50, 53	6	7		

Occult blood, pre-dose, Day 1, 2+, n=50, 53	2	0		
Occult blood, pre-dose, Day 1, 3+, n=50, 53	1	0		
Occult blood, pre-dose, Day 1, 4+, n=50, 53	0	0		
Occult blood, pre-dose, Day 1, 5+, n=50, 53	0	0		
Occult blood, Day 4 to 8, negative, n=48, 53	45	49		
Occult blood, Day 4 to 8, trace, n=48, 53	0	0		
Occult blood, Day 4 to 8, 1+, n=48, 53	1	1		
Occult blood, Day 4 to 8, 2+, n=48, 53	2	0		
Occult blood, Day 4 to 8, 3+, n=48, 53	0	3		
Occult blood, Day 4 to 8, 4+, n=48, 53	0	0		
Occult blood, Day 4 to 8, 5+, n=48, 53	0	0		
Protein, pre-dose, Day 1, negative, n=50, 53	37	39		
Protein, pre-dose, Day 1, trace, n=50, 53	8	9		
Protein, pre-dose, Day 1, 1+, n=50, 53	4	5		
Protein, pre-dose, Day 1, 2+, n=50, 53	1	0		
Protein, pre-dose, Day 1, 3+, n=50, 53	0	0		
Protein, pre-dose, Day 1, 4+, n=50, 53	0	0		
Protein, pre-dose, Day 1, 5+, n=50, 53	0	0		
Protein, Day 4 to 8, negative, n=48, 53	42	43		
Protein, Day 4 to 8, trace, n=48, 53	4	7		
Protein, Day 4 to 8, 1+, n=48, 53	2	2		
Protein, Day 4 to 8, 2+, n=48, 53	0	1		
Protein, Day 4 to 8, 3+, n=48, 53	0	0		
Protein, Day 4 to 8, 4+, n=48, 53	0	0		
Protein, Day 4 to 8, 5+, n=48, 53	0	0		
pH, pre-dose, Day 1, pH 5, n=50, 53	2	1		
pH, pre-dose, Day 1, pH 5.5, n=50, 53	5	8		
pH, pre-dose, Day 1, pH 6, n=50, 53	13	8		
pH, pre-dose, Day 1, pH 6.5, n=50, 53	12	14		
pH, pre-dose, Day 1, pH 7, n=50, 53	12	14		
pH, pre-dose, Day 1, pH 7.5, n=50, 53	4	7		
pH, pre-dose, Day 1, pH 8, n=50, 53	2	1		
pH, Day 4 to 8, pH 5, n=48, 53	0	0		
pH, Day 4 to 8, pH 5.5, n=48, 53	10	11		
pH, Day 4 to 8, pH 6, n=48, 53	13	15		
pH, Day 4 to 8, pH 6.5, n=48, 53	9	14		
pH, Day 4 to 8, pH 7, n=48, 53	10	7		
pH, Day 4 to 8, pH 7.5, n=48, 53	5	3		
pH, Day 4 to 8, pH 8, n=48, 53	1	3		

Notes:

[35] - Safety Population

[36] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from start of the study treatment (Day1) until Test-of-Cure visit (Day 4 to 8).

Adverse event reporting additional description:

On-treatment SAEs and non-serious (AEs) are reported for Safety Population which comprised of all randomized participants who received any dose of study medication.

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

Dictionary used

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

Dictionary version	19.1
--------------------	------

Reporting groups

Reporting group title	GSK2140944 1500 mg
-----------------------	--------------------

Reporting group description:

Participants were randomized to receive oral dose of GSK2140944 1500 mg (3 immediate-release capsules of 500 mg each) with food and 240 milliliters (mL) of water. Additional 100 mL of water was given to assist in swallowing a large number of capsules. Participants who tested positive for chlamydia trachomatis at the Baseline visit, received a single 1 gram dose of azithromycin or local standard of care at the TOC visit.

Reporting group title	GSK2140944 3000 mg
-----------------------	--------------------

Reporting group description:

Participants were randomized to receive oral dose of GSK2140944 3000 mg (6 immediate-release capsules of 500 mg each) with food and 240 mL of water. Additional 100 mL of water was given to assist in swallowing a large number of capsules. Participants who tested positive for chlamydia trachomatis at the Baseline visit, received a single 1 gram dose of azithromycin or local standard of care at the TOC visit.

Serious adverse events	GSK2140944 1500 mg	GSK2140944 3000 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)	0 / 53 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	GSK2140944 1500 mg	GSK2140944 3000 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 52 (42.31%)	28 / 53 (52.83%)	
Nervous system disorders			
Dizziness			

subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	6 / 53 (11.32%) 6	
Somnolence subjects affected / exposed occurrences (all)	0 / 52 (0.00%) 0	3 / 53 (5.66%) 3	
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 3	5 / 53 (9.43%) 6	
Feeling hot subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	4 / 53 (7.55%) 4	
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 4	2 / 53 (3.77%) 3	
Abdominal pain subjects affected / exposed occurrences (all)	6 / 52 (11.54%) 6	10 / 53 (18.87%) 11	
Diarrhoea subjects affected / exposed occurrences (all)	9 / 52 (17.31%) 10	19 / 53 (35.85%) 21	
Eructation subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	3 / 53 (5.66%) 3	
Faeces soft subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	3 / 53 (5.66%) 4	
Flatulence subjects affected / exposed occurrences (all)	14 / 52 (26.92%) 17	10 / 53 (18.87%) 10	
Nausea subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 3	11 / 53 (20.75%) 13	
Skin and subcutaneous tissue disorders			

Hyperhidrosis subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1	6 / 53 (11.32%) 6	
---	---------------------	----------------------	--

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2016	Added optional interim analyses for success or futility. Removed the 2-hour post-dose ECG, vital sign measurements, and PK requirements and removed the ECG at the Test-of-Cure (Day 4 to 8) visit. Incorporated Protocol Administration Letters 1, 2, 3, and 4. Clarified that treatment for Chlamydia trachomatis at the Test-of-Cure (Day 4 to 8) visit should be administered after all study procedures have been completed. Clarified that the laboratory manual, in addition to the study procedures manual, provides instructions for sample collection, processing, and shipment. Updated medical monitor information. Updated the list of authors. Updated the investigator's brochure (IB) document number and added IB supplement 1 reference. Updated formatting and stylistic inconsistencies and minor administrative edits.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported