Clinical trial results:
A phase II observer blind, randomised, controlled study to evaluate the safety, reactogenicity and immunogenicity of GSK Biologicals' candidate tuberculosis vaccine GSK 692342 when administered to adults aged 18 to 59 years with TB disease

Summary

EudraCT number	2012-001820-36
Trial protocol	EE
Global end of trial date	10 April 2014

Results information

Result version number	v1
This version publication date	03 March 2016
First version publication date	22 May 2015

Trial information

Trial identification

Sponsor protocol code	114886

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

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	Interim
Date of interim/final analysis	20 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2014
Global end of trial reached?	Yes
Global end of trial date	10 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and reactogenicity of GSK Biologicals' candidate TB vaccine M72/AS01E in the study population.

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 November 2011
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	Estonia: 36
Country: Number of subjects enrolled	Taiwan: 106
Worldwide total number of subjects	142
EEA total number of subjects	36

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)	142
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following was performed: informed consent was obtained and signed from parents or guardians of subjects, check for inclusion/exclusion criteria and contraindications/precautions was performed, and medical history of subjects was collected. Prior to vaccination, subjects' pre-vaccination body temperature was evaluated.

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, Monitor, Carer

Blinding implementation details:

During the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoints have been unaware of which vaccine was administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	TB Treatment GSK 692342 Group

Arm description:

Subjects having completed the intensive phase of treatment, i.e. 2 to 4 months post initiation of treatment, who received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1.

Arm type	Experimental
Investigational medicinal product name	GSK 692342
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses of vaccine were administered intramuscularly in the deltoid region of the arm, on a 0, 1 Months schedule

Arm title	TB Treatment Saline Group

Arm description:

Subjects having completed the intensive phase of treatment, i.e. 2 to 4 months post initiation of treatment who received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.

Arm type	Placebo
Investigational medicinal product name	Physiological Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Doses were administered intramuscularly in the deltoid of the arm at Months 0 and 1

Arm title	TB Treated GSK 692342 Group

Arm description:

Subjects having successfully completed treatment for TB disease at least 1 year prior to the study, who during this study received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1

Arm type	Experimental
Investigational medicinal product name	GSK 692342
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses of vaccine were administered intramuscularly in the deltoid region of the arm, on a 0, 1 Months schedule

Arm title	TB Treated Saline Group

Arm description:

Subjects having successfully completed treatment for TB disease at least 1 year prior to the study, who in this study received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.

Arm type	Placebo
Investigational medicinal product name	Physiological Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Doses were administered intramuscularly in the deltoid of the arm at Months 0 and 1

Arm title	TB Naive GSK 692342 Group

Arm description:

Subjects unaffected by tuberculosis who received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1.

Arm type	Experimental
Investigational medicinal product name	GSK 692342
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses of vaccine were administered intramuscularly in the deltoid region of the arm, on a 0, 1 Months schedule

Arm title	TB Naive Saline Group

Arm description:

Subjects unaffected by tuberculosis who received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.

Arm type	Placebo
Investigational medicinal product name	Physiological Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Doses were administered intramuscularly in the deltoid of the arm at Months 0 and 1

Number of subjects in period 1	TB Treatment GSK 692342 Group	TB Treatment Saline Group	TB Treated GSK 692342 Group
Started	7	6	24
Completed	6	5	22
Not completed	1	1	2
Consent withdrawn by subject	1	1	1
Lost to follow-up	-	-	1

Number of subjects in period 1	TB Treated Saline Group	TB Naive GSK 692342 Group	TB Naive Saline Group
Started	25	40	40
Completed	25	40	40
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Lost to follow-up	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	TB Treatment GSK 692342 Group
Reporting group description:	
Subjects having completed the intensive phase of treatment, i.e. 2 to 4 months post initiation of treatment, who received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1.	
Reporting group title	TB Treatment Saline Group
Reporting group description:	
Subjects having completed the intensive phase of treatment, i.e. 2 to 4 months post initiation of treatment who received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.	
Reporting group title	TB Treated GSK 692342 Group
Reporting group description:	
Subjects having successfully completed treatment for TB disease at least 1 year prior to the study, who during this study received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1	
Reporting group title	TB Treated Saline Group
Reporting group description:	
Subjects having successfully completed treatment for TB disease at least 1 year prior to the study, who in this study received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.	
Reporting group title	TB Naive GSK 692342 Group
Reporting group description:	
Subjects unaffected by tuberculosis who received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1.	
Reporting group title	TB Naive Saline Group
Reporting group description:	
Subjects unaffected by tuberculosis who received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.	

Reporting group values	TB Treatment GSK 692342 Group	TB Treatment Saline Group	TB Treated GSK 692342 Group
Number of subjects	7	6	24
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	42.9	44.7	44.5
standard deviation	± 11.5	± 11.8	± 10.3
Gender categorical Units: Subjects			
Female	1	2	13

End points

End points reporting groups

Reporting group title	TB Treatment GSK 692342 Group
Reporting group description:	
Subjects having completed the intensive phase of treatment, i.e. 2 to 4 months post initiation of treatment, who received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1.	
Reporting group title	TB Treatment Saline Group
Reporting group description:	
Subjects having completed the intensive phase of treatment, i.e. 2 to 4 months post initiation of treatment who received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.	
Reporting group title	TB Treated GSK 692342 Group
Reporting group description:	
Subjects having successfully completed treatment for TB disease at least 1 year prior to the study, who during this study received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1	
Reporting group title	TB Treated Saline Group
Reporting group description:	
Subjects having successfully completed treatment for TB disease at least 1 year prior to the study, who in this study received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.	
Reporting group title	TB Naive GSK 692342 Group
Reporting group description:	
Subjects unaffected by tuberculosis who received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1.	
Reporting group title	TB Naive Saline Group
Reporting group description:	
Subjects unaffected by tuberculosis who received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.	

Primary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms[1]
End point description:	
End point type	Primary
End point timeframe:	
During the 7 day (Days 0-6), after each vaccine dose	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	TB Treatment GSK 692342 Group	TB Treatment Saline Group	TB Treated GSK 692342 Group	TB Treated Saline Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	24	25
Units: Subjects				
Pain, D1 (N=7,6,24,25,40,40)	6	1	21	2
Redness, D1 (N=7,6,24,25,40,40)	2	0	4	0
Swelling, D1 (N=7,6,24,25,40,40)	2	0	5	1
Pain, D2 (N=6,5,21,25,39,39)	5	1	19	1

Redness, D2 (N=6,5,21,25,39,39)	3	0	7	0
Swelling, D2 (N=6,5,21,25,39,39)	3	0	4	0
Pain, Across (N=7,6,24,25,40,40)	6	1	22	3
Redness, Across (N=7,6,24,25,40,40)	3	0	8	0
Swelling, Across (N=7,6,24,25,40,40)	3	0	6	1

End point values	TB Naive GSK 692342 Group	TB Naive Saline Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: Subjects				
Pain, D1 (N=7,6,24,25,40,40)	38	5		
Redness, D1 (N=7,6,24,25,40,40)	7	0		
Swelling, D1 (N=7,6,24,25,40,40)	4	0		
Pain, D2 (N=6,5,21,25,39,39)	36	6		
Redness, D2 (N=6,5,21,25,39,39)	6	0		
Swelling, D2 (N=6,5,21,25,39,39)	11	0		
Pain, Across (N=7,6,24,25,40,40)	39	8		
Redness, Across (N=7,6,24,25,40,40)	10	0		
Swelling, Across (N=7,6,24,25,40,40)	11	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms[2]

End point description:

End point type	Primary

End point timeframe:

During the 7 day (Days 0-6), after each vaccine dose

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: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	TB Treatment GSK 692342 Group	TB Treatment Saline Group	TB Treated GSK 692342 Group	TB Treated Saline Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	24	25
Units: Subjects				
Fatigue, D1 (N=7,6,24,25,40,40)	1	2	14	6
Gastrointestinal symptoms, D1 (N=7,6,24,25,40,40)	0	0	4	2
Headache, D1 (N=7,6,24,25,40,40)	1	0	11	4
Malaise, D1 (N=7,6,24,25,40,40)	1	1	11	2

Myalgia, D1 (N=7,6,24,25,40,40)	2	0	13	4
Temperature/(Axillary), D1 (N=7,6,24,25,40,40)	0	0	1	0
Fatigue, D2 (N=6,5,21,25,39,39)	3	1	13	5
Gastrointestinal symptoms, D2 (N=6,5,21,25,39,39)	2	0	7	3
Headache, D2 (N=6,5,21,25,39,39)	3	1	12	2
Malaise, D2 (N=6,5,21,25,39,39)	3	2	11	5
Myalgia, D2 (N=6,5,21,25,39,39)	3	1	14	4
Temperature/(Axillary), D2 (N=6,5,21,25,39,39)	4	1	9	0
Fatigue, Across (N=7,6,24,25,40,40)	3	2	17	8
Gastrointestinal symptoms, Across (N=7,6,24,25,40,	2	0	10	4
Headache, Across (N=7,6,24,25,40,40)	3	1	18	4
Malaise, Across (N=7,6,24,25,40,40)	3	2	16	6
Myalgia, Across (N=7,6,24,25,40,40)	3	1	18	5
Temperature/(Axillary), Across (N=7,6,24,25,40,40)	4	1	10	0

End point values	TB Naive GSK 692342 Group	TB Naive Saline Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: Subjects				
Fatigue, D1 (N=7,6,24,25,40,40)	19	8		
Gastrointestinal symptoms, D1 (N=7,6,24,25,40,40)	5	5		
Headache, D1 (N=7,6,24,25,40,40)	8	5		
Malaise, D1 (N=7,6,24,25,40,40)	14	8		
Myalgia, D1 (N=7,6,24,25,40,40)	24	7		
Temperature/(Axillary), D1 (N=7,6,24,25,40,40)	2	0		
Fatigue, D2 (N=6,5,21,25,39,39)	33	7		
Gastrointestinal symptoms, D2 (N=6,5,21,25,39,39)	13	3		
Headache, D2 (N=6,5,21,25,39,39)	22	3		
Malaise, D2 (N=6,5,21,25,39,39)	32	3		
Myalgia, D2 (N=6,5,21,25,39,39)	28	3		
Temperature/(Axillary), D2 (N=6,5,21,25,39,39)	16	0		
Fatigue, Across (N=7,6,24,25,40,40)	36	10		
Gastrointestinal symptoms, Across (N=7,6,24,25,40,	16	6		
Headache, Across (N=7,6,24,25,40,40)	24	6		
Malaise, Across (N=7,6,24,25,40,40)	35	9		
Myalgia, Across (N=7,6,24,25,40,40)	34	7		
Temperature/(Axillary), Across (N=7,6,24,25,40,40)	17	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with adverse events (AEs)

End point title	Number of subjects with adverse events (AEs)[3]

End point description:

End point type	Primary

End point timeframe:

During the 30 day (Days 0-29) after vaccination

Notes:

[3] - 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: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	TB Treatment GSK 692342 Group	TB Treatment Saline Group	TB Treated GSK 692342 Group	TB Treated Saline Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	24	25
Units: Subjects				
Any AEs	1	2	14	7

End point values	TB Naive GSK 692342 Group	TB Naive Saline Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: Subjects				
Any AEs	19	8		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)[4]

End point description:

End point type	Primary

End point timeframe:

Up to day 210

Notes:

[4] - 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: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	TB Treatment GSK 692342 Group	TB Treatment Saline Group	TB Treated GSK 692342 Group	TB Treated Saline Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	24	25
Units: Subjects				
Any SAEs	0	0	2	2

End point values	TB Naive GSK 692342 Group	TB Naive Saline Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: Subjects				
Any SAEs	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: During the 7 day (Days 0-6), after each vaccine dose, unsolicited AEs: During the 30 day (Days 0-29) after vaccination, SAEs: Up to day 210

Adverse event reporting additional description:

Results presented per group consist of a summary of the events (SAEs and AEs other than SAEs, respectively) reported, compiling overall number of subjects with events across the different periods of assessment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	TB Treatment GSK 692342 Group

Reporting group description:

Subjects having completed the intensive phase of treatment, i.e. 2 to 4 months post initiation of treatment, who received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1.

Reporting group title	TB Treatment Saline Group

Reporting group description:

Subjects having completed the intensive phase of treatment, i.e. 2 to 4 months post initiation of treatment who received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.

Reporting group title	TB Treated GSK 692342 Group

Reporting group description:

Subjects having successfully completed treatment for TB disease at least 1 year prior to the study, who during this study received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1

Reporting group title	TB Treated Saline Group

Reporting group description:

Subjects having successfully completed treatment for TB disease at least 1 year prior to the study, who in this study received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.

Reporting group title	TB Naive GSK 692342 Group

Reporting group description:

Subjects unaffected by tuberculosis who received the GSK 692342 vaccine according to a 2-dose schedule at Months 0 and 1.

Reporting group title	TB Naive Saline Group

Reporting group description:

Subjects unaffected by tuberculosis who received a placebo (physiological saline) according to a 2-dose schedule at Months 0 and 1.

Serious adverse events	TB Treatment GSK 692342 Group	TB Treatment Saline Group	TB Treated GSK 692342 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 24 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Immune system disorders			
Hypersensitivity			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal fistula			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	TB Treated Saline Group	TB Naive GSK 692342 Group	TB Naive Saline Group
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 25 (8.00%)	1 / 40 (2.50%)	0 / 40 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Immune system disorders			
Hypersensitivity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 25 (0.00%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal fistula			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 25 (0.00%)	1 / 40 (2.50%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 25 (0.00%)	1 / 40 (2.50%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 25 (0.00%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 25 (4.00%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	TB Treatment GSK 692342 Group	TB Treatment Saline Group	TB Treated GSK 692342 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	2 / 6 (33.33%)	22 / 24 (91.67%)
Investigations			
Hepatic enzyme increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Nervous system disorders			
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	6 / 7 (85.71%)	1 / 6 (16.67%)	22 / 24 (91.67%)
occurrences (all)	6	1	22
Redness			

subjects affected / exposed	3 / 7 (42.86%)	0 / 6 (0.00%)	8 / 24 (33.33%)
occurrences (all)	3	0	8
Swelling			
subjects affected / exposed	3 / 7 (42.86%)	0 / 6 (0.00%)	6 / 24 (25.00%)
occurrences (all)	3	0	6
Fatigue			
subjects affected / exposed	3 / 7 (42.86%)	2 / 6 (33.33%)	17 / 24 (70.83%)
occurrences (all)	3	2	17
Gastrointestinal symptoms			
subjects affected / exposed	2 / 7 (28.57%)	0 / 6 (0.00%)	10 / 24 (41.67%)
occurrences (all)	2	0	10
Headache (solicited)			
subjects affected / exposed	3 / 7 (42.86%)	1 / 6 (16.67%)	18 / 24 (75.00%)
occurrences (all)	3	1	18
Malaise			
subjects affected / exposed	3 / 7 (42.86%)	2 / 6 (33.33%)	16 / 24 (66.67%)
occurrences (all)	3	2	16
Myalgia			
subjects affected / exposed	3 / 7 (42.86%)	1 / 6 (16.67%)	18 / 24 (75.00%)
occurrences (all)	3	1	18
Temperature/(Axillary)			
subjects affected / exposed	4 / 7 (57.14%)	1 / 6 (16.67%)	10 / 24 (41.67%)
occurrences (all)	4	1	10
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	3 / 24 (12.50%)
occurrences (all)	0	0	3
Infections and infestations			
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	3 / 24 (12.50%)
occurrences (all)	0	0	3
Gastroenteritis			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 24 (8.33%)
occurrences (all)	0	0	2

Non-serious adverse events	TB Treated Saline Group	TB Naive GSK 692342 Group	TB Naive Saline Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 25 (32.00%)	39 / 40 (97.50%)	10 / 40 (25.00%)

subjects affected / exposed	8 / 25 (32.00%)	36 / 40 (90.00%)	10 / 40 (25.00%)
occurrences (all)	8	36	10
Gastrointestinal symptoms			
subjects affected / exposed	4 / 25 (16.00%)	16 / 40 (40.00%)	6 / 40 (15.00%)
occurrences (all)	4	16	6
Headache (solicited)			
subjects affected / exposed	4 / 25 (16.00%)	24 / 40 (60.00%)	6 / 40 (15.00%)
occurrences (all)	4	24	6
Malaise			
subjects affected / exposed	6 / 25 (24.00%)	35 / 40 (87.50%)	9 / 40 (22.50%)
occurrences (all)	6	35	9
Myalgia			
subjects affected / exposed	5 / 25 (20.00%)	34 / 40 (85.00%)	7 / 40 (17.50%)
occurrences (all)	5	34	7
Temperature/(Axillary)			
subjects affected / exposed	0 / 25 (0.00%)	17 / 40 (42.50%)	0 / 40 (0.00%)
occurrences (all)	0	17	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 25 (0.00%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 25 (0.00%)	4 / 40 (10.00%)	3 / 40 (7.50%)
occurrences (all)	0	4	3
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 25 (0.00%)	2 / 40 (5.00%)	1 / 40 (2.50%)
occurrences (all)	0	2	1
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 25 (0.00%)	1 / 40 (2.50%)	0 / 40 (0.00%)
occurrences (all)	0	1	0

Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 25 (0.00%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 May 2012	• At the European Medicines Agency's (EMA) request, GSK Biologicals has updated its procedure for emergency unblinding during the conduct of a clinical study. According to the revised procedure, the responsibility and the decision to break the treatment code in emergency situations resides solely with the investigator and consequently, the investigator will have full authority to break the treatment code. • Change in the number of participating countries in this study. • It has been clarified that TB treatment for subjects belonging to the TB-treatment cohort will be provided independent of this study. • Additional minor modifications have been implemented.
18 February 2013	This amendment aims to correct the centre-specific information provided in the protocol. However, as centre-specific information is available in other documents included in the clinical trial application, it was decided to remove centre-specific information from the protocol to avoid future amendments in case enrolment of subjects in the TB treated and TB treatment cohorts remains difficult and additional centres/countries might need to be added to the study.
16 January 2014	Due to a safety signal identified in the TB treatment cohort (increased local solicited symptoms post-dose 2), the protocol was amended to include exploratory testing on blood samples taken at Days 0, 7, 30, 37, 60 and 210.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
10 April 2014	A safety signal was observed during a planned interim safety review. In consequence the trial was put on hold. After careful consideration further conduct of this safety study is not considered the best course of action and enrolment in the study was terminated.	-

Notes:

Limitations and caveats

None reported