



Clinical trial results:

A Phase III, randomised, observer-blind, placebo-controlled, multicentre clinical study to assess the immunogenicity and safety of GSK Biologicals? HZ/su candidate vaccine when administered intramuscularly on a 0- and 1- to 2-months schedule to adults > 18 years of age with renal transplant.

Summary

EudraCT number	2012-005059-18
Trial protocol	ES CZ BE FI IT
Global end of trial date	30 May 2017

Results information

Result version number	v2
This version publication date	26 April 2018
First version publication date	27 May 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	116886
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02058589
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 Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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	08 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 May 2016
Global end of trial reached?	Yes
Global end of trial date	30 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate vaccine response rate (VRR) for anti-glycoprotein E (anti-gE) humoral immune responses at Month 2, following a two-dose administration of the HZ/su vaccine, in all subjects.

Criterion to be used:

The objective was met if the lower limit of the 95% confidence interval (CI) of the VRR for anti-gE antibody (Ab) concentrations at Month 2 in the HZ/su vaccine group was at least 60%.

- To evaluate the safety following administration of HZ/su vaccine, as compared to placebo, from the first vaccination up to 30 days post last vaccination in all subjects.

Protection of trial subjects:

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	20 March 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 17
Country: Number of subjects enrolled	Canada: 26
Country: Number of subjects enrolled	Czech Republic: 25
Country: Number of subjects enrolled	Finland: 10
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Korea, Republic of: 39
Country: Number of subjects enrolled	Panama: 8
Country: Number of subjects enrolled	Spain: 119
Country: Number of subjects enrolled	Taiwan: 14
Worldwide total number of subjects	265
EEA total number of subjects	178

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)	222
From 65 to 84 years	43
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	265
----------------------------	-----

Number of subjects completed	264
------------------------------	-----

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Study vaccine not received: 1
----------------------------	-------------------------------

Period 1

Period 1 title	Overall Study (overall period)
----------------	--------------------------------

Is this the baseline period?	Yes
------------------------------	-----

Allocation method	Randomised - controlled
-------------------	-------------------------

Blinding used	Single blind
---------------	--------------

Roles blinded	Subject
---------------	---------

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	GSK1437173A Group
------------------	-------------------

Arm description:

Subjects, aged 18 years or older, received 2 doses of the GSK 1437173A vaccine, adjuvanted with AS01B at Day 0, and Month 1, administered intramuscularly, in the deltoid muscle of an arm.

Arm type	Experimental
----------	--------------

Investigational medicinal product name	Herpes Zoster vaccine GSK1437173A
--	-----------------------------------

Investigational medicinal product code	
--	--

Other name	
------------	--

Pharmaceutical forms	Powder and solvent for suspension for injection
----------------------	---

Routes of administration	Intramuscular use
--------------------------	-------------------

Dosage and administration details:

2 doses at Day 0, and Month 1

Arm title	Control Group
------------------	---------------

Arm description:

Subjects, aged 18 years or older, received 2 doses of Placebo (lyophilised sucrose reconstituted with saline [NaCl] solution) at Day 0, and Month 1, administered intramuscularly, in the deltoid muscle of an arm.

Arm type	Placebo
----------	---------

Investigational medicinal product name	Placebo
--	---------

Investigational medicinal product code	
--	--

Other name	lyophilised sucrose reconstituted with saline [NaCl] solution
------------	---

Pharmaceutical forms	Powder and solution for solution for injection
----------------------	--

Routes of administration	Intramuscular use
--------------------------	-------------------

Dosage and administration details:

2 doses at Day 0, and Month 1

Number of subjects in period 1^[1]	GSK1437173A Group	Control Group
Started	132	132
Completed	129	132
Not completed	3	0
Adverse event, non-fatal	3	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 1 enrolled subject did not receive vaccination and hence did not start the study.

Baseline characteristics

Reporting groups

Reporting group title	GSK1437173A Group
-----------------------	-------------------

Reporting group description:

Subjects, aged 18 years or older, received 2 doses of the GSK 1437173A vaccine, adjuvanted with AS01B at Day 0, and Month 1, administered intramuscularly, in the deltoid muscle of an arm.

Reporting group title	Control Group
-----------------------	---------------

Reporting group description:

Subjects, aged 18 years or older, received 2 doses of Placebo (lyophilised sucrose reconstituted with saline [NaCl] solution) at Day 0, and Month 1, administered intramuscularly, in the deltoid muscle of an arm.

Reporting group values	GSK1437173A Group	Control Group	Total
Number of subjects	132	132	264
Age categorical Units: Subjects			

Age continuous Units: years geometric mean standard deviation	52.3 ± 12.5	52.4 ± 12.8	-
Gender categorical Units: Subjects			
Female	38	41	79
Male	94	91	185
Race/Ethnicity Units: Subjects			
African Heritage / African American	3	1	4
Asian - Central/South Asian Heritage	1	2	3
Asian - East Asian Heritage	20	22	42
Asian - Japanese Heritage	0	1	1
Asian - South East Asian Heritage	10	3	13
White - Arabic / North African Heritage	2	2	4
White - Caucasian / European Heritage	88	97	185
Other	8	4	12

End points

End points reporting groups

Reporting group title	GSK1437173A Group
Reporting group description: Subjects, aged 18 years or older, received 2 doses of the GSK 1437173A vaccine, adjuvanted with AS01B at Day 0, and Month 1, administered intramuscularly, in the deltoid muscle of an arm.	
Reporting group title	Control Group
Reporting group description: Subjects, aged 18 years or older, received 2 doses of Placebo (lyophilised sucrose reconstituted with saline [NaCl] solution) at Day 0, and Month 1, administered intramuscularly, in the deltoid muscle of an arm.	

Primary: Number of subjects with a Vaccine response for anti-gE humoral immunogenicity

End point title	Number of subjects with a Vaccine response for anti-gE humoral immunogenicity ^[1]
End point description: Vaccine response was determined by ELISA	
End point type	Primary
End point timeframe: At Month 2.	

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: There were no statistical analyses needed for this endpoint as it was descriptive.

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	119		
Units: Participants				
Participants	97	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms ^[2]
End point description: Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) of injection site.	
End point type	Primary
End point timeframe: Within 7 days (Days 0-6) after each vaccination.	

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: There were no statistical analyses needed for this endpoint as it was descriptive.

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	132		
Units: Participants				
Any Pain, Dose 1	107	8		
Grade 3 Pain, Dose 1	10	0		
Any Redness, Dose 1	24	1		
Grade 3 Redness, Dose 1	0	0		
Any Swelling, Dose 1	10	1		
Grade 3 Swelling, Dose 1	0	0		
Any Pain, Dose 2	93	6		
Grade 3 Pain, Dose 2	9	0		
Any Redness, Dose 2	21	1		
Grade 3 Redness, Dose 2	1	0		
Any Swelling, Dose 2	11	0		
Grade 3 Swelling, Dose 2	1	0		
Any Pain, Across doses	114	11		
Grade 3 Pain, Across doses	13	0		
Any Redness, Across doses	33	2		
Grade 3 Redness, Across doses	1	0		
Any Swelling, Across doses	15	1		
Grade 3 Swelling, Across doses	1	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 ^[3]
-----------------	---

End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal symptoms, headache, myalgia, shivering and fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)] . Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.0 °C. Related = symptom assessed by the investigator as related to the vaccination. Gastrointestinal symptoms (Gastro. sympt.) included nausea, vomiting, diarrhoea and/or abdominal pain.

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

End point timeframe:

Within 7 days (Days 0-6) after each 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: There were no statistical analyses needed for this endpoint as it was descriptive.

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	132		
Units: Participants				
Any Fatigue, Dose 1	47	42		
Grade 3 Fatigue, Dose 1	3	3		
Related Fatigue, Dose 1	8	2		
Any Gastro. sympt., Dose 1	17	16		
Grade 3 Gastro. sympt., Dose 1	1	0		
Related Gastro. sympt., Dose 1	1	1		
Any Headache, Dose 1	32	25		
Grade 3 Headache, Dose 1	1	4		
Related Headache, Dose 1	5	3		
Any Myalgia, Dose 1	43	23		
Grade 3 Myalgia, Dose 1	4	1		
Related Myalgia, Dose 1	11	2		
Any Shivering, Dose 1	10	13		
Grade 3 Shivering, Dose 1	0	1		
Related Shivering, Dose 1	3	2		
Any Temperature, Dose 1	13	6		
Grade 3 Temperature, Dose 1	0	0		
Related Temperature, Dose 1	3	0		
Any Fatigue, Dose 2	49	36		
Grade 3 Fatigue, Dose 2	4	4		
Related Fatigue, Dose 2	8	4		
Any Gastro. sympt., Dose 2	14	14		
Grade 3 Gastro. sympt., Dose 2	0	1		
Related Gastro. sympt., Dose 2	1	2		
Any Headache, Dose 2	35	22		
Grade 3 Headache, Dose 2	2	3		
Related Headache, Dose 2	9	1		
Any Myalgia, Dose 2	47	19		
Grade 3 Myalgia, Dose 2	8	3		
Related Myalgia, Dose 2	14	3		
Any Shivering, Dose 2	23	9		
Grade 3 Shivering, Dose 2	4	2		
Related Shivering, Dose 2	9	0		
Any Temperature, Dose 2	21	7		
Grade 3 Temperature, Dose 2	1	0		
Related Temperature, Dose 2	6	0		
Any Fatigue, Across doses	62	53		
Grade 3 Fatigue, Across doses	4	6		
Related Fatigue, Across doses	15	4		
Any Gastro. sympt., Across doses	24	24		
Grade 3 Gastro. sympt., Across doses	1	1		
Related Gastro. sympt., Across doses	2	3		
Any Headache, Across doses	44	34		
Grade 3 Headache, Across doses	2	5		
Related Headache, Across doses	12	4		
Any Myalgia, Dose Across doses	65	31		
Grade 3 Myalgia, Dose Across doses	9	3		

Related Myalgia, Dose Across doses	21	4		
Any Shivering, Dose Across doses	29	16		
Grade 3 Shivering, Dose Across doses	4	2		
Related Shivering, Dose Across doses	11	2		
Any Temperature, Dose Across doses	31	13		
Grade 3 Temperature, Dose Across doses	1	0		
Related Temperature, Dose Across doses	9	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with unsolicited symptoms (AEs)

End point title	Number of subjects with unsolicited symptoms (AEs) ^[4]
-----------------	---

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

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

End point timeframe:

During 30 days (Days 0-29) after each vaccination

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: There were no statistical analyses needed for this endpoint as it was descriptive.

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	132		
Units: Participants				
At least one symptom	51	44		
Subjects with grade 3 AEs	7	5		
Subjects with related AEs	7	3		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any potential immune-mediated diseases (pIMDs)

End point title	Number of subjects with any potential immune-mediated diseases (pIMDs) ^[5]
-----------------	---

End point description:

Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and

other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology

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

End point timeframe:

From first vaccination up to 30 days post last vaccination.

Notes:

[5] - 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: There were no statistical analyses needed for this endpoint as it was descriptive.

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	132		
Units: Participants				
Participants	0	0		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any and related serious adverse events (SAEs) ^[6]
-----------------	--

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, or result in disability /incapacity.

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

End point timeframe:

From first vaccination up to 30 days post last vaccination

Notes:

[6] - 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: There were no statistical analyses needed for this endpoint as it was descriptive.

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	132		
Units: Participants				
Participants	6	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with biopsy confirmed renal allograft rejection

End point title	Number of subjects with biopsy confirmed renal allograft
-----------------	--

End point description:

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

End point timeframe:

From the first vaccination up to 30 days post last vaccination.

Notes:

[7] - 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: There were no statistical analyses needed for this endpoint as it was descriptive.

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	132		
Units: Participants				
Rejection confirmed	0	0		
Rejection not confirmed	0	3		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with changes in allograft function

End point title	Number of subjects with changes in allograft function ^[8]
-----------------	--

End point description:

Allograft function was indicated by an increase in levels of serum creatinine. The number of subjects with declining allograft function, as determined by serum creatinine measurements post-vaccination (up to 30 days post-last vaccination) compared to pre-vaccination were presented.

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

End point timeframe:

From the first vaccination up to 30 days post last vaccination

Notes:

[8] - 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: There were no statistical analyses needed for this endpoint as it was descriptive.

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	107		
Units: Participants				
≥1.20 fold increase	5	7		
≥1.50 fold increase	0	1		
≥1.75 fold increase	0	1		
≥2 fold increase	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of days with solicited local symptoms

End point title	Number of days with solicited local symptoms ^[9]
End point description: Assessed solicited local symptoms were pain, redness and swelling.	
End point type	Primary
End point timeframe: Within 7 days (Days 0-6) after each vaccination	

Notes:

[9] - 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: There were no statistical analyses needed for this endpoint as it was descriptive.

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	132		
Units: Days				
log mean (inter-quartile range (Q1-Q3))				
Pain, Dose 1 (N=132, 132)	3.0 (2.0 to 4.0)	1.9 (1.0 to 2.5)		
Pain, Dose 2 (N=126, 128)	2.8 (2.0 to 3.0)	1.3 (1.0 to 2.0)		
Pain, Overall (N=258, 260)	2.9 (2.0 to 4.0)	1.6 (1.0 to 2.0)		
Redness, Dose 1 (N=132, 132)	5.0 (3.0 to 7.0)	4.0 (4.0 to 4.0)		
Redness, Dose 2 (N=126, 128)	5.0 (2.0 to 7.0)	2.0 (2.0 to 2.0)		
Redness, Overall (N=258, 260)	5.0 (2.0 to 7.0)	3.0 (2.0 to 4.0)		
Swelling, Dose 1 (N=132, 132)	5.3 (2.0 to 7.0)	4.0 (4.0 to 4.0)		
Swelling, Dose 2 (N=126, 128)	3.9 (1.0 to 6.0)	0.0 (0.0 to 0.0)		
Swelling, Overall (N=258, 260)	4.6 (2.0 to 7.0)	4.0 (4.0 to 4.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of days with solicited general symptoms

End point title	Number of days with solicited general symptoms ^[10]
End point description: Assessed solicited general symptoms were fatigue, gastrointestinal symptoms, headache, myalgia, shivering and fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)].	
End point type	Primary
End point timeframe: Within 7 days (Days 0-6) after each vaccination	

Notes:

[10] - 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: There were no statistical analyses needed for this endpoint as it was descriptive.

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	132		
Units: Days				
arithmetic mean (inter-quartile range (Q1-Q3))				
Fatigue, Dose 1 (N=132, 132)	3.6 (2.0 to 6.0)	4.0 (1.0 to 7.0)		
Fatigue, Dose 2 (N=126, 128)	3.4 (2.0 to 5.0)	4.4 (2.0 to 7.0)		
Fatigue, Overall (N=258, 260)	3.5 (2.0 to 5.5)	4.1 (2.0 to 7.0)		
Gastrointestinal symptoms, Dose 1 (N=132, 132)	1.9 (1.0 to 2.0)	3.4 (1.0 to 4.5)		
Gastrointestinal symptoms, Dose 2 (N=126, 128)	2.3 (1.0 to 7.0)	2.6 (1.0 to 3.0)		
Gastrointestinal symptoms, Overall (N=258, 260)	2.1 (1.0 to 7.0)	3.0 (1.0 to 7.0)		
Headache, Dose 1 (N=132, 132)	1.8 (1.0 to 2.0)	2.4 (1.0 to 3.0)		
Headache, Dose 2 (N=126, 128)	2.4 (1.0 to 3.0)	2.6 (1.0 to 4.0)		
Headache, Overall (N=258, 260)	2.1 (1.0 to 3.0)	2.5 (1.0 to 3.0)		
Myalgia, Dose 1 (N=132, 132)	3.6 (2.0 to 4.0)	3.8 (1.0 to 7.0)		
Myalgia, Dose 2 (N=126, 128)	2.8 (1.0 to 4.0)	4.9 (2.0 to 7.0)		
Myalgia, Overall (N=258, 260)	3.2 (1.0 to 4.0)	4.3 (1.0 to 7.0)		
Shivering, Dose 1 (N=132, 132)	2.7 (1.0 to 4.0)	3.3 (1.0 to 7.0)		
Shivering, Dose 2 (N=126, 128)	1.9 (1.0 to 2.0)	4.1 (2.0 to 7.0)		
Shivering, Overall (N=258, 260)	2.1 (1.0 to 7.0)	3.6 (1.0 to 7.0)		
Temperature, Dose 1 (N=132, 132)	1.2 (1.0 to 2.0)	1.2 (1.0 to 2.0)		
Temperature, Dose 2 (N=126, 128)	1.0 (1.0 to 1.0)	1.1 (1.0 to 2.0)		
Temperature, Overall (N=258, 260)	1.1 (1.0 to 2.0)	1.2 (1.0 to 2.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-gE antibody concentrations

End point title	Anti-gE antibody concentrations
End point description:	Varicella Zoster Virus.glycoprotein E Ab.Immunoglobulin G was determined by ELISA assay.
End point type	Secondary
End point timeframe:	At Months 0, 1, 2, 7 and 13

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	119		
Units: mIU/mL				
geometric mean (confidence interval 95%)				

anti-gE, Month 0	1354.4 (1118.3 to 1640.4)	1495.7 (1202.3 to 1860.8)		
anti-gE, Month 1	9530.5 (7111.3 to 12772.7)	1501.9 (1231.3 to 1832.0)		
anti-gE, Month 2	19163.8 (15041.5 to 24416.0)	1489.4 (1215.8 to 1824.7)		
anti-gE, Month 7	13066.7 (10291.5 to 16590.4)	1533.7 (1249.6 to 1882.3)		
anti-gE, Month 13	8545.1 (6753.7 to 10811.5)	1572.7 (1269.6 to 1948.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a vaccine response for anti-gE humoral immunogenicity

End point title	Number of subjects with a vaccine response for anti-gE humoral immunogenicity
End point description: Cut-off value for the vaccine response was 97 milli-international units per millilitre (mIU/mL).	
End point type	Secondary
End point timeframe: At Months 1, 7 and 13	

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	119		
Units: Participants				
anti-gE, Month 1	77	3		
anti-gE, Month 7	83	5		
anti-gE, Month 13	74	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequencies of gE-specific CD4+ T-cells

End point title	Frequencies of gE-specific CD4+ T-cells
End point description: gE-specific CD4+ T-cells, expressing at least two activation markers (from among interferon gamma [IFN-γ], interleukin-2 [IL-2], tumour necrosis factor alpha [TNF-α] and CD40L), as determined by in	

vitro ICS

End point type	Secondary
End point timeframe:	
At Months 0, 2 and 13	

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	32		
Units: gE-specific CD4+ T-cells/million T-cells				
arithmetic mean (standard deviation)				
Month 0	110.9 (± 182.09)	165.75 (± 242.92)		
Month 2	2433.07 (± 2102.29)	156.98 (± 274.81)		
Month 13	1320.92 (± 1823.64)	129.41 (± 197.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Vaccine response for gE-specific CD4+ T-cells

End point title	Number of subjects with Vaccine response for gE-specific CD4+ T-cells
-----------------	---

End point description:

Vaccine response for gE-specific CD4+ T-cells expressing at least two activation markers (from among IFN- γ , IL-2, TNF- α and CD40L), as determined by in vitro ICS

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

End point timeframe:

At Months 2 and 13

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	28		
Units: Participants				
Month 2	20	0		
Month 13	17	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and related serious adverse events (SAEs)

End point title	Number of subjects with any and related serious adverse events (SAEs)
End point description: Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, or result in disability /incapacity.	
End point type	Secondary
End point timeframe: From 30 days post last vaccination until study end (Month 13).	

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	132		
Units: Participants				
Any SAEs	21	29		
Related SAEs	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any potential immune-mediated diseases (pIMDs)

End point title	Number of subjects with any potential immune-mediated diseases (pIMDs)
End point description: Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology	
End point type	Secondary
End point timeframe: From 30 days post last vaccination until study end (Month 13).	

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	132		
Units: Participants				
Participants	4	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with biopsy confirmed renal allograft rejection

End point title	Number of subjects with biopsy confirmed renal allograft rejection
-----------------	--

End point description:

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

End point timeframe:

From 30 days post last vaccination until study end (Month 13).

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	132	132		
Units: Participants				
Rejection confirmed	4	7		
Rejection not confirmed	12	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with changes in allograft function

End point title	Number of subjects with changes in allograft function
-----------------	---

End point description:

Allograft function was indicated by an increase in the levels of serum creatinine. The number of subjects with declining allograft function, as determined by serum creatinine measurements post-vaccination (after 30 days post-last vaccination to study end) compared to pre-vaccination were presented.

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

End point timeframe:

From 30 days post last vaccination until study end at Month 13

End point values	GSK1437173A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	132		
Units: Participants				
≥1.20 fold increase	17	22		
≥1.50 fold increase	4	3		
≥1.75 fold increase	3	1		
≥2 fold increase	2	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 7-day (Days 0-6) post-vaccination period following each dose and across doses, unsolicited symptoms: during the 30-day (Days 0-29) post-vaccination period, serious adverse events: up to study end at Month 13.

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Placebo Group
-----------------------	---------------

Reporting group description:

Subjects, aged 18 years or older, received 2 doses of Placebo (lyophilised sucrose reconstituted with saline [NaCl] solution) at Day 0, and Month 1, administered intramuscularly, in the deltoid muscle of the non-dominant arm.

Reporting group title	GSK1437173A Group
-----------------------	-------------------

Reporting group description:

Subjects, aged 18 years or older, received 2 doses of the GSK 1437173A vaccine, adjuvanted with AS01B at Day 0, and Month 1, administered intramuscularly, in the deltoid muscle of the non-dominant arm.

Serious adverse events	Placebo Group	GSK1437173A Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 132 (25.00%)	26 / 132 (19.70%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign gastrointestinal neoplasm			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burkitt's lymphoma			

subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous incomplete			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Mucosal inflammation			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Kidney transplant rejection			
subjects affected / exposed	2 / 132 (1.52%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant rejection			
subjects affected / exposed	4 / 132 (3.03%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	3 / 132 (2.27%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft stenosis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft thrombosis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Beta haemolytic streptococcal infection			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium colitis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Erysipelas			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	4 / 132 (3.03%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter gastritis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	4 / 132 (3.03%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 132 (0.00%)	3 / 132 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			

subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 132 (0.76%)	4 / 132 (3.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal graft infection			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 132 (2.27%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo Group	GSK1437173A Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 132 (59.09%)	121 / 132 (91.67%)	
Nervous system disorders			
Headache			
subjects affected / exposed	35 / 132 (26.52%)	44 / 132 (33.33%)	
occurrences (all)	48	68	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	16 / 132 (12.12%)	29 / 132 (21.97%)	
occurrences (all)	22	33	
Fatigue			
subjects affected / exposed	54 / 132 (40.91%)	62 / 132 (46.97%)	
occurrences (all)	79	96	
Pain			
subjects affected / exposed	11 / 132 (8.33%)	114 / 132 (86.36%)	
occurrences (all)	14	202	
Pyrexia			
subjects affected / exposed	14 / 132 (10.61%)	32 / 132 (24.24%)	
occurrences (all)	14	37	
Swelling			
subjects affected / exposed	1 / 132 (0.76%)	15 / 132 (11.36%)	
occurrences (all)	1	21	
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	24 / 132 (18.18%)	24 / 132 (18.18%)	
occurrences (all)	30	31	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	2 / 132 (1.52%)	33 / 132 (25.00%)	
occurrences (all)	2	45	
Musculoskeletal and connective tissue disorders			
Myalgia			

subjects affected / exposed	31 / 132 (23.48%)	65 / 132 (49.24%)	
occurrences (all)	42	90	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2012	<ul style="list-style-type: none">• Eligibility criteria have been added and modified for one or more of the following reasons: to respond to FDA/CBER comments, to increase the homogeneity of the subject population and/or to increase safety of the subjects• To allow expedited reporting, renal allograft rejections will always be recorded on SAE screens• As per CBER's request, any medical condition including the occurrence of a new pIMD or the exacerbation of an existing pIMD that, in the opinion of the investigator, exposes the subject to unacceptable risk from subsequent vaccination, constitutes contraindications to further administration of HZ/su vaccine.• To add the endpoint of allograft dysfunction, as measured by serum creatinine, to the safety objectives (co-primary and secondary)
06 August 2014	<ul style="list-style-type: none">• GSK has revised the allowed intervals for the ATP cohort for analysis of immunogenicity.• The cut-off of the gE-specific ELISA assay has been changed from 18 to 97 mIU/mL.• Modifications were made to some of the eligibility criteria: 1) the inclusion criterion for stable renal function can now also be met based upon investigator review of more than the last two creatinine measurements or calculated GFR; 2) Diabetes mellitus (type 1 and 2) with diabetic nephropathy as the primary kidney disease prompting transplantation was added as an exception to autoimmune or potential immune-mediated diseases; 3) added that use of anti-B cell monoclonal antibody agents as therapeutic immunosuppressive therapy for prevention of allograft rejections is not permitted and use of these agents within 9 months of first dose of study vaccine is not permitted; 4) other edits to eligibility criteria were minor clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported