



Clinical trial results:

A phase III, randomised, open-label, multicentre, clinical trial to assess the safety and immunogenicity of GSK Biologicals' HZ/su vaccine when administered intramuscularly according to a 0,2-month schedule, a 0,6-month schedule or a 0,12-month schedule in adults aged 50 years or older.

Summary

EudraCT number	2012-004456-11
Trial protocol	EE
Global end of trial date	08 April 2015

Results information

Result version number	v2 (current)
This version publication date	06 November 2020
First version publication date	22 April 2016
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Results have been amended to account for consistency with other registries.

Trial information

Trial identification

Sponsor protocol code	116697
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01751165
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, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, 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	Final
Date of interim/final analysis	20 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 May 2014
Global end of trial reached?	Yes
Global end of trial date	08 April 2015
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 (gE) humoral immune responses at one month (1 mth) post-dose 2 (PD2) in the 0,6-mth and 0,12-mth schedule groups.

Criterion:

*The lower limit of the 97,5% confidence interval (CI) of the VRR for anti-gE ELISA antibody concentrations at 1 mth PD2 in the 0,6-mth or 0,12-mth schedule groups is at least 60%.

If the objectives are met for the 0,6-mth and 0,12-mth schedules, the following objective will be evaluated:

-Non-inferiority in terms of anti-gE humoral immune response 1 mth PD2 given according to a 0,6-mth schedule compared to a 0,2-mth schedule and a 0,12-mth schedule compared to a 0,2-mth schedule.

Criteria for non-inferiority:

*The upper limit of the 97,5% CI for the anti-gE ELISA geometric mean concentration (GMC) ratio (0,2-mth schedule over 0,6-mth schedule) at 1 mth PD2 is <1.5.

*The upper limit of the 97,5% CI for the anti-gE ELISA GMC ratio (0,2-mth schedule over 0,12-mth schedule) at 1 mth PD2 is <1.5.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Subjects were followed-up for 30 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 March 2013
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: 277
Country: Number of subjects enrolled	United States: 77
Worldwide total number of subjects	354
EEA total number of subjects	277

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)	194
From 65 to 84 years	159
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK1437173A-0,2 M Group
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	GSK1437173A
Investigational medicinal product code	
Other name	Herpes Zoster (HZ) vaccine GSK1437173A
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses of the study vaccine on a 0, 2 months schedule, by intramuscular injection into the deltoid region of the non-dominant arm.

Arm title	GSK1437173A-0,6 M Group
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	GSK1437173A
Investigational medicinal product code	
Other name	Herpes Zoster (HZ) vaccine GSK1437173A
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses of the study vaccine on a 0, 6 months schedule, by intramuscular injection into the deltoid region of the non-dominant arm.

Arm title	GSK1437173A-0,12 M Group
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	GSK1437173A
Investigational medicinal product code	
Other name	Herpes Zoster (HZ) vaccine GSK1437173A
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses of the study vaccine on a 0, 12 months schedule, by intramuscular injection into the deltoid region of the non-dominant arm.

Number of subjects in period 1	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group
Started	119	119	116
Completed	117	116	113
Not completed	2	3	3
Adverse event, serious fatal	1	-	1
Consent withdrawn by subject	-	-	1
SAE	-	2	-
Lost to follow-up	1	1	1

Baseline characteristics

Reporting groups

Reporting group title	GSK1437173A-0,2 M Group
Reporting group description: -	
Reporting group title	GSK1437173A-0,6 M Group
Reporting group description: -	
Reporting group title	GSK1437173A-0,12 M Group
Reporting group description: -	

Reporting group values	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group
Number of subjects	119	119	116
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	64.5	64	64.1
standard deviation	± 8.9	± 8.6	± 9.2
Gender categorical Units: Subjects			
Female	90	77	79
Male	29	42	37

Reporting group values	Total		
Number of subjects	354		
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	0 0 0 0 0 0 0 0		

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	246		
Male	108		

End points

End points reporting groups

Reporting group title	GSK1437173A-0,2 M Group
Reporting group description: -	
Reporting group title	GSK1437173A-0,6 M Group
Reporting group description: -	
Reporting group title	GSK1437173A-0,12 M Group
Reporting group description: -	

Primary: Number of subjects with vaccine response to anti-glicoprotein E (anti-gE) antibodies as determined by the enzyme-linked immunosorbent assay (ELISA).

End point title	Number of subjects with vaccine response to anti-glicoprotein E (anti-gE) antibodies as determined by the enzyme-linked immunosorbent assay (ELISA). ^{[1][2]}
End point description:	Vaccine response was defined as: for initially seronegative subjects, antibody concentration at post-vaccination ≥ 4 fold the cut-off for Anti-gE (4x97 mIU/mL); for initially seropositive subjects, antibody concentration at post-vaccination ≥ 4 fold the pre-vaccination antibody concentration. The objective required a comparison of VRR between 0,6-months and 0,12-months schedules.
End point type	Primary
End point timeframe:	
At one month (M1) after Dose 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: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint only required results for the groups on the 0,6 and 0,12 months vaccination schedule.

End point values	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	110		
Units: Subjects				
Anti-gE, M1 [N=114,110]	110	104		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of antibodies against anti-gE as determined by ELISA.

End point title	Concentrations of antibodies against anti-gE as determined by ELISA.
End point description:	
End point type	Primary

End point timeframe:

At one month (M1) after Dose 2

End point values	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	118	114	111	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-gE, M1 [N=118,114,111]	44376.3 (39697 to 49607.2)	38153.7 (34205.8 to 42557.3)	37435.8 (30813.8 to 45480.8)	

Statistical analyses

Statistical analysis title	Anti-gE immune response for 0,2-0,6 months.
Statistical analysis description: To demonstrate the non-inferiority in terms of anti-gE humoral immune response one month post-dose 2 given according to a 0,6-month schedule compared to a 0,2-month schedule.	
Comparison groups	GSK1437173A-0,2 M Group v GSK1437173A-0,6 M Group
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	1.16
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.98
upper limit	1.39

Notes:

[3] - Non inferiority criteria:

The upper limit (UL) of the 97.5% confidence interval (CI) for the anti-gE ELISA geometric mean concentration (GMC) ratio (0,2-month schedule over 0,6-month schedule) at one month post-dose 2 had to be below 1.5

Statistical analysis title	Anti-gE immune response for 0,2-0,12 months.
Statistical analysis description: To demonstrate the non-inferiority in terms of anti-gE humoral immune response one month post-dose 2 given according to a 0,12-month schedule compared to a 0,2-month schedule.	
Comparison groups	GSK1437173A-0,2 M Group v GSK1437173A-0,12 M Group
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[4]
Method	ANCOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	1.19

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.93
upper limit	1.53

Notes:

[4] - The upper limit (UL) of the 97.5% confidence interval (CI) for the anti-gE ELISA geometric mean concentration (GMC) ratio (0,2-month schedule over 0,12-month schedule) at one month post-dose 2 had to be below 1.5

Secondary: Concentrations of antibodies against anti-gE as determined by ELISA.

End point title	Concentrations of antibodies against anti-gE as determined by ELISA.
-----------------	--

End point description:

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

End point timeframe:

Prior (PRE) to vaccination and twelve (M12) post Dose 2

End point values	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	118	115	110	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-gE, PRE [N=118,114,110]	1079.1 (891.9 to 1305.5)	1066.1 (891.3 to 1275.3)	1019.4 (858.6 to 1210.2)	
Anti-gE, M12 [N=117,115,110]	14245.4 (12450.8 to 16298.6)	12911.5 (11412.7 to 14607.2)	11892.1 (10236.4 to 13815.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms.

End point title	Number of subjects with solicited local symptoms.
-----------------	---

End point description:

Solicited local symptoms assessed include pain, redness and swelling. "Grade 3 pain" was defined as crying when limb was moved/spontaneously painful. "Grade 3 swelling/redness" was defined as swelling/redness larger than (>) 100 millimeters (mm). "Any" is defined as incidence of the specified symptom regardless of intensity.

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

End point timeframe:

During the 7 day period (Days 0-6) following each vaccination

End point values	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	119	116	
Units: Subjects				
Any Pain, D1 [N=119,119,115]	84	77	80	
Grade 3 Pain, D1 [N=119,119,115]	1	0	2	
Any Redness, D1 [N=119,119,115]	37	39	32	
Grade 3 Redness, D1 [N=119,119,115]	0	0	1	
Any Swelling, D1 [N=119,119,115]	17	23	25	
Grade 3 Swelling, D1 [N=119,119,115]	0	0	0	
Any Pain, D2 [N=118,117,111]	71	83	87	
Grade 3 Pain, D2 [N=118,117,111]	6	6	10	
Any Redness, D2 [N=118,117,111]	28	27	37	
Grade 3 Redness, D2 [N=118,117,111]	2	0	0	
Any Swelling, D2 [N=118,117,111]	15	9	24	
Grade 3 Swelling, D2 [N=118,117,111]	0	0	0	
Any Pain, Across [N=119,119,116]	91	95	98	
Grade 3, Across [N=119,119,116]	7	6	12	
Any Redness, Across [N=119,119,116]	48	50	53	
Grade 3 Redness, Across [N=119,119,116]	2	0	1	
Any Swelling, Across [N=119,119,116]	26	28	39	
Grade 3 Swelling, Across [N=119,119,116]	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms.

End point title	Number of subjects with solicited general symptoms.
End point description:	
Assessed solicited general symptoms were Fatigue, Gastrointestinal (meaning nausea, vomiting, diarrhoea and/or abdominal pain), Headache, Myalgia, Shivering and Temperature (temperature higher than \geq 37.5 degrees Celsius [$^{\circ}$ C]). "Any" = occurrence of the specified solicited general symptom, regardless of intensity or relationship to vaccination. "Related" = occurrence of the specified symptom assessed by the investigators as causally related to vaccination. "Grade 3 Fatigue" = fatigue that prevented normal activity. "Grade 3 Gastrointestinal" = gastrointestinal that prevented normal every day activities. "Grade 3 Headache" = headache that prevented normal activity. "Grade 3 Myalgia" = myalgia that prevented normal activity. "Grade 3 Shivering" = shivering that prevented normal activity. "Grade 3 Temperature" = temperature higher than ($>$) 39.0 $^{\circ}$ C.	
End point type	Secondary
End point timeframe:	
During the 7 day period (Days 0-6) following each vaccination	

End point values	GSK1437173A- 0,2 M Group	GSK1437173A- 0,6 M Group	GSK1437173A- 0,12 M Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	119	116	
Units: Subjects				
Any Fatigue, D1 [N=119,119,115]	42	50	46	
Grade 3 Fatigue, D1 [N=119,119,115]	3	1	0	
Related Fatigue, D1 [N=119,119,115]	37	49	38	
Any Gastrointestinal, D1 [N=119,119,115]	22	17	17	
Grade 3 Gastrointestinal, D1 [N=119,119,115]	3	1	0	
Related Gastrointestinal, D1 [N=119,119,115]	19	14	12	
Any Headache, D1 [N=119,119,115]	35	39	34	
Grade 3 Headache, D1 [N=119,119,115]	1	1	0	
Related Headache, D1 [N=119,119,115]	31	31	26	
Any Myalgia, D1 [N=119,119,115]	43	38	46	
Grade 3 Myalgia, D1 [N=119,119,115]	2	2	0	
Related Myalgia, D1 [N=119,119,115]	36	33	40	
Any Shivering, D1 [N=119,119,115]	25	25	29	
Grade 3 Shivering, D1 [N=119,119,115]	1	0	0	
Related Shivering, D1 [N=119,119,115]	22	22	26	
Any Temperature, D1 [N=119,119,115]	21	22	14	
Grade 3 Temperature, D1 [N=119,119,115]	1	0	0	
Related Temperature, D1 [N=119,119,115]	19	21	13	
Any Fatigue, D2 [N=118,117,111]	43	46	59	
Grade 3 Fatigue, D2 [N=118,117,111]	4	4	4	
Related Fatigue, D2 [N=118,117,111]	41	41	56	
Any Gastrointestinal, D2 [N=118,117,111]	14	5	12	
Grade 3 Gastrointestinal, D2 [N=118,117,111]	0	1	1	
Related Gastrointestinal, D2 [N=118,117,111]	14	5	10	
Any Headache, D2 [N=118,117,111]	36	27	37	
Grade 3 Headache, D2 [N=118,117,111]	2	3	5	
Related Headache, D2 [N=118,117,111]	32	22	33	
Any Myalgia, D2 [N=118,117,111]	48	42	43	
Grade 3 Myalgia, D2 [N=118,117,111]	5	2	3	
Related Myalgia, D2 [N=118,117,111]	46	39	38	
Any Shivering, D2 [N=118,117,111]	25	23	35	
Grade 3 Shivering, D2 [N=118,117,111]	3	3	3	
Related Shivering, D2 [N=118,117,111]	24	20	31	
Any Temperature, D2 [N=118,117,111]	20	16	26	
Grade 3 Temperature, D2 [N=118,117,111]	0	0	2	
Related Temperature, D2 [N=118,117,111]	19	16	24	
Any Fatigue, Across [N=119,119,116]	54	63	71	
Grade 3 Fatigue, Across [N=119,119,116]	7	5	4	

Related Fatigue, Across [N=119,119,116]	49	57	65	
Any Gastrointestinal, Across [N=119,119,116]	27	20	27	
Grade 3 Gastrointestinal, Across [N=119,119,116]	3	2	1	
Related Gastrointestinal, Across [N=119,119,116]	26	17	21	
Any Headache, Across [N=119,119,116]	47	47	53	
Grade 3 Headache, Across [N=119,119,116]	2	4	5	
Related Headache, Across [N=119,119,116]	41	38	45	
Any Myalgia, Across [N=119,119,116]	63	57	64	
Grade 3 Myalgia, Across [N=119,119,116]	7	4	3	
Related Myalgia, Across [N=119,119,116]	57	52	57	
Any Shivering, Across [N=119,119,116]	37	35	48	
Grade 3 Shivering, Across [N=119,119,116]	4	3	3	
Related Shivering, Across [N=119,119,116]	34	29	43	
Any Temperature, Across [N=119,119,116]	32	32	33	
Grade 3 Temperature, Across [N=119,119,116]	1	0	2	
Related Temperature, Across [N=119,119,116]	29	31	30	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs).

End point title	Number of subjects with unsolicited adverse events (AEs).
-----------------	---

End point description:

An adverse event (AE) is 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.

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

End point timeframe:

During the 30 Days (Day 0-29) following vaccination

End point values	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	119	116	
Units: Subjects				
Any AEs [N=119,119,116]	27	27	23	
Grade 3 AEs [N=119,119,116]	4	4	4	
Related AEs [N=119,119,116]	9	5	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs).

End point title	Number of subjects with 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, result in disability/incapacity.

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

End point timeframe:

From first vaccination up to one month (30 Days) post last vaccination

End point values	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	119	116	
Units: Subjects				
Any SAEs [N=119,119,116]	0	4	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with SAE(s).

End point title	Number of subjects with SAE(s).
-----------------	---------------------------------

End point description:

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

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

End point timeframe:

Starting from 30 Days post last vaccine administration up to study end at Month 24

End point values	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	119	116	
Units: Subjects				
Any SAEs [N=119,119,116]	5	6	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with solicited local symptoms.

End point title	Number of days with solicited local symptoms.
End point description:	
Each dose was abbreviated as follows: D1 = Dose 1, D2 = Dose 2	
End point type	Secondary
End point timeframe:	
During the 7 Days (Day 0-6) following vaccination	

End point values	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	119	116	
Units: Days				
Days with Pain, D1 [N=119,119,116]	84	77	80	
Days with Pain, D2 [N=119,119,116]	71	83	87	
Days with Redness, D1 [119,119,116]	37	39	32	
Days with Redness, D2 [119,119,116]	28	27	37	
Days with Swelling, D1 [N=119,119,116]	17	23	25	
Days with Swelling, D2 [N=119,119,116]	15	9	24	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with solicited general symptoms.

End point title	Number of days with solicited general symptoms.
End point description:	
Each dose was abbreviated as follows: D1 = Dose 1, D2 = Dose 2	
End point type	Secondary
End point timeframe:	
During the 7 Days (Day 0-6) following vaccination	

End point values	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	119	116	
Units: Days				
Days with Fatigue, D1 [N=119,119,116]	42	50	46	
Days with Fatigue, D2 [N=119,119,116]	43	46	59	
Days with Gastrointestinal, D1 [119,119,116]	22	17	17	
Days with Gastrointestinal, D2 [119,119,116]	14	5	12	
Days with Headache, D1 [N=119,119,116]	35	39	34	
Days with Headache, D2 [N=119,119,116]	36	27	37	
Days with Myalgia, D1 [N=119,119,116]	43	38	46	
Days with Myalgia, D2 [N=119,119,116]	48	42	43	
Days with Shivering, D1 [N=119,119,116]	25	25	29	
Days with Shivering, D2 [N=119,119,116]	25	23	35	
Days with Temperature, D1 [N=119,119,116]	21	22	14	
Days with Temperature, D2 [N=119,119,116]	20	16	26	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with potential immune-mediated disease (pIMDs).

End point title	Number of subjects with potential immune-mediated disease (pIMDs).
-----------------	--

End point description:

Potential immune-mediated diseases (pIMDs) are a subset of Adverse Events (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 Dose 1 up to one month (30 days) following the last vaccine dose administration (Dose 2)

End point values	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	119	116	
Units: Subjects				
Any pIMDs [N=119,119,116]	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with pIMDs.

End point title	Number of subjects with pIMDs.
End point description: Potential immune-mediated diseases (pIMDs) are a subset of Adverse Events (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 one month (30 Days) following the last vaccine administration up to study end at Month 24	

End point values	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	119	119	116	
Units: Subjects				
Any pIMDs [N=119,119,116]	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events were collected during the entire study period (up to Month 24). Other Adverse Events were collected during the 30 Day post-vaccination period (Day 0 - Day 29).

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

Dictionary used

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

Dictionary version	18.1
--------------------	------

Reporting groups

Reporting group title	GSK1437173A-0,2 M Group
-----------------------	-------------------------

Reporting group description: -	
--------------------------------	--

Reporting group title	GSK1437173A-0,6 M Group
-----------------------	-------------------------

Reporting group description: -	
--------------------------------	--

Reporting group title	GSK1437173A-0,12 M Group
-----------------------	--------------------------

Reporting group description: -	
--------------------------------	--

Serious adverse events	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 119 (4.20%)	9 / 119 (7.56%)	12 / 116 (10.34%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal adenocarcinoma			
subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Lung neoplasm malignant			
subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			

subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Venous thrombosis limb			
subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	1 / 119 (0.84%)	0 / 119 (0.00%)	0 / 116 (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
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Cardiac disorders			
Atrial flutter			

subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Ventricular extrasystoles			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Atrial fibrillation			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Bradycardia			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Cardiovascular disorder			
subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Coronary artery disease			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Nervous system disorders			
Carotid artery disease			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Cerebral infarction			

subjects affected / exposed	0 / 119 (0.00%)	2 / 119 (1.68%)	0 / 116 (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
Cerebral haemorrhage			
subjects affected / exposed	1 / 119 (0.84%)	0 / 119 (0.00%)	0 / 116 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
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			
Diverticulum			
subjects affected / exposed	1 / 119 (0.84%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mallory-weiss syndrome			
subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varices oesophageal			
subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 119 (0.00%)	0 / 116 (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
Hepatobiliary disorders			

Cholecystitis acute			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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			
Nephrolithiasis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	0 / 116 (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
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 119 (0.00%)	0 / 116 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 119 (0.84%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	1 / 119 (0.84%)	0 / 119 (0.00%)	0 / 116 (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			
Helicobacter gastritis			
subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dyslipidaemia			

subjects affected / exposed	0 / 119 (0.00%)	0 / 119 (0.00%)	1 / 116 (0.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	GSK1437173A-0,2 M Group	GSK1437173A-0,6 M Group	GSK1437173A-0,12 M Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	107 / 119 (89.92%)	106 / 119 (89.08%)	107 / 116 (92.24%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed	91 / 119 (76.47%)	95 / 119 (79.83%)	98 / 116 (84.48%)
occurrences (all)	91	95	98
Erythema			
subjects affected / exposed	48 / 119 (40.34%)	51 / 119 (42.86%)	53 / 116 (45.69%)
occurrences (all)	48	50	53
Swelling			
subjects affected / exposed	26 / 119 (21.85%)	28 / 119 (23.53%)	39 / 116 (33.62%)
occurrences (all)	26	28	39
Fatigue			
subjects affected / exposed	54 / 119 (45.38%)	63 / 119 (52.94%)	71 / 116 (61.21%)
occurrences (all)	54	63	71
Gastrointestinal			
subjects affected / exposed	27 / 119 (22.69%)	20 / 119 (16.81%)	27 / 116 (23.28%)
occurrences (all)	27	20	27
Headache			
subjects affected / exposed	48 / 119 (40.34%)	48 / 119 (40.34%)	53 / 116 (45.69%)
occurrences (all)	47	47	53
Myalgia			
subjects affected / exposed	63 / 119 (52.94%)	57 / 119 (47.90%)	64 / 116 (55.17%)
occurrences (all)	63	57	64
Chills			
subjects affected / exposed	37 / 119 (31.09%)	35 / 119 (29.41%)	48 / 116 (41.38%)
occurrences (all)	37	35	48
Pyrexia			

subjects affected / exposed	32 / 119 (26.89%)	32 / 119 (26.89%)	33 / 116 (28.45%)
occurrences (all)	32	32	33

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 May 2014	The cut-off of the gE-specific ELISA assay has been changed from 18 to 97 mIU/mL. The definition of the ATP cohort for safety was updated. Other minor changes were implemented.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported