Clinical trial results:
A Phase III, randomised, observer-blind, placebo-controlled, multicentre study to assess the safety, immunogenicity and efficacy of GSK Biologicals' Herpes Zoster HZ/su candidate vaccine when administered intramuscularly on a two-dose schedule to adults aged 18 years and older with haematologic malignancies.

Summary

EudraCT number	2012-003438-18
Trial protocol	SE BE FI ES IT CZ GB PL
Global end of trial date	06 January 2017

Results information

Result version number	v1 (current)
This version publication date	03 January 2018
First version publication date	03 January 2018

Trial information

Trial identification

Sponsor protocol code	116428

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01767467
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	Final
Date of interim/final analysis	27 October 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the safety and tolerability following administration of the HZ/su vaccine compared to placebo from the first vaccination up to 30 days post last vaccination in subjects with haematologic malignancies, aged 18 years and older.
- 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 subjects with haematologic malignancies excluding subjects with Non-Hodgkin B-cell Lymphoma and Chronic Lymphocytic Leukaemia.
- To evaluate anti-gE humoral immune responses at Month 2 following a two-dose administration of the HZ/su vaccine, as compared to placebo, in subjects with haematologic malignancies excluding subjects with Non-Hodgkin B-cell Lymphoma and Chronic Lymphocytic Leukaemia.

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	01 March 2013
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	Australia: 29
Country: Number of subjects enrolled	Belgium: 31
Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	Czech Republic: 13
Country: Number of subjects enrolled	Finland: 10
Country: Number of subjects enrolled	France: 28
Country: Number of subjects enrolled	Hong Kong: 3
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Korea, Republic of: 107
Country: Number of subjects enrolled	New Zealand: 11
Country: Number of subjects enrolled	Pakistan: 12
Country: Number of subjects enrolled	Panama: 14
Country: Number of subjects enrolled	Poland: 31
Country: Number of subjects enrolled	Russian Federation: 27

Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Spain: 64
Country: Number of subjects enrolled	Sweden: 26
Country: Number of subjects enrolled	Taiwan: 29
Country: Number of subjects enrolled	Turkey: 52
Country: Number of subjects enrolled	United Kingdom: 48
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	606
EEA total number of subjects	274

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)	370
From 65 to 84 years	219
85 years and over	17

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of the 568 subjects enrolled, only 562 subjects received vaccination as per protocol and hence started the study.

Pre-assignment period milestones

Number of subjects started	606
Number of subjects completed	562

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Study vaccine dose not administered AT ALL but sub: 44

Period 1

Period 1 title	Vaccination Phase (up to Month 2)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Subject, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK1437173A Group

Arm description:

Subjects who received GSK1437173A vaccine according to a 0, 1 Months schedule (The second dose of study vaccine could be administered 1 - 2 months after the first dose).

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:

Administered according to a 0, 1 Months schedule (The second dose of study vaccine/placebo could be administered 1 - 2 months after the first dose)

Arm title	Placebo Group

Arm description:

Subjects who received placebo doses according to a 0, 1 Months schedule (The second dose of placebo could be administered 1 - 2 months after the first dose).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Administered according to a 0, 1 Months schedule (The second dose of study vaccine/placebo could be administered 1 - 2 months after the first dose)

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.
Justification: The blinding was presented as per the protocol.

Number of subjects in period 1[2]	GSK1437173A Group	Placebo Group
Started	283	279
Completed	266	259
Not completed	17	20
Consent withdrawn by subject	7	10
Physician decision	1	-
Adverse event, non-fatal	8	8
Subject Unavailable	-	1
Suspected Herpes Zoster episode	-	1
Protocol deviation	1	-

Notes:

[2] - 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: Out of the enrolled subjects, some received subject numbers but did not receive the study vaccination, hence they were excluded from study start.

Period 2

Period 2 title	End of Study Phase (up to Month 13)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind[3]
Roles blinded	Subject, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK1437173A Group

Arm description:

Subjects who received GSK1437173A vaccine according to a 0, 1 Months schedule (The second dose of study vaccine could be administered 1 - 2 months after the first dose).

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:

Administered according to a 0, 1 Months schedule (The second dose of study vaccine/placebo could be administered 1 - 2 months after the first dose)

Arm title	Placebo Group

Arm description:

Subjects who received placebo doses according to a 0, 1 Months schedule (The second dose of placebo could be administered 1 - 2 months after the first dose).

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Administered according to a 0, 1 Months schedule (The second dose of study vaccine/placebo could be administered 1 - 2 months after the first dose)

Notes:

[3] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.
Justification: The blinding was presented as per the protocol.

Number of subjects in period 2	GSK1437173A Group	Placebo Group
Started	266	259
Completed	236	216
Not completed	30	43
Consent withdrawn by subject	2	4
Migrated/Moved from study area	-	3
Adverse event, non-fatal	21	31
Subject Unavailable	-	1
Lost to follow-up	6	4
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	GSK1437173A Group
Reporting group description:	
Subjects who received GSK1437173A vaccine according to a 0, 1 Months schedule (The second dose of study vaccine could be administered 1 - 2 months after the first dose).	
Reporting group title	Placebo Group
Reporting group description:	
Subjects who received placebo doses according to a 0, 1 Months schedule (The second dose of placebo could be administered 1 - 2 months after the first dose).	

Reporting group values	GSK1437173A Group	Placebo Group	Total
Number of subjects	283	279	562
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	56.8	57.8	
standard deviation	± 15.5	± 14.9	-
Gender categorical Units: Subjects			
Female	114	114	228
Male	169	165	334
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American	1	1	2
American Indian or Alaskan Native	0	1	1
Asian - Central / South Asian Heritage	5	6	11
Asian - East Asian Heritage	57	60	117
Asian - South East Asian Heritage	4	1	5
White - Arabic / North African Heritage	0	1	1
White - Caucasian / European Heritage	198	186	384
Other	7	12	19
Missing	11	11	22

End points

End points reporting groups

Reporting group title	GSK1437173A Group
Reporting group description:	
Subjects who received GSK1437173A vaccine according to a 0, 1 Months schedule (The second dose of study vaccine could be administered 1 - 2 months after the first dose).	
Reporting group title	Placebo Group
Reporting group description:	
Subjects who received placebo doses according to a 0, 1 Months schedule (The second dose of placebo could be administered 1 - 2 months after the first dose).	
Reporting group title	GSK1437173A Group
Reporting group description:	
Subjects who received GSK1437173A vaccine according to a 0, 1 Months schedule (The second dose of study vaccine could be administered 1 - 2 months after the first dose).	
Reporting group title	Placebo Group
Reporting group description:	
Subjects who received placebo doses according to a 0, 1 Months schedule (The second dose of placebo could be administered 1 - 2 months after the first dose).	
Subject analysis set title	GSK1437173A HZ cases Sub-Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects who received GSK1437173A vaccine according to a 0, 1 Months schedule (The second dose of study vaccine could be administered 1 - 2 months after the first dose), with confirmed Herpes Zoster (HZ).	
Subject analysis set title	GSK1437173A Non-HZ cases Sub-Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects who received GSK1437173A vaccine according to a 0, 1 Months schedule (The second dose of study vaccine could be administered 1 - 2 months after the first dose), with non-confirmed Herpes Zoster (HZ).	
Subject analysis set title	Placebo HZ cases Sub-Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects who received placebo doses according to a 0, 1 Months schedule (The second dose of placebo could be administered 1 - 2 months after the first dose), with confirmed Herpes Zoster (HZ).	
Subject analysis set title	Placebo Non-HZ cases Sub-Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects who received placebo doses according to a 0, 1 Months schedule (The second dose of placebo could be administered 1 - 2 months after the first dose), with non-confirmed Herpes Zoster (HZ).	

Primary: Vaccine response rates (VRR) for anti-glycoprotein E (anti-gE) antibody concentrations

End point title	Vaccine response rates (VRR) for anti-glycoprotein E (anti-gE) antibody concentrations[1]
End point description:	
Vaccine response rate refers to the percentage of subjects with a vaccine response, as determined by Enzyme-Linked Immunosorbent Assay (ELISA). Vaccine response was defined as: For initially seronegative subjects, antibody concentration at Month 2 greater than or equal to (≥) 4 fold the cut-off for Anti-gE [4x97 milli-international units per milliliter (mIU/mL)]. For initially seropositive subjects, antibody concentration at Month 2 ≥ 4 fold the pre-vaccination antibody concentration. This analysis was performed on subjects with haematologic malignancies excluding subjects with Non-Hodgkin B-cell Lymphoma and Chronic Lymphocytic Leukaemia.	
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: This endpoint was descriptive, hence no statistical anaylses were performed.

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	130		
Units: Percentage				
number (confidence interval 95%)				
Percentage	80.4 (73.1 to 86.5)	0.8 (0.0 to 4.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Adjusted geometric mean concentration of anti-gE antibodies

End point title	Adjusted geometric mean concentration of anti-gE antibodies

End point description:

The Adjusted geometric mean concentration was measured in all subjects excluding those with Non-Hodgkin B-cell Lymphoma and Chronic Lymphocytic Leukaemia.

End point type	Primary

End point timeframe:

At Month 2

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	130		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
mIU/mL	22132.9 (16642.8 to 32153.9)	777.6 (702.8 to 860.3)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The objective aimed to evaluate anti-gE humoral immune responses at Month 2 following a two-dose administration of the GSK1437173A vaccine, as compared to placebo, in subjects with haematologic malignancies excluding subjects with Non-Hodgkin B-cell Lymphoma and Chronic Lymphocytic

Leukaemia.

Comparison groups	Placebo Group v GSK1437173A Group
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.0001 [3]
Method	Repeated measurement model
Parameter estimate	Adjusted Geometric Mean Concentration
Point estimate	29.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.09
upper limit	41.96

Notes:

[2] - The objective was met if the lower limit of the 95% CI of the Geometric Mean (GM) ratio (GSK1437173A vaccine over placebo) for anti-gE ELISA antibody concentrations at Month 2 was greater than (>) 3.
[3] - The p-value is relative to the null hypothesis Ho: Vaccine / Placebo = 1

Primary: Number of subjects with any and Grade 3 solicited local symptoms

End point title	Number of subjects with any and Grade 3 solicited local symptoms[4]

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:

During the 7-day (Days 0-6) post-vaccination period following each dose and across doses

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: This endpoint was descriptive, hence no statistical anaylses were performed.

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	274		
Units: Participants				
Any Pain, Dose 1	199	26		
Grade 3 Pain, Dose 1	16	0		
Any Redness, Dose 1	80	1		
Grade 3 Redness, Dose 1	2	0		
Any Swelling, Dose 1	47	2		
Grade 3 Swelling, Dose 1	1	0		
Any Pain, Dose 2	172	31		
Grade 3 Pain, Dose 2	20	0		
Any Redness, Dose 2	82	5		
Grade 3 Redness, Dose 2	10	0		
Any Swelling, Dose 2	42	1		
Grade 3 Swelling, Dose 2	5	0		
Any Pain, Across doses	221	45		
Grade 3 Pain, Across doses	29	0		

Any Redness, Across doses	115	5		
Grade 3 Redness, Across doses	12	0		
Any Swelling, Across doses	63	2		
Grade 3 Swelling, Across doses	5	0		

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[5]

End point description:

Solicited local symptoms: pain, redness, swelling and their number of days were recorded after each vaccination dose.

End point type	Primary

End point timeframe:

Within the 7-day (Days 0-6) post-vaccination period

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: This endpoint was descriptive, hence no statistical anaylses were performed.

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	271		
Units: Days				
median (inter-quartile range (Q1-Q3))				
Pain, Dose 1	3.0 (2.0 to 4.0)	1.0 (1.0 to 2.0)		
Pain, Dose 2	3.0 (2.0 to 4.0)	2.0 (1.0 to 3.0)		
Redness, Dose 1	3.0 (2.0 to 5.0)	1.0 (1.0 to 1.0)		
Redness, Dose 2	3.0 (2.0 to 5.0)	4.0 (2.0 to 6.0)		
Swelling, Dose 1	3.0 (2.0 to 4.0)	1.5 (1.0 to 2.0)		
Swelling, Dose 2	3.0 (2.0 to 4.0)	4.0 (4.0 to 4.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any, Grade 3 and related solicited general symptoms

End point title	Number of subjects with any, Grade 3 and related solicited general symptoms[6]

End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal symptoms (included nausea, vomiting, diarrhoea and/or abdominal pain), headache, myalgia, shivering and fever [defined as oral, axillary or tympanic route measured 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.

End point type	Primary

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each dose and across doses

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: This endpoint was descriptive, hence no statistical anaylses were performed.

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	274		
Units: Participants				
Any fatigue, Dose 1	122	73		
Grade 3 fatigue, Dose 1	11	8		
Related fatigue, Dose 1	37	11		
Any gastrointestinal, Dose 1	48	24		
Grade 3 gastrointestinal, Dose 1	5	2		
Related gastrointestinal, Dose 1	13	1		
Any headache, Dose 1	70	40		
Grade 3 headache, Dose 1	3	3		
Related headache, Dose 1	29	10		
Any myalgia, Dose 1	80	35		
Grade 3 myalgia, Dose 1	11	0		
Related myalgia, Dose 1	33	10		
Any shivering, Dose 1	39	16		
Grade 3 shivering, Dose 1	2	0		
Related shivering, Dose 1	14	2		
Any temperature, Dose 1	33	15		
Grade 3 temperature, Dose 1	0	1		
Related temperature, Dose 1	18	3		
Any fatigue, Dose 2	126	67		
Grade 3 fatigue, Dose 2	16	6		
Related fatigue, Dose 2	49	13		
Any gastrointestinal, Dose 2	53	16		
Grade 3 gastrointestinal, Dose 2	5	2		
Related gastrointestinal, Dose 2	20	4		
Any headache, Dose 2	90	42		
Grade 3 headache, Dose 2	10	3		
Related headache, Dose 2	42	9		
Any myalgia, Dose 2	93	25		
Grade 3 myalgia, Dose 2	14	5		
Related myalgia, Dose 2	50	7		
Any shivering, Dose 2	48	7		
Grade 3 shivering, Dose 2	9	0		
Related shivering, Dose 2	27	1		
Any temperature, Dose 2	51	11		
Grade 3 teamperature, Dose 2	3	0		
Related temperature, Dose 2	28	3		
Any fatigue, Across doses	162	102		
Grade 3 fatigue, Across doses	23	10		

Related fatigue, Across doses	63	22		
Any gastrointestinal, Across doses	76	29		
Grade 3 gastrointestinal, Across doses	9	3		
Related gastrointestinal, Across doses	28	5		
Any headache, Across doses	115	64		
Grade 3 headache, Across doses	12	6		
Related headache, Across doses	52	16		
Any myalgia, Across doses	122	48		
Grade 3 myalgia, Across doses	22	5		
Related myalgia, Across doses	63	15		
Any shivering, Across doses	69	18		
Grade 3 shivering, Across doses	11	0		
Related shivering, Across doses	36	2		
Any temperature, Across doses	68	21		
Grade 3 temperature, Across doses	3	1		
Related teamperature, Across doses	36	4		

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[7]

End point description:

Solicited general symptoms: fatigue, gastrointestinal symptoms, headache, myalgia, shivering, temperature and their number of days were recorded after each vaccination dose.

End point type	Primary

End point timeframe:

Withing the 7-day (Day 0-6) post-vaccination period

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: This endpoint was descriptive, hence no statistical anaylses were performed.

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	271		
Units: Days				
median (inter-quartile range (Q1-Q3))				
Fatigue, Dose 1	3.0 (1.0 to 6.0)	3.0 (2.0 to 7.0)		
Fatigue, Dose 2	3.0 (2.0 to 5.0)	3.0 (1.0 to 7.0)		
Gastrointestinal symptoms, Dose 1	2.5 (1.0 to 5.0)	3.5 (1.5 to 6.0)		
Gastrointestinal symptoms, Dose 2	2.0 (1.0 to 3.0)	6.0 (2.5 to 7.0)		
Headache, Dose 1	2.0 (1.0 to 3.0)	1.5 (1.0 to 3.0)		
Headache, Dose 2	2.0 (1.0 to 3.0)	1.0 (1.0 to 3.0)		
Myalgia, Dose 1	3.5 (2.0 to 5.5)	3.0 (1.0 to 4.0)		
Myalgia, Dose 2	2.0 (2.0 to 4.0)	3.0 (1.0 to 7.0)		
Shivering, Dose 1	2.0 (1.0 to 3.0)	2.0 (1.0 to 3.5)		
Shivering, Dose 2	1.0 (1.0 to 2.0)	4.0 (2.0 to 4.0)		

Temperature, Dose 1	1.0 (1.0 to 2.0)	2.0 (1.0 to 3.0)		
Temperature, Dose 2	1.0 (1.0 to 2.0)	2.0 (1.0 to 4.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any, Grade 3 and related unsolicited adverse events (AEs)

End point title	Number of subjects with any, Grade 3 and related unsolicited adverse events (AEs)[8]

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. It also included 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:

Within the 30-day (Days 0-29) post-vaccination period

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: This endpoint was descriptive, hence no statistical anaylses were performed.

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	279		
Units: Participants				
Any AEs	134	128		
Grade 3 AEs	25	28		
Related AEs	19	5		

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)[9]

End point description:

A Serious adverse event (SAE) is any untoward medical occurrence that result in death, is life threatening, requires hospitalisation or prolongation of existing hospitalisation, results in disability/incapacity, or is a congenital anomaly/birth defect in the offspring of a study subject. Related = SAEs assessed by the investigator as causally related to the study vaccination

End point type	Primary

End point timeframe:

From first vaccination up to 30 days post last 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: This endpoint was descriptive, hence no statistical anaylses were performed.

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	279		
Units: Participants				
At least one SAE	17	29		
Related SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting any and related potential immune-mediated diseases (pIMDs)

End point title	Number of subjects reporting any and related potential immune-mediated diseases (pIMDs)[10]

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. Related = pIMds assessed by the investigator as causally related to the study vaccination

End point type	Primary

End point timeframe:

From first vaccination up to 30 days post last 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: This endpoint was descriptive, hence no statistical anaylses were performed.

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	279		
Units: Participants				
Any pIMDs	1	0		
Related pIMDs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine response rate (VRR) for anti-gE antibody concentrations

End point title	Vaccine response rate (VRR) for anti-gE antibody

	concentrations

End point description:

Vaccine response rate refers to the percentage of subjects with a vaccine response, as determined by ELISA. Vaccine response was defined as: For initially seronegative subjects, antibody concentration at Month 2 ≥ 4 fold the cut-off for Anti-gE (4x97 mIU/mL). For initially seropositive subjects, antibody concentration at Month 2 ≥ 4 fold the pre -vaccination antibody concentration. This analysis was performed on subjects with haematologic malignancies, excluding subjects with Non-Hodgkin B-cell Lymphoma.

End point type	Secondary

End point timeframe:

At Month 2

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	165		
Units: Percentage				
number (confidence interval 95%)				
Percentage	69.0 (61.8 to 75.6)	0.6 (0.0 to 3.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-gE antibody concentrations

End point title	Anti-gE antibody concentrations

End point description:

Antibody concentrations were determined by ELISA, presented as geometric mean concentrations (GMCs) and expressed in milli-international units per milliliter (mIU/mL).This parameter was assessed in subjects with haematologic malignancies, excluding subjects with Non-Hodgkin B-cell Lymphoma.

End point type	Secondary

End point timeframe:

At Month 2

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	165		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
mIU/mL	15795.5 (11603.3 to 21502.2)	791.6 (648.9 to 965.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-gE antibody concentrations

End point title	Anti-gE antibody concentrations

End point description:

Antibody concentrations were determined by ELISA, presented as geometric mean concentrations (GMCs) and expressed in milli-international units per milliliter (mIU/mL). This parameter was assessed in all vaccinated subjects.

End point type	Secondary

End point timeframe:

At Months 0, 1, 2 and 13

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	198		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-gE, Month 0	964.0 (814.5 to 1140.8)	883.7 (749.9 to 1041.4)		
Anti-gE, Month 1	4216.5 (3328.6 to 5341.4)	824.2 (699.4 to 971.3)		
Anti-gE, Month 2	13445.6 (10158.9 to 17795.6)	832.0 (701.1 to 987.3)		
Anti-gE, Month 13	5202.7 (4074.8 to 6642.8)	895.4 (734.5 to 1091.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine response rate (VRR) for anti-gE antibody concentrations

End point title	Vaccine response rate (VRR) for anti-gE antibody concentrations

End point description:

Vaccine response rate refers to the percentage of subjects with a vaccine response, as determined by ELISA. Vaccine response was defined as: For initially seronegative subjects, antibody concentration at Month 2 ≥ 4 fold the cut-off for anti-gE (4x97 mIU/mL). For initially seropositive subjects, antibody

concentration at Month 2 ≥ 4 fold the pre -vaccination antibody concentration. Vaccine response was measured in all subjects.

End point type	Secondary

End point timeframe:

At Months 1, 2 and 13

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	198		
Units: Percentage				
number (confidence interval 95%)				
VRR, anti-gE, Month 1	44.2 (37.4 to 51.1)	0.0 (0.0 to 1.9)		
VRR, anti-gE, Month 2	65.4 (58.7 to 71.7)	0.5 (0.0 to 2.8)		
VRR, anti-gE, Month 13	52.1 (44.2 to 59.9)	3.6 (1.2 to 8.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of gE -specific cluster of differentiation 4 (CD4) [2+] T-cells expressing at least 2 activation markers

End point title	Frequency of gE -specific cluster of differentiation 4 (CD4) [2+] T-cells expressing at least 2 activation markers

End point description:

Among markers expressed were interferon-gamma (IFN-γ), interleukin-2 (IL-2), tumour necrosis factor-alpha (TNF-α) and cluster of differentiation 40 ligand (CD40L), as determined by in vitro intracellular cytokine staining (ICS).

End point type	Secondary

End point timeframe:

At Months 0, 1, 2 and 13

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	51		
Units: CD4 [2+] T-cells/million T-cells				
arithmetic mean (standard deviation)				
CD4 [2+], Month 0	226.78 (± 659.84)	147.30 (± 191.91)		
CD4 [2+], Month 1	1261.67 (± 2318.36)	196.74 (± 332.52)		
CD4 [2+], Month 2	6083.98 (± 10467.57)	318.20 (± 1000.90)		

CD4 [2+], Month 13	3626.87 (± 7758.18)	181.23 (± 387.90)		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine response rates (VRR) for gE-specific CD4 [2+] T-cells, expressing at least 2 activation markers

End point title	Vaccine response rates (VRR) for gE-specific CD4 [2+] T-cells, expressing at least 2 activation markers

End point description:

Among markers expressed were IFN-γ, IL-2, TNF-α and CD40L, as determined by in vitro ICS. Vaccine response was defined as: For initially subjects with pre-vaccination T-cell frequencies below the threshold, at least a 2-fold increase as compared to the threshold (2x<320> Events/106 CD4+ T cells). For initially subjects with pre-vaccination T-cell frequencies above the threshold, at least a 2-fold increase as compared to pre-vaccination T-cell frequencies.

End point type	Secondary

End point timeframe:

At Months 1, 2 and 13

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: Percentage				
number (confidence interval 95%)				
CD4 [2+], Month 1	37.5 (24.0 to 52.6)	2.1 (0.1 to 11.3)		
CD4 [2+], Month 2	83.7 (69.3 to 93.2)	6.8 (1.4 to 18.7)		
CD4 [2+], Month 13	66.7 (48.2 to 82.0)	6.5 (0.8 to 21.4)		

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:

A Serious adverse event (SAE) is any untoward medical occurrence that result in death, is life threatening, requires hospitalisation or prolongation of existing hospitalisation, results in disability/incapacity, or is a congenital anomaly/birth defect in the offspring of a study subject. Related = SAEs assessed by the investigator as causally related to the study vaccination

End point type	Secondary

End point timeframe:

From first vaccination at Month 0 up to study end at Month 13

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	279		
Units: Participants				
At least one SAE, up to Month 6	50	60		
Related SAEs, up to Month 6	0	1		
At least one SAE, up to Month 13	66	82		
Related SAEs, up to Month 13	1	1		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reporting 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 first vaccination at Month 0 up to study end at Month 13

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	279		
Units: Participants				
Up to Month 6	3	1		
Up to Month 13	3	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to occurrence of any confirmed HZ case

End point title	Time to occurrence of any confirmed HZ case

End point description:

Time to occurrence of any confirmed HZ case is expressed in terms of incidence rate of subjects with at least one event. Hence, person-year rate = number of episodes (n)/ sum of follow-up period (censored at the first occurrence of an event) expressed in years (T[year)]). Follow-up period starts Day 1 of vaccination. Any clinically suspected case of HZ (defined as (1) a new rash characteristic of HZ (e.g., unilateral, dermatomal and accompanied by pain broadly defined to include allodynia, pruritus or other sensations), or a vesicular rash suggestive of Varicella Zoster Virus (VZV) infection regardless of the distribution, and no alternative diagnosis; or (2) a clinical presentation (symptoms and/or signs) and specific laboratory findings suggestive of VZV infection in the absence of characteristic HZ or VZV rash.) The endpoint is confirmed in two ways: (1) By Polymerase Chain Reaction (PCR) or (2) By the HZ Ascertainment Committee. The PCR is used as primary classification method.

End point type	Secondary

End point timeframe:

From Month 0 until study end (Month 13)

End point values	GSK1437173A Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	279		
Units: Person-Year rate				
number (confidence interval 95%)	0.02 (0.009 to 0.045)	0.071 (0.045 to 0.111)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean concentrations (GMCs) of anti-gE antibodies

End point title	Geometric mean concentrations (GMCs) of anti-gE antibodies

End point description:

GMCs of anti-gE antibodies were tabulated per study group and HZ confirmed/non-confirmed status and expressed in milli-international units per milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

At Months 0 and 2

End point values	GSK1437173A HZ cases Sub-Group	GSK1437173A Non-HZ cases Sub-Group	Placebo HZ cases Sub-Group	Placebo Non-HZ cases Sub-Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	257	12	240
Units: mIU/mL				
geometric mean (confidence interval 95%)				
PRE (N=2,257,12,240)	115.9 (0 to 7406196)	973.6 (835.6 to 1134.4)	984.5 (500.7 to 1935.7)	866.3 (745.5 to 1006.6)
Month 2 (N=2, 253, 12, 234)	184.0 (0 to 4187800000)	12517.4 (9662.0 to 16216.6)	960.5 (454.2 to 2031.1)	802.9 (686.7 to 938.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Geometric Increase (MGI) of anti-gE antibody ELISA concentrations

End point title	Mean Geometric Increase (MGI) of anti-gE antibody ELISA concentrations

End point description:

MGI was tabulated per study group and HZ confirmed/non-confirmed status. MGI was defined as the Geometric mean of the within subject ratios of the post-vaccination reciprocal anti-gE concentration to the Month 0 reciprocal anti-gE concentration.

End point type	Secondary

End point timeframe:

At Month 2

End point values	GSK1437173A HZ cases Sub-Group	GSK1437173A Non-HZ cases Sub-Group	Placebo HZ cases Sub-Group	Placebo Non-HZ cases Sub-Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	253	12	233
Units: Fold Increase				
log mean (confidence interval 95%)	1.59 (0.00 to 565.45)	13.07 (9.93 to 17.22)	0.98 (0.80 to 1.19)	0.94 (0.88 to 1.00)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited and unsolicited symptoms: within the 30-day (Days 0-29) post-vaccination period; SAEs: up to study end, at Month 13.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Placebo Group

Reporting group description:

Subjects who received placebo doses according to a 0, 1 Months schedule (The second dose of placebo could be administered 1 - 2 months after the first dose).

Reporting group title	GSK1437173A Group

Reporting group description:

Subjects who received GSK1437173A vaccine according to a 0, 1 Months schedule (The second dose of study vaccine could be administered 1 - 2 months after the first dose).

Serious adverse events	Placebo Group	GSK1437173A Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	82 / 279 (29.39%)	66 / 283 (23.32%)	
number of deaths (all causes)	37	29	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	1 / 279 (0.36%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Acute myeloid leukaemia			
subjects affected / exposed	8 / 279 (2.87%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 7	0 / 2	
Anaplastic large-cell lymphoma			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blastic plasmacytoid dendritic cell neoplasia			

subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Brain neoplasm			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cervix cancer metastatic			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	2 / 279 (0.72%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Haemangioma			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	1 / 279 (0.36%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Leukaemia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant melanoma			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			

subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to peritoneum			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myeloid leukaemia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-hodgkin's lymphoma			
subjects affected / exposed	2 / 279 (0.72%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Plasma cell leukaemia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	6 / 279 (2.15%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 5	0 / 2	
Post transplant lymphoproliferative disorder			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Precursor t-lymphoblastic lymphoma/leukaemia			

subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
T-cell lymphoma			
subjects affected / exposed	2 / 279 (0.72%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
T-cell type acute leukaemia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 279 (0.36%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Embolism			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypotension			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	2 / 279 (0.72%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Surgical and medical procedures			

Finger amputation			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stem cell transplant			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (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			
Adhesion			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	2 / 279 (0.72%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death neonatal			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
General physical health deterioration			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Malaise			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nodule			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 279 (1.08%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Acute graft versus host disease in skin			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Graft versus host disease			
subjects affected / exposed	1 / 279 (0.36%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease in gastrointestinal tract			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft versus host disease in liver			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst ruptured			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dyspnoea			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			

subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 279 (0.72%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 279 (0.72%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Rhinorrhoea			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Disorientation			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

Oxygen saturation decreased			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body in gastrointestinal tract			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	2 / 279 (0.72%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Spinal compression fracture			
subjects affected / exposed	2 / 279 (0.72%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	0 / 279 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiovascular disorder			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (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 / 279 (0.36%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	2 / 279 (0.72%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			

subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dysarthria			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-barre syndrome			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhagic transformation stroke			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic encephalopathy			

subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Loss of consciousness			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinsonism			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post herpetic neuralgia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 279 (0.36%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytopenia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Febrile neutropenia			

subjects affected / exposed	11 / 279 (3.94%)	14 / 283 (4.95%)	
occurrences causally related to treatment / all	0 / 16	0 / 16	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 279 (0.72%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancytopenia			
subjects affected / exposed	2 / 279 (0.72%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 279 (0.36%)	4 / 283 (1.41%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Ear and labyrinth disorders			
Deafness neurosensory			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmoplegia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Anal fistula			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastritis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 279 (0.72%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			

subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatitis fulminant			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema nodosum			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			

subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	4 / 279 (1.43%)	5 / 283 (1.77%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Hydronephrosis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Fasciitis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Spondylolisthesis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Aspergillus infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 279 (0.36%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 279 (0.36%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 279 (0.00%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter colitis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corynebacterium bacteraemia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus colitis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	0 / 279 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ecthyma			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottitis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			

subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fungal infection			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis b			
subjects affected / exposed	0 / 279 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Herpes zoster			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infection			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	2 / 279 (0.72%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (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 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis aseptic			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis cryptococcal			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis externa			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perichondritis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			

subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	11 / 279 (3.94%)	11 / 283 (3.89%)	
occurrences causally related to treatment / all	0 / 12	0 / 12	
deaths causally related to treatment / all	0 / 5	0 / 4	
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia klebsiella			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia parainfluenzae viral			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			

subjects affected / exposed	1 / 279 (0.36%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia streptococcal			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mycosis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyomyositis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	2 / 279 (0.72%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			

subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	6 / 279 (2.15%)	5 / 283 (1.77%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 5	0 / 1	
Septic shock			
subjects affected / exposed	3 / 279 (1.08%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Sinusitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 279 (0.36%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Staphylococcal infection			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Subcutaneous abscess			

subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic candida			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
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 / 279 (0.00%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella zoster virus infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			

subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid retention			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (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	146 / 279 (52.33%)	252 / 283 (89.05%)	
Nervous system disorders			
Headache			
subjects affected / exposed	65 / 279 (23.30%)	115 / 283 (40.64%)	
occurrences (all)	86	166	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	19 / 279 (6.81%)	69 / 283 (24.38%)	
occurrences (all)	24	89	
Fatigue			
subjects affected / exposed	102 / 279 (36.56%)	163 / 283 (57.60%)	
occurrences (all)	140	250	
Pain			

subjects affected / exposed	46 / 279 (16.49%)	221 / 283 (78.09%)	
occurrences (all)	60	372	
Pyrexia			
subjects affected / exposed	24 / 279 (8.60%)	74 / 283 (26.15%)	
occurrences (all)	30	96	
Swelling			
subjects affected / exposed	2 / 279 (0.72%)	63 / 283 (22.26%)	
occurrences (all)	3	89	
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	29 / 279 (10.39%)	76 / 283 (26.86%)	
occurrences (all)	40	101	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	6 / 279 (2.15%)	116 / 283 (40.99%)	
occurrences (all)	7	165	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	48 / 279 (17.20%)	123 / 283 (43.46%)	
occurrences (all)	60	175	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 February 2013	• Section 7.5 has been amended to indicate that the second vaccination is contraindicated in subjects who experience a pIMD between dose 1 and dose 2 of study vaccine or placebo. This amendment is being implemented to fulfil a request of the Swedish Medical Products Agency (MPA). The amendment is not in response to any safety concern arising from an event or series of events in any completed or ongoing clinical studies that have been or are being conducted as part of GSK's Zoster vaccine program or in studies conducted as part of other GSK vaccine programs. • Also in response to Sweden's MPA request, text has been added to Section 8.1.5.1 to clarify how pIMDs are handled by GSK Biologicals when reported by the investigator. • Two sentences were added to Section 7.6.1 (Recording of concomitant medications/products and concomitant vaccination) for clarification: Any concomitant vaccination administered in the period starting 30 days before the first dose of study vaccine and ending within 30 days post last dose. Any concomitant medications/products/vaccines listed in Section 7.6.2 • Minor typographical and document formatting errors throughout the protocol have been corrected.
14 July 2014	• For clarification, it has been detailed in the glossary of terms that cancer therapy, as included in the inclusion criteria in this protocol, pertains to treatments that may put the subject at an increased risk for HZ and it comprises direct anti-cancer treatments (chemotherapy and/or immunotherapy; if radiotherapy it must be in combination with either chemotherapy or immunotherapy) that are immunosuppressive, and immunosuppressive therapies administered as part of the anti-cancer treatment or to avoid/treat complications of the anti-cancer treatment. • To address a request from the Food and Drug Administration (FDA), the objective to evaluate anti-gE humoral immune responses at Month 2 following a two-dose administration of the HZ/su vaccine, as compared to placebo, in subjects with haematologic malignancies excluding subjects with Non-Hodgkin B-cell Lymphoma and Chronic Lymphocytic Leukaemia, has been promoted from secondary to primary confirmatory objective. • The cut-off of the gE-specific ELISA assay has been changed from 18 to 97 mIU/mL. Background signal has been measured with the anti-gE ELISA on samples from Varicella Zoster Virus (VZV) naïve paediatric subjects. • The list of potential immune-mediated diseases has been updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported