Clinical trial results:
A Phase IIIB, randomized, open-label, multicenter clinical trial to assess the immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A when co-administered with Prevenar13 in adults aged 50 years and older.

Summary

EudraCT number	2017-001220-22
Trial protocol	DE EE
Global end of trial date	03 March 2020

Results information

Result version number	v2 (current)
This version publication date	21 January 2022
First version publication date	11 March 2021
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	204487

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03439657
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	GSK Response Center, GlaxoSmithKline, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 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	18 January 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To determine the vaccine response rate (VRR) to HZ/su (based on humoral immune response) one month after the second vaccine dose, when the first dose of HZ/su is co-administered with Prevenar13 (Co-Ad group). • To demonstrate non-inferiority of the humoral immune response to two doses of HZ/su at one month after the last vaccine dose, when the first dose of HZ/su is co-administered with Prevenar13 (Co-Ad group) compared to when two doses of HZ/su are administered subsequent to Prevenar13 (Control Group). • To demonstrate non-inferiority of the humoral immune response to Prevenar13 at one month after the vaccine dose, when Prevenar13 is co-administered with the first HZ/su dose (Co-Ad group) compared to when Prevenar13 is administered separately from HZ/su (Control group), for the 13 serotypes included in Prevenar13 analyzed sequentially.

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 12 months after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 April 2018
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	Canada: 362
Country: Number of subjects enrolled	Estonia: 122
Country: Number of subjects enrolled	Germany: 290
Country: Number of subjects enrolled	United States: 139
Worldwide total number of subjects	913
EEA total number of subjects	412

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)	536
From 65 to 84 years	368
85 years and over	9

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 4 countries (Canada, Estonia, Germany & United States)

Pre-assignment

Screening details:

Out of 913 subjects enrolled in the study, 1 subject violated protocol prior to randomization. 912 subjects were vaccinated and included in the Exposed Set, 901 subjects completed the study.

Period 1

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

Blinding implementation details:

This is not applicable as there was no blinding in this study (open-label)

Arms

Are arms mutually exclusive?	Yes
Arm title	Co-Ad Group

Arm description:

Adults aged ≥50 years of age who received the first dose of GSK1437173A and one dose of Prevenar13 at Day 1 and the second dose of GSK1437173A at Month 2. Both vaccines were administered intramuscularly, GSK1437173A was administered in the deltoid muscle of the non-dominant arm, while Prevenar13 was administered in the deltoid muscle of the dominant arm

Arm type	Experimental
Investigational medicinal product name	HZ/su vaccine GSK1437173A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.5 mL of the vaccine in a 0,2 Months schedule. Administered by intramuscular injection into the deltoid muscle of the non-dominant arm.

Investigational medicinal product name	Prevenar13
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of 0.5 mL of the vaccine. Administered by intramuscu-lar injection into the deltoid muscle of the dominant arm.

Arm title	Control Group

Arm description:

Adults aged ≥50 years of age who received one dose of Prevenar13 at Day 1, the first dose of GSK1437173A at Month 2 and the second dose of GSK1437173A at Month 4. Both vaccines were administered intramuscularly, GSK1437173A was administered in the deltoid muscle of the non-dominant arm, while Prevenar13 was administered in the deltoid muscle of the dominant arm

Arm type	Placebo

Investigational medicinal product name	HZ/su vaccine GSK1437173A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection, Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.5 mL of the vaccine in a 0,2 Months schedule. Administered by intramuscular injection into the deltoid muscle of the non-dominant arm.

Investigational medicinal product name	Prevenar13
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of 0.5 mL of the vaccine. Administered by intramuscu-lar injection into the deltoid muscle of the dominant arm.

Number of subjects in period 1[1]	Co-Ad Group	Control Group
Started	449	463
Completed	442	459
Not completed	7	4
Adverse event, non-fatal	2	3
Lost to follow-up	1	-
Consent withdrawal, not due to an Adverse Event	3	-
Protocol deviation	1	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of 913 subjects enrolled in the study, 1 subject violated protocol. 912 subjects were vaccinated and included in the Exposed Set.

Baseline characteristics

Reporting groups	
Reporting group title	Co-Ad Group
Reporting group description:	
Adults aged ≥50 years of age who received the first dose of GSK1437173A and one dose of Prevenar13 at Day 1 and the second dose of GSK1437173A at Month 2. Both vaccines were administered intramuscularly, GSK1437173A was administered in the deltoid muscle of the non-dominant arm, while Prevenar13 was administered in the deltoid muscle of the dominant arm	
Reporting group title	Control Group
Reporting group description:	
Adults aged ≥50 years of age who received one dose of Prevenar13 at Day 1, the first dose of GSK1437173A at Month 2 and the second dose of GSK1437173A at Month 4. Both vaccines were administered intramuscularly, GSK1437173A was administered in the deltoid muscle of the non-dominant arm, while Prevenar13 was administered in the deltoid muscle of the dominant arm	

Reporting group values	Co-Ad Group	Control Group	Total
Number of subjects	449	463	912
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	271	265	536
From 65-84 years	175	192	367
85 years and over	3	6	9
Age continuous Units: years			
arithmetic mean	63.1	63.2	
standard deviation	± 8.3	± 8.4	-
Sex: Female, Male Units: Participants			
Female	259	284	543
Male	190	179	369
Race/Ethnicity, Customized Units: Subjects			
American Indian Or Alaska Native	1	0	1
Black Or African American	8	8	16
Mixed Origin	0	2	2
White - Arabic / North African Heritage	1	1	2
White - Caucasian / European Heritage	439	452	891

End points

End points reporting groups

Reporting group title	Co-Ad Group

Reporting group description:

Adults aged ≥50 years of age who received the first dose of GSK1437173A and one dose of Prevenar13 at Day 1 and the second dose of GSK1437173A at Month 2. Both vaccines were administered intramuscularly, GSK1437173A was administered in the deltoid muscle of the non-dominant arm, while Prevenar13 was administered in the deltoid muscle of the dominant arm

Reporting group title	Control Group

Reporting group description:

Adults aged ≥50 years of age who received one dose of Prevenar13 at Day 1, the first dose of GSK1437173A at Month 2 and the second dose of GSK1437173A at Month 4. Both vaccines were administered intramuscularly, GSK1437173A was administered in the deltoid muscle of the non-dominant arm, while Prevenar13 was administered in the deltoid muscle of the dominant arm

Primary: Percentage of subjects with a Vaccine response for Anti-glycoprotein E (Anti-gE) in Co-Ad Group

End point title	Percentage of subjects with a Vaccine response for Anti-glycoprotein E (Anti-gE) in Co-Ad Group[1][2]

End point description:

Vaccine response rate (VRR) for Varicella Zoster Virus (VZV) anti-glycoprotein E (gE) humoral immunogenicity was determined by Enzyme Limked Immunosorbent Assay (ELISA). The VRR for anti-gE is defined as the percentage of subjects who had at least: a 4-fold increase in the anti-gE antibodies concentration as compared to the pre-vaccination anti-gE antibodies concentration, for subjects who are seropositive at baseline, or, a 4-fold increase in the anti-gE antibodies concentration as compared to the anti-gE antibodies cut-off value for seropositivity, for subjects who are seronegative at baseline. Analysis was performed on the Per-Protocol Set (PPS) for immunogenicity that included all evaluable subjects who met all eligibility criteria, who complied with the procedures and intervals allowed for the analysis and for whom data concerning immunogenicity outcome measures were available.

End point type	Primary

End point timeframe:

One month post-dose 2 (Month 3)

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 Co-Ad group.

End point values	Co-Ad Group			
Subject group type	Reporting group			
Number of subjects analysed	426			
Units: Percentage of subjects				
number (confidence interval 95%)	99.1 (97.6 to 99.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Anti-gE antibody concentrations

End point title	Anti-gE antibody concentrations[3]

End point description:

Anti-gE antibody concentrations in terms of Geometric Mean concentrations (GMC) were determined by ELISA and expressed as milli-international units per milliliter (mIU/mL). Analysis was performed on the PPS for immunogenicity that included all evaluable subjects who met all eligibility criteria, who complied with the procedures and intervals allowed for the analysis and for whom data concerning immunogenicity outcome measures were available.

End point type	Primary

End point timeframe:

One month post-dose 2 (at Month 3 for the Co-Ad and Month 5 for the Control group).

Notes:

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

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	426	436		
Units: mIU/mL				
geometric mean (confidence interval 95%)	54789.9 (51586.3 to 58192.4)	59126.7 (55973.8 to 62457.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Anti-pneumococcal antibody titers

End point title	Anti-pneumococcal antibody titers[4]

End point description:

Anti-pneumococcal antibody titers for the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F) were determined by Multiplex Opsonophagocytosis Assay (MOPA). Analysis was performed on the PPS for immunogenicity that included all evaluable subjects who met all eligibility criteria, who complied with the procedures and intervals allowed for the analysis and for whom data concerning immunogenicity outcome measures were available.

End point type	Primary

End point timeframe:

At one month post-dose 1 (Month 1)

Notes:

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

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	425	434		
Units: Titers				
geometric mean (confidence interval 95%)				
MOPA-1 [N=425,434]	144.2 (120.5 to 172.6)	151.5 (126.0 to 182.1)		
MOPA-3 [N=425,434]	99.8 (87.2 to 114.1)	100.2 (88.0 to 114.1)		
MOPA-4 [N=425,434]	1127.2 (975.5 to 1302.5)	1392.4 (1206.5 to 1607.0)		
MOPA-5 [N=424,434]	279.4 (231.2 to 337.7)	292.8 (243.5 to 352.1)		
MOPA-6A [N=425,434]	1839.3 (1570.0 to 2154.9)	2354.9 (2015.0 to 2752.2)		
MOPA-6B [N=425,433]	1499.4 (1241.2 to 1811.4)	2025.9 (1715.5 to 2392.4)		
MOPA-7F [N=425,434]	1981 (1735.2 to 2261.5)	2387.5 (2112.7 to 2698.0)		
MOPA-9V [N=425,434]	2541.9 (2219.2 to 2911.7)	3049.3 (2693.7 to 3451.9)		
MOPA-14 [N=424,432]	1752.6 (1505.2 to 2040.6)	2096 (1796.6 to 2445.2)		
MOPA-18C [N=425,434]	1450.3 (1262.5 to 1666.1)	1606.6 (1402.6 to 1840.4)		
MOPA-19A [N=425,434]	1684.9 (1477.2 to 1921.9)	1664.3 (1465.7 to 1889.7)		
MOPA-19F [N=425,434]	712 (617.1 to 821.6)	802.4 (696.2 to 924.8)		
MOPA-23F [N=425,434]	758.1 (644.9 to 891.2)	925.5 (782.5 to 1094.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Adjusted Geometric Mean Concentrations (GMCs) for anti-gE antibody

End point title	Adjusted Geometric Mean Concentrations (GMCs) for anti-gE antibody

End point description:

Anti-gE antibody concentrations (GMCs) adjusted for age and baseline concentrations were determined using Analysis Of Covariance (ANCOVA) model. Adjusted GMCs were expressed in milli-international units per milliliter (mIU/mL). Analysis was performed on the PPS for immunogenicity that included all evaluable subjects who met all eligibility criteria, who complied with the procedures and intervals allowed for the analysis and for whom data concerning immunogenicity outcome measures were available.

End point type	Primary

End point timeframe:

One month post-dose 2 (at Month 3 for the Co-Ad and Month 5 for the Control group).

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	426	435		
Units: mIU/mL				
geometric mean (confidence interval 95%)	54634.9 (51546.0 to 57909.0)	58526.8 (55248.5 to 61999.7)		

Statistical analyses

Statistical analysis title	Anti-gE GMCs (non-inferiority)

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean concentrations (GMCs) for anti-gE antibodies, one month after the administration of last vaccine dose.

Comparison groups	Control Group v Co-Ad Group
Number of subjects included in analysis	861
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Method	ANCOVA
Parameter estimate	GMC ratio
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.16

Notes:

[5] - Upper limit (UL) of the 95% confidence interval (CI) for the anti-gE antibodies Geometric Mean Concentration (GMC) ratio between the Control group and the Co-Ad group should be <1.5.

Primary: Adjusted Geometric Mean Titers (GMTs) of anti-pneumococcal antibodies

End point title	Adjusted Geometric Mean Titers (GMTs) of anti-pneumococcal antibodies

End point description:

Geometric mean antibody (anti-pneumococcal antibodies: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F) titers adjusted for age and baseline concentration were determined using ANCOVA model. Analysis was performed on the PPS for immunogenicity that included all evaluable subjects who met all eligibility criteria, who complied with the procedures and intervals allowed for the analysis and for whom data concerning immunogenicity outcome measures were available.

End point type	Primary

End point timeframe:

At one month post-dose 1 (Month 1)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	425	433		
Units: Titers				
geometric mean (confidence interval 95%)				
MOPA-1 [N=433,425]	141.2 (118.7 to 167.9)	147.1 (123.9 to 174.7)		
MOPA-3 [N=431,425]	97.3 (86.0 to 110.0)	99.6 (88.1 to 112.6)		
MOPA-4 [N=432,423]	1066.9 (924.2 to 1231.5)	1331.6 (1155.2 to 1535.0)		
MOPA-5 [N=433,423]	269.1 (225.8 to 320.8)	278.9 (234.4 to 331.8)		
MOPA-6A [N=433,424]	1784.4 (1530.2 to 2080.8)	2253.8 (1935.6 to 2624.3)		
MOPA-6B [N=431,424]	1445.4 (1219.3 to 1713.4)	1967.3 (1661.5 to 2329.3)		
MOPA-7F [N=432,423]	1935.1 (1704.3 to 2197.1)	2337.3 (2061.2 to 2650.5)		
MOPA-9V [N=431,420]	2553.5 (2244.2 to 2905.4)	2955.8 (2601.9 to 3357.9)		
MOPA-14 [N=430,423]	1730.7 (1491.3 to 2008.5)	1992.3 (1718.5 to 2309.7)		
MOPA-18C [N=433,423]	1403.8 (1226.4 to 1606.8)	1558.9 (1363.9 to 1781.9)		
MOPA-19A [N=431,425]	1619.2 (1433.7 to 1828.7)	1663.5 (1474.0 to 1877.2)		
MOPA-19F [N=433,424]	696.4 (608.2 to 797.3)	760.2 (664.8 to 869.2)		
MOPA-23F [N=432,425]	748.2 (637.6 to 878.0)	896.6 (765.0 to 1050.9)		

Statistical analyses

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers (GMTs) for anti-pneumococcal antibody (MOPA-1), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Control Group v Co-Ad Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.33

Notes:

[6] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers (GMTs) for anti-pneumococcal antibody (MOPA-3), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.22

Notes:

[7] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers (GMTs) for anti-pneumococcal antibody (MOPA-4), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.52

Notes:

[8] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers

(GMTs) for anti-pneumococcal antibody (MOPA-5), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.32

Notes:

[9] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers (GMTs) for anti-pneumococcal antibody (MOPA-6B), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.73

Notes:

[10] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers (GMTs) for anti-pneumococcal antibody (MOPA-6A), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.26

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.56

Notes:

[11] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers (GMTs) for anti-pneumococcal antibody (MOPA-7F), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.44

Notes:

[12] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers (GMTs) for anti-pneumococcal antibody (MOPA-9V), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.39

Notes:

[13] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers

(GMTs) for anti-pneumococcal antibody (MOPA-14), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.42

Notes:

[14] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers (GMTs) for anti-pneumococcal antibody (MOPA-18C), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Co-Ad Group v Control Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.34

Notes:

[15] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers (GMTs) for anti-pneumococcal antibody (MOPA-19A), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Control Group v Co-Ad Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.03

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.22

Notes:

[16] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers (GMTs) for anti-pneumococcal antibody (MOPA-19F), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Control Group v Co-Ad Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.32

Notes:

[17] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Statistical analysis title	Anti-pneumococcal antibody titers

Statistical analysis description:

Non-inferiority comparison between Control Group and Co-Ad Group in terms of geometric mean titers (GMTs) for anti-pneumococcal antibody (MOPA-23F), one month after the administration of Prevnar 13 vaccine dose.

Comparison groups	Control Group v Co-Ad Group
Number of subjects included in analysis	858
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Method	ANCOVA
Parameter estimate	GMT ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.5

Notes:

[18] - Upper limit (UL) of 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group should be <2.

Secondary: Number of subjects with any and grade 3 solicited local symptoms by vaccine and dose

End point title	Number of subjects with any and grade 3 solicited local

	symptoms by vaccine and dose

End point description:

Assessed solicited local symptoms were pain, erythema and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 erythema/swelling = erythema/swelling that had spread beyond 100 millimeters (mm) of injection site. The Co-Ad Group received only 2 vaccine doses. Analysis was performed on Exposed Set (ES) which included all subjects with at least one vaccine administration documented and who provided solicited safety data.

End point type	Secondary

End point timeframe:

Within 7 days (Day 1 - 7) after each vaccination

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	447	463		
Units: Participants				
Any Erythema, GSK1437173A, Dose1 [N=447,0]	120	0		
Grade3 Erythema, GSK1437173A, Dose1 [N=447,0]	5	0		
Any Erythema, Prevenar13, Dose1 [N=447,463]	48	31		
Grade3 Erythema, Prevenar13, Dose1 [N=447,463]	2	1		
Any Pain, GSK1437173A, Dose1 [N=447,0]	332	0		
Grade3 Pain, GSK1437173A, Dose1 [N=447,0]	25	0		
Any Pain, Prevenar13, Dose1 [N=447,463]	233	241		
Grade3 Pain, Prevenar13, Dose1 [N=447,463]	11	9		
Any Swelling, GSK1437173A, Dose1 [N=447,0]	69	0		
Grade3 Swelling, GSK1437173A, Dose1 [N=447,0]	0	0		
Any Swelling, Prevenar13, Dose1 [N=447,463]	33	21		
Grade3 Swelling, Prevenar13, Dose1 [N=447,463]	1	0		
Any Erythema, GSK1437173A, Dose2 [N=444,458]	147	128		
Grade3 Erythema, GSK1437173A, Dose2 [N=444,458]	9	5		
Any Pain, GSK1437173A, Dose2 [N=444,458]	326	359		
Grade3 Pain, GSK1437173A, Dose2 [N=444,458]	28	32		
Any Swelling, GSK1437173A, Dose2 [N=444,458]	70	72		
Grade3 Swelling, GSK1437173A, Dose2 [N=444,458]	1	2		
Any Erythema, GSK1437173A, Dose3 [N=0,459]	0	123		
Grade3 Erythema, GSK1437173A, Dose3 [N=0,459]	0	1		

Any Pain, GSK1437173A, Dose3 [N=0,459]	0	350		
Grade3 Pain, GSK1437173A, Dose3 [N=0,459]	0	41		
Any Swelling, GSK1437173A, Dose3 [N=0,459]	0	60		
Grade3 Swelling, GSK1437173A, Dose3 [N=0,459]	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with each solicited local symptoms

End point title	Number of days with each solicited local symptoms

End point description:

The number of days with any local symptoms had been assessed during the post-vaccination period. Analysis was performed on ES which included all subjects with at least one vaccine administration documented and who provided solicited safety data and for those who experienced the specified symptom for the specific dose.

End point type	Secondary

End point timeframe:

Within 7 days (Day 1 - 7) after each vaccination

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	359		
Units: Days				
median (inter-quartile range (Q1-Q3))				
Any erythema,Dose1 [N=131,31]	3 (2 to 5)	2 (1 to 4)		
Any pain,Dose1 [N=347,241]	3 (2 to 4)	2 (1 to 2)		
Any swelling, Dose1 [N=76,21]	2 (2 to 4)	2 (1 to 3)		
Any erythema, Dose2 [N=147,128]	3 (2 to 4)	2 (2 to 4)		
Any pain,Dose2 [N=326,359]	3 (2 to 4)	3 (2 to 4)		
Any swelling, Dose2 [N=70,72]	3 (2 to 4)	2 (1.5 to 4)		
Any erythema,Dose3 [N=0,123]	0 (0 to 0)	2 (2 to 3)		
Any pain,Dose3 [N=0,350]	0 (0 to 0)	3 (2 to 3)		
Any swelling,Dose3 [N=0,60]	0 (0 to 0)	2 (1 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: 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

End point description:

Assessed solicited general symptoms were fatigue, fever [defined as oral temperature ≥ 38.0 degrees Celsius (°C)/ 100.4 degrees Fahrenheit (°F)], GastroIntestinal (GI) symptoms, headache, myalgia and shivering. 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. Analysis was performed on ES which included all subjects with at least one vaccine administration documented and who provided solicited safety data.

End point type	Secondary

End point timeframe:

Within 7 days (Day 1 - 7) after each vaccination

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	448	463		
Units: Participants				
Any Fatigue, Dose1 [N=448,463]	166	85		
Grade3 Fatigue, Dose1 [N=448,463]	21	5		
Related Fatigue, Dose1 [N=448,463]	149	67		
Any Fever, Dose1 [N=448,463]	10	2		
Grade3 Fever, Dose1 [N=448,463]	1	0		
Related Fever, Dose1 [N=448,463]	8	0		
Any GI symptoms, Dose1 [N=448,463]	61	37		
Grade3 GI symptoms, Dose1 [N=448,463]	6	1		
Related GI symptoms, Dose1 [N=448,463]	55	30		
Any Headache, Dose1 [N=448,463]	130	72		
Grade3 Headache, Dose1 [N=448,463]	10	0		
Related Headache, Dose1 [N=448,463]	113	59		
Any Myalgia, Dose1 [N=448,463]	168	102		
Grade3 Myalgia, Dose1 [N=448,463]	17	4		
Related Myalgia, Dose1 [N=448,463]	150	86		
Any Shivering, Dose1 [N=448,463]	78	7		
Grade3 Shivering, Dose1 [N=448,463]	9	0		
Related Shivering, Dose1 [N=448,463]	71	7		
Any Fatigue, Dose2 [N=444,458]	192	152		
Grade3 Fatigue, Dose2 [N=444,458]	22	17		
Related Fatigue, Dose2 [N=444,458]	177	141		
Any Fever, Dose2 [N=444,458]	16	7		
Grade3 Fever, Dose2 [N=444,458]	2	2		
Related Fever, Dose2 [N=444,458]	10	2		
Any GI symptoms, Dose2 [N=444,458]	57	47		
Grade3 GI symptoms, Dose2 [N=444,458]	8	4		
Related GI symptoms, Dose2 [N=444,458]	50	44		
Any Headache, Dose2 [N=444,458]	156	115		
Grade3 Headache, Dose2 [N=444,458]	18	7		
Related Headache, Dose2 [N=444,458]	143	99		
Any Myalgia, Dose2 [N=444,458]	203	174		

Grade3 Myalgia, Dose2 [N=444,458]	23	24		
Related Myalgia, Dose2 [N=444,458]	186	163		
Any Shivering, Dose2 [N=444,458]	95	50		
Grade3 Shivering, Dose2 [N=444,458]	12	8		
Related Shivering, Dose2 [N=444,458]	86	47		
Any Fatigue, Dose3 [N=0,459]	0	210		
Grade3 Fatigue, Dose3 [N=0,459]	0	27		
Related Fatigue, Dose3 [N=0,459]	0	202		
Any Fever, Dose3 [N=0,459]	0	23		
Grade3 Fever, Dose3 [N=0,459]	0	2		
Related Fever, Dose3 [N=0,459]	0	17		
Any GI symptoms, Dose3 [N=0,459]	0	69		
Grade3 GI symptoms, Dose3 [N=0,459]	0	3		
Related GI symptoms, Dose3 [N=0,459]	0	63		
Any Headache, Dose3 [N=0,459]	0	180		
Grade3 Headache, Dose3 [N=0,459]	0	23		
Related Headache, Dose3 [N=0,459]	0	168		
Any Myalgia, Dose3 [N=0,459]	0	224		
Grade3 Myalgia, Dose3 [N=0,459]	0	37		
Related Myalgia, Dose3 [N=0,459]	0	215		
Any Shivering, Dose3 [N=0,459]	0	122		
Grade3 Shivering, Dose3 [N=0,459]	0	20		
Related Shivering, Dose3 [N=0,459]	0	117		

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:

The number of days with any general symptoms had been assessed during the post-vaccination period. Assessed solicited general symptoms were fatigue, fever, GastroIntestinal (GI) symptoms, headache, myalgia and shivering. Analysis was performed on ES which included all subjects with at least one vaccine administration documented and who provided solicited safety data and for those who experienced the specified symptom for the specific dose.

End point type	Secondary

End point timeframe:

Within 7 days (Day 1 - 7) after each vaccination

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	224		
Units: Days				
median (inter-quartile range (Q1-Q3))				
Any fatigue,Dose1 [N=166,85]	2 (1 to 3)	2 (1 to 3)		
Any GI symptoms,Dose1 [N=61,37]	2 (1 to 2)	1 (1 to 2)		

Any headache,Dose1 [N=130,72]	2 (1 to 3)	1 (1 to 2)		
Any myalgia,Dose1 [N=168,102]	2 (1 to 3)	2 (1 to 3)		
Any shivering,Dose1 [N=78,7]	1 (1 to 2)	1 (1 to 3)		
Any fever,Dose1 [N=10,2]	1 (1 to 1)	1 (1 to 1)		
Any fatigue,Dose2 [N=192,152]	2 (1 to 3)	2 (1 to 3)		
Any GI symptoms,Dose2 [N=57,47]	1 (1 to 2)	1 (1 to 2)		
Any headache,Dose2 [N=156,115]	2 (1 to 3)	2 (1 to 3)		
Any myalgia,Dose2 [N=203,174]	2 (1 to 3)	2 (1 to 3)		
Any shivering,Dose2 [N=95,50]	1 (1 to 2)	1 (1 to 2)		
Any fever,Dose2 [N=16,7]	1 (1 to 1)	1 (1 to 3)		
Any fatigue,Dose3 [N=0,210]	0 (0 to 0)	2 (1 to 3)		
Any GI symptoms,Dose3 [N=0,69]	0 (0 to 0)	1 (1 to 2)		
Any headache,Dose3 [N=0,180]	0 (0 to 0)	1.5 (1 to 2)		
Any myalgia,Dose3 [N=0,224]	0 (0 to 0)	2 (1 to 3)		
Any shivering,Dose3 [N=0,122]	0 (0 to 0)	1 (1 to 2)		
Any fever,Dose3 [N=0,23]	0 (0 to 0)	1 (1 to 1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, Grade 3 and related unsolicited Adverse Events (AE)

End point title	Number of subjects with any, Grade 3 and related unsolicited Adverse Events (AE)

End point description:

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

End point type	Secondary

End point timeframe:

Within 30 days (Day 1 to 30) after each vaccination

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	449	463		
Units: Participants				
Subjects with any AEs	95	107		
Subjects with Grade 3 AEs	9	13		
Subjects with related AEs	35	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and related Serious Adverse Events (SAE) from Day 1 to 30 days post last vaccination

End point title	Number of subjects with any and related Serious Adverse Events (SAE) from Day 1 to 30 days post last vaccination

End point description:

SAEs assessed included medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity. Related SAEs= SAEs assessed by the investigator as causally related to the study vaccination. Analysis was performed on ES which included all subjects with at least one vaccine administered.

End point type	Secondary

End point timeframe:

From first vaccination at Day 1 up to 30 days post last vaccination

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	449	463		
Units: Participants				
Subjects with any SAEs	7	8		
Subjects with related SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and related SAEs from 30 days post last vaccination up to study end.

End point title	Number of subjects with any and related SAEs from 30 days post last vaccination up to study end.

End point description:

Serious adverse events (SAEs) assessed included medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity. Related SAEs= SAEs assessed by the investigator as causally related to the study vaccination. Analysis was performed on ES which included all subjects with at least one vaccine administered.

End point type	Secondary

End point timeframe:

From 30 days post last vaccination up to study end (Month 14 for the Co-Ad group and Month 16 for the Control group)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	449	463		
Units: Participants				
Subjects with any SAEs	10	10		
Subjects with related SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and related Potential immune-mediated diseases (pIMDs) from Day 1 to 30 days post last vaccination

End point title	Number of subjects with any and related Potential immune-mediated diseases (pIMDs) from Day 1 to 30 days post last vaccination

End point description:

pIMDs assessed were a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which might or might not had an autoimmune aetiology. Related pIMDs= pIMDs assessed by the investigator as causally related to the study vaccination. Analysis was performed on ES which included all subjects with at least one vaccine administered.

End point type	Secondary

End point timeframe:

From first vaccination at Day 1 up to 30 days post last vaccination.

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	449	463		
Units: Participants				
Subjects with any pIMDs	1	1		
Subjects with related pIMDs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any pIMDs from 30 days post last vaccination up to study end.

End point title	Number of subjects with any pIMDs from 30 days post last vaccination up to study end.

End point description:

pIMDs assessed were a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which might or might not had an autoimmune aetiology. Analysis was performed on ES which included all subjects with at least one vaccine administered.

End point type	Secondary

End point timeframe:

From 30 days post last vaccination up to study end (Month 14 for the Co-Ad group and Month 16 for the Control group)

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	449	463		
Units: Participants	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms by dose

End point title	Number of subjects with any and Grade 3 solicited local symptoms by dose

End point description:

Assessed solicited local symptoms were pain, erythema and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 erythema/swelling = erythema/swelling that had spread beyond 100 millimeters (mm) of injection site. The Co-Ad Group received only 2 vaccine doses. Analysis was performed on Exposed Set (ES) which included all subjects with at least one vaccine administration documented and who provided solicited safety data.

End point type	Secondary

End point timeframe:

Within 7 days (Day 1 - 7) after each vaccination

End point values	Co-Ad Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	448	463		
Units: Participants				
Any Erythema, Dose1 [N=448,463]	131	31		
Grade3 Erythema, Dose1 [N=448,463]	7	1		
Any Pain, Dose1 [N=448,463]	347	241		
Grade3 Pain, Dose1 [N=448,463]	28	9		
Any Swelling, Dose1 [N=448,463]	76	21		
Grade3 Swelling, Dose1 [N=448,463]	1	0		
Any Erythema, Dose2 [N=444,458]	147	128		
Grade3 Erythema, Dose2 [N=444,458]	9	5		
Any Pain, Dose2 [N=444,458]	326	359		
Grade3 Pain, Dose2 [N=444,458]	28	32		
Any Swelling, Dose2 [N=444,458]	70	72		
Grade3 Swelling, Dose2 [N=444,458]	1	2		
Any Erythema, Dose3 [N=0,459]	0	123		

Grade3 Erythema, Dose3 [N=0,459]	0	1		
Any Pain, Dose3 [N=0,459]	0	350		
Grade3 Pain, Dose3 [N=0,459]	0	41		
Any Swelling, Dose3 [N=0,459]	0	60		
Grade3 Swelling, Dose3 [N=0,459]	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: During the 7-day (Days 1 to 7) after each vaccination, Unsolicited AEs: During the 30 day (Days 1 to 30) after any vaccination, SAEs:throughout the study period [Day 1 to study end (Month 14 for Co-Ad group and Month-16 for Control Group)]

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Control Group

Reporting group description:

Adults aged ≥50 years of age who received one dose of Prevenar13 at Day 1, the first dose of GSK1437173A at Month 2 and the second dose of GSK1437173A at Month 4. Both vaccines were administered intramuscularly, GSK1437173A was administered in the deltoid muscle of the non-dominant arm, while Prevenar13 was administered in the deltoid muscle of the dominant arm

Reporting group title	Co-Ad Group

Reporting group description:

Adults aged ≥50 years of age who received the first dose of GSK1437173A and one dose of Prevenar13 at Day 1 and the second dose of GSK1437173A at Month 2. Both vaccines were administered intramuscularly, GSK1437173A was administered in the deltoid muscle of the non-dominant arm, while Prevenar13 was administered in the deltoid muscle of the dominant arm

Serious adverse events	Control Group	Co-Ad Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 463 (3.46%)	16 / 449 (3.56%)	
number of deaths (all causes)	4	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			

subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic carcinoma of the bladder			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neoplasm malignant			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Monoclonal gammopathy			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (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			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Reproductive system and breast disorders			
Ovarian cyst			

subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (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			
Pneumothorax			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
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			
Road traffic accident			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			

subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 463 (0.22%)	2 / 449 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dressler's syndrome			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive heart disease			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (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	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			

subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebral haematoma			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Volvulus			

subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (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			
Nephrotic syndrome			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			

subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
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	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Control Group	Co-Ad Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	427 / 463 (92.22%)	419 / 449 (93.32%)	
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	5 / 463 (1.08%)	3 / 449 (0.67%)	
occurrences (all)	5	3	
Circulatory collapse			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Lymphoedema			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
General disorders and administration			

site conditions			
Administration site pruritus			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Asthenia			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Feeling hot			
subjects affected / exposed	2 / 463 (0.43%)	2 / 449 (0.45%)	
occurrences (all)	2	2	
Fatigue			
subjects affected / exposed	261 / 463 (56.37%)	243 / 449 (54.12%)	
occurrences (all)	448	361	
Chills			
subjects affected / exposed	143 / 463 (30.89%)	139 / 449 (30.96%)	
occurrences (all)	179	174	
Chest pain			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Axillary pain			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Injection site bruising			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Injection site erythema			
subjects affected / exposed	190 / 463 (41.04%)	192 / 449 (42.76%)	
occurrences (all)	286	278	
Injection site hypoaesthesia			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Injection site movement impairment			

subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Injection site oedema			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Injection site pain			
subjects affected / exposed	406 / 463 (87.69%)	389 / 449 (86.64%)	
occurrences (all)	952	673	
Injection site pruritus			
subjects affected / exposed	7 / 463 (1.51%)	7 / 449 (1.56%)	
occurrences (all)	10	9	
Injection site rash			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Injection site reaction			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Injection site swelling			
subjects affected / exposed	117 / 463 (25.27%)	108 / 449 (24.05%)	
occurrences (all)	156	146	
Injection site warmth			
subjects affected / exposed	2 / 463 (0.43%)	1 / 449 (0.22%)	
occurrences (all)	2	1	
Peripheral swelling			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Pain			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Non-cardiac chest pain			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Malaise			

subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Pyrexia			
subjects affected / exposed	29 / 463 (6.26%)	23 / 449 (5.12%)	
occurrences (all)	32	26	
Sensation of foreign body			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Seasonal allergy			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Breast pain			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Bronchospasm			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Dyspnoea			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Dysphonia			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Dry throat			

subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	2 / 463 (0.43%)	2 / 449 (0.45%)	
occurrences (all)	2	3	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Epistaxis			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Lower respiratory tract congestion			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Haemoptysis			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	2	
Nasal congestion			
subjects affected / exposed	2 / 463 (0.43%)	0 / 449 (0.00%)	
occurrences (all)	2	0	
Nasal discomfort			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 463 (0.22%)	3 / 449 (0.67%)	
occurrences (all)	1	3	
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Throat irritation			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Psychiatric disorders			
Acute stress disorder			

subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Restlessness			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	2 / 463 (0.43%)	0 / 449 (0.00%)	
occurrences (all)	2	0	
Arthropod bite			
subjects affected / exposed	2 / 463 (0.43%)	0 / 449 (0.00%)	
occurrences (all)	2	0	
Mallet finger			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Limb injury			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Joint dislocation			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Head injury			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Procedural pain			

subjects affected / exposed	2 / 463 (0.43%)	0 / 449 (0.00%)	
occurrences (all)	2	0	
Road traffic accident			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Burning sensation			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	2 / 463 (0.43%)	3 / 449 (0.67%)	
occurrences (all)	2	3	
Hypoaesthesia			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	241 / 463 (52.05%)	206 / 449 (45.88%)	
occurrences (all)	376	287	
Dysgeusia			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	3	0	
Neuralgia			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
VIth nerve paresis			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Trigeminal neuralgia			

subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Neuromuscular blockade			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Pseudolymphoma			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Presbyacusis			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Vertigo			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Retinal detachment			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Aphthous ulcer			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	0 / 463 (0.00%)	3 / 449 (0.67%)	
occurrences (all)	0	3	
Diarrhoea			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Dental caries			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Hypoaesthesia oral			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Gastrointestinal disorder			
subjects affected / exposed	119 / 463 (25.70%)	102 / 449 (22.72%)	
occurrences (all)	153	118	
Food poisoning			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Mouth haemorrhage			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	

Enteritis			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Rectal fissure			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Tongue eruption			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Dermatitis			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Alopecia			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Night sweats			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Erythema			
subjects affected / exposed	4 / 463 (0.86%)	6 / 449 (1.34%)	
occurrences (all)	6	7	
Peau d'orange			

subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	2 / 463 (0.43%)	2 / 449 (0.45%)	
occurrences (all)	2	3	
Rash			
subjects affected / exposed	2 / 463 (0.43%)	1 / 449 (0.22%)	
occurrences (all)	2	1	
Rash erythematous			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Urinary retention			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 463 (1.73%)	5 / 449 (1.11%)	
occurrences (all)	10	6	
Flank pain			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Bursitis			
subjects affected / exposed	2 / 463 (0.43%)	0 / 449 (0.00%)	
occurrences (all)	2	0	
Back pain			

subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Axillary mass			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Arthritis			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Limb discomfort			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Joint swelling			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	284 / 463 (61.34%)	260 / 449 (57.91%)	
occurrences (all)	501	373	
Neck pain			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Osteoarthritis			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Plantar fasciitis			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	3 / 463 (0.65%)	4 / 449 (0.89%)	
occurrences (all)	3	5	
Synovial cyst			

subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Tendon disorder			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 463 (0.22%)	5 / 449 (1.11%)	
occurrences (all)	1	5	
Cystitis			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Erysipelas			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Fungal skin infection			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	3 / 463 (0.65%)	0 / 449 (0.00%)	
occurrences (all)	3	0	
Herpes simplex			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Genital infection fungal			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	

Impetigo			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Injection site cellulitis			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Influenza			
subjects affected / exposed	3 / 463 (0.65%)	2 / 449 (0.45%)	
occurrences (all)	3	2	
Infection			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Otitis externa			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Oral herpes			
subjects affected / exposed	2 / 463 (0.43%)	1 / 449 (0.22%)	
occurrences (all)	2	1	
Nasopharyngitis			
subjects affected / exposed	7 / 463 (1.51%)	3 / 449 (0.67%)	
occurrences (all)	7	3	
Lower respiratory tract infection			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Laryngitis			
subjects affected / exposed	1 / 463 (0.22%)	1 / 449 (0.22%)	
occurrences (all)	1	1	
Pneumonia			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Pulpitis dental			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Rash pustular			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	

Pharyngitis streptococcal			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	4 / 463 (0.86%)	0 / 449 (0.00%)	
occurrences (all)	4	0	
Otitis media			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	7 / 463 (1.51%)	4 / 449 (0.89%)	
occurrences (all)	7	4	
Urinary tract infection			
subjects affected / exposed	2 / 463 (0.43%)	0 / 449 (0.00%)	
occurrences (all)	2	0	
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 463 (0.86%)	1 / 449 (0.22%)	
occurrences (all)	4	1	
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 463 (0.22%)	0 / 449 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	
Dyslipidaemia			
subjects affected / exposed	0 / 463 (0.00%)	2 / 449 (0.45%)	
occurrences (all)	0	2	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 463 (0.00%)	1 / 449 (0.22%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 October 2017	• Following the initial approval of the GlaxoSmithKline (GSK) Biologicals' HZ/su vaccine, this protocol was amended to indicate that the Trademark is Shingrix. In addition, the term "candidate" vaccine has been replaced by "study" vaccine throughout the protocol and the term "investigational" vaccine has been replaced by "study" vaccine.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported