Clinical trial results:
A phase III, randomized, open-label, multicenter clinical trial to assess the immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A when co-administered with Pneumovax 23 in adults aged 50 years and older.

Summary

EudraCT number	2012-005314-19
Trial protocol	EE
Global end of trial date	22 June 2017

Results information

Result version number	v2 (current)
This version publication date	05 May 2021
First version publication date	08 July 2017
Version creation reason	• Correction of full data set Results have been amended to account for consistency with other registries.

Trial information

Trial identification

Sponsor protocol code	116889

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02045836
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 March 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 June 2017
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 the HZ/su vaccine (based on humoral immune response) one month after the last vaccine dose in the HZ/su – Pneumovax 23 co-administration (Co-Ad) group.
To demonstrate non-inferiority of the humoral immune response to two doses of the HZ/su vaccine when Pneumovax 23 is co-administered with the first HZ/su vaccine dose compared to two doses of HZ/su vaccine (administered separately from Pneumovax 23), one month after the last vaccine dose.
To demonstrate non-inferiority of the humoral immune response to Pneumovax 23 when co-administered with HZ/su vaccine at first vaccine dose compared to Pneumovax 23 (administered separately from HZ/su), for the following 12 serotypes included in Pneumovax 23, one month after the vaccine dose: 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified ad 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	05 May 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Estonia: 400
Country: Number of subjects enrolled	Canada: 299
Country: Number of subjects enrolled	United States: 166
Worldwide total number of subjects	865
EEA total number of subjects	400

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)	502
From 65 to 84 years	356
85 years and over	7

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Period 1

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

Arms

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

Arm description:

Subjects received one dose of the GSK1437173A study vaccine and one dose of the Pneumovax 23 vaccine at Day 0 and a second dose of GSK1437173A study vaccine at Month 2. GSK1437173A vaccine was administered intramuscularly, in the deltoid region of the non-dominant arm. Pneumovax 23 was administered intramuscularly, in the deltoid region of the dominant arm .

Arm type	Experimental
Investigational medicinal product name	GSK1437173A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of the vaccine at Day 0 and a second dose at Month 2.

Investigational medicinal product name	Pneumovax 23
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of the vaccine at Day 0.

Arm title	Control group

Arm description:

Subjects received one dose of the Pneumovax 23 vaccine at Day 0, one dose of the GSK1437173A study vaccine at Month 2 and a second dose of the GSK1437173A study vaccine at Month 4. GSK1437173A vaccine was administered intramuscularly, in the deltoid region of the non-dominant arm. Pneumovax 23 was administered intramuscularly, in the deltoid region of the dominant arm .

Arm type	Active comparator
Investigational medicinal product name	GSK1437173A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of the vaccine at Day 0 and a second dose at Month 2.

Investigational medicinal product name	Pneumovax 23
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose of the vaccine at Day 0.

Number of subjects in period 1	Co-Ad group	Control group
Started	432	433
Completed	423	419
Not completed	9	14
Consent withdrawn by subject	1	1
Adverse event, non-fatal	4	4
Lost to follow-up	4	9

Baseline characteristics

Reporting groups	
Reporting group title	Co-Ad group
Reporting group description:	
Subjects received one dose of the GSK1437173A study vaccine and one dose of the Pneumovax 23 vaccine at Day 0 and a second dose of GSK1437173A study vaccine at Month 2. GSK1437173A vaccine was administered intramuscularly, in the deltoid region of the non-dominant arm. Pneumovax 23 was administered intramuscularly, in the deltoid region of the dominant arm .	
Reporting group title	Control group
Reporting group description:	
Subjects received one dose of the Pneumovax 23 vaccine at Day 0, one dose of the GSK1437173A study vaccine at Month 2 and a second dose of the GSK1437173A study vaccine at Month 4. GSK1437173A vaccine was administered intramuscularly, in the deltoid region of the non-dominant arm. Pneumovax 23 was administered intramuscularly, in the deltoid region of the dominant arm .	

Reporting group values	Co-Ad group	Control group	Total
Number of subjects	432	433	865
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	63.2	63.2	
standard deviation	± 8.4	± 8.4	-
Gender categorical Units: Subjects			
Female	264	252	516
Male	168	181	349
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American	12	9	21
American Indian or Alaskan Native	1	3	4
Asian - East Asian Heritage	3	7	10
Asian - Japanese Heritage	0	1	1
Asian - South East Asian Heritage	4	2	6
Other	2	5	7
White - Arabic / North African Heritage	2	0	2
White - Caucasian / European Heritage	408	406	814

End points

End points reporting groups

Reporting group title	Co-Ad group

Reporting group description:

Subjects received one dose of the GSK1437173A study vaccine and one dose of the Pneumovax 23 vaccine at Day 0 and a second dose of GSK1437173A study vaccine at Month 2. GSK1437173A vaccine was administered intramuscularly, in the deltoid region of the non-dominant arm. Pneumovax 23 was administered intramuscularly, in the deltoid region of the dominant arm .

Reporting group title	Control group

Reporting group description:

Subjects received one dose of the Pneumovax 23 vaccine at Day 0, one dose of the GSK1437173A study vaccine at Month 2 and a second dose of the GSK1437173A study vaccine at Month 4. GSK1437173A vaccine was administered intramuscularly, in the deltoid region of the non-dominant arm. Pneumovax 23 was administered intramuscularly, in the deltoid region of the dominant arm .

Primary: Number of subjects with a vaccine response for anti-gE antibodies

End point title	Number of subjects with a vaccine response for anti-gE antibodies[1][2]

End point description:

Vaccine response rate for anti-gE antibody concentrations, as determined by enzyme-linked immunosorbent assay (ELISA), in subjects from the Co-Ad group. Vaccine response defined as: For initially seronegative subjects, antibody concentration at post-vaccination ≥ 4 fold the cut-off for Anti-gE (4x 97 mIU/mL). For initially seropositive subjects, antibody concentration at post-vaccination ≥ 4 fold the pre-vaccination antibody concentration.

End point type	Primary

End point timeframe:

At 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 end point was descriptive, no statistical hypothesis test was performed.
[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: As only the Co-ad Group received vaccination containing gE antigen, only this group had results.

End point values	Co-Ad group			
Subject group type	Reporting group			
Number of subjects analysed	401			
Units: Subjects				
Subjects	394			

Statistical analyses

No statistical analyses for this end point

Primary: Anti-glicoprotein E (gE) antibody concentrations

End point title	Anti-glicoprotein E (gE) antibody concentrations[3]

End point description:

Antibody concentrations were determined by ELISA, presented as geometric mean concentrations and expressed as milli international units per milliliter (mIU/mL).

End point type	Primary

End point timeframe:

At one month post-dose 2 (Month 3 for the Co-Ad Group 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 end point was descriptive, no statistical hypothesis test was performed.

End point values	Co-Ad group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	407	402		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
mIU/mL	49918 (47143 to 52856.3)	50327.9 (47200.4 to 53662.7)		

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 were presented as geometric mean titers (GMTs) for the 12 following serotypes as determined by Opsonophagocytic Assay (OPA): 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.

End point type	Primary

End point timeframe:

At one month post-dose (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 end point was descriptive, no statistical hypothesis test was performed.

End point values	Co-Ad group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	410	413		
Units: Titers				
geometric mean (confidence interval 95%)				
MOPA-1 [N=410, 413]	65.1 (54.2 to 78.1)	68.6 (56.9 to 82.7)		
MOPA-9V [N=410, 413]	1898.4 (1618.1 to 2227.2)	1991.3 (1716 to 2310.8)		

MOPA-14 [N=410, 413]	2629.4 (2297.4 to 3009.3)	2612.8 (2230.7 to 3060.3)		
MOPA-3 [N=410, 413]	106.7 (92.6 to 122.9)	107.4 (92.7 to 124.4)		
MOPA-4 [N=410, 412]	1079.4 (924 to 1260.9)	1328.8 (1141 to 1547.6)		
MOPA-5 [N=410, 413]	161.4 (134.6 to 193.6)	149.5 (123.5 to 181)		
MOPA-6B [N=410, 413]	1619 (1354.5 to 1935)	1564.4 (1303.5 to 1877.6)		
MOPA-7F [N=410, 413]	2352.5 (2049.5 to 2700.3)	2460.4 (2128.7 to 2843.8)		
MOPA-18C [N=410, 413]	1077.4 (921.1 to 1260.2)	1076 (918.2 to 1260.9)		
MOPA-19A [N=410, 413]	1349.6 (1152.1 to 1580.8)	1573.1 (1350.7 to 1832.2)		
MOPA-19F [N=409, 413]	904.3 (779.6 to 1049)	953 (814.8 to 1114.6)		
MOPA-23F [N=409, 413]	431.4 (356.1 to 522.7)	367.3 (300.8 to 448.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Adjusted ratios of Geometric Mean Titers (GMTs) between groups

End point title	Adjusted ratios of Geometric Mean Titers (GMTs) between groups

End point description:

The Adjusted ratios of GMTs between groups (Control group and Co-Ad group) were presented for each individual pneumococcal conjugate serotype Opsonophagocytic Activity (OPA).

End point type	Primary

End point timeframe:

At 1 month after vaccination

End point values	Co-Ad group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	411	408		
Units: Titers				
geometric mean (confidence interval 95%)				
MOPA-1 [N=411, 408]	67.6 (56.9 to 80.2)	65.6 (55.2 to 119.5)		
MOPA-3 [N=411, 408]	105 (92.2 to 119.5)	108.9 (95.7 to 124.1)		
MOPA-4 [N=409, 408]	1264.1 (1089.9 to 1466.2)	1117.2 (963.1 to 1296.1)		

MOPA-5 [N=411, 408]	152.6 (129.1 to 180.3)	159.8 (135.1 to 188.9)		
MOPA-6B [N=409, 408]	1536.8 (1307.9 to 1805.7)	1666.6 (1418 to 1958.6)		
MOPA-7F [N=409, 407]	2491.3 (2179.8 to 2847.5)	2324.7 (2033.3 to 2657.9)		
MOPA-9V [N=410, 406]	1911.8 (1651.6 to 2212.9)	1970.3 (1700.9 to 2282.3)		
MOPA-14 [N=411, 407]	2610.1 (2281.6 to 2986)	2678.1 (2339.4 to 3065.8)		
MOPA-18C [N=411, 405]	1040.9 (902.7 to 1200.4)	1099.8 (952.8 to 1269.6)		
MOPA-19A [N=406, 406]	1558.6 (1361.8 to 1783.8)	1350.5 (1180 to 1545.7)		
MOPA-19F [N=409, 407]	938.2 (814.6 to 1080.7)	914.1 (793.4 to 1053.3)		
MOPA-23F [N=410, 405]	372.8 (316 to 439.8)	419.1 (354.9 to 494.9)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-1.	
Comparison groups	Control group v Co-Ad group
Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.31

Notes:

[5] - Non Inferiority criterion used: Upper Limit (UL) of the 95% CI for each individual pneumococcal conjugate serotype Opsonophagocytic Assay (OPA) GMT ratio of the Control group over the Co-Ad group had to be below 2.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-3	
Comparison groups	Control group v Co-Ad group

Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.16

Notes:

[6] - Non Inferiority criterion used: Upper Limit (UL) of the 95% CI for each individual pneumococcal conjugate serotype Opsonophagocytic Assay (OPA) GMT ratio of the Control group over the Co-Ad group had to be below 2.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-4

Comparison groups	Co-Ad group v Control group
Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.4

Notes:

[7] - Non Inferiority criterion used: Upper Limit (UL) of the 95% CI for each individual pneumococcal conjugate serotype Opsonophagocytic Assay (OPA) GMT ratio of the Control group over the Co-Ad group had to be below 2.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-5

Comparison groups	Co-Ad group v Control group
Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.21

Notes:

[8] - Non Inferiority criterion used: Upper Limit (UL) of the 95% CI for each individual pneumococcal conjugate serotype Opsonophagocytic Assay (OPA) GMT ratio of the Control group over the Co-Ad group had to be below 2.

Statistical analysis title	Statistical analysis 5
Statistical analysis description:	
Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-6B	
Comparison groups	Co-Ad group v Control group
Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.16

Statistical analysis title	Statistical analysis 6
Statistical analysis description:	
Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-7F	
Comparison groups	Co-Ad group v Control group
Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.29

Notes:

[9] - Non Inferiority criterion used: Upper Limit (UL) of the 95% CI for each individual pneumococcal conjugate serotype Opsonophagocytic Assay (OPA) GMT ratio of the Control group over the Co-Ad group had to be below 2.

Statistical analysis title	Statistical analysis 7
Statistical analysis description:	
Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-9V	
Comparison groups	Co-Ad group v Control group

Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.19

Notes:

[10] - Non Inferiority criterion used: Upper Limit (UL) of the 95% CI for each individual pneumococcal conjugate serotype Opsonophagocytic Assay (OPA) GMT ratio of the Control group over the Co-Ad group had to be below 2.

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-14

Comparison groups	Co-Ad group v Control group
Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.18

Notes:

[11] - Non Inferiority criterion used: Upper Limit (UL) of the 95% CI for each individual pneumococcal conjugate serotype Opsonophagocytic Assay (OPA) GMT ratio of the Control group over the Co-Ad group had to be below 2.

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-18C

Comparison groups	Co-Ad group v Control group
Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.16

Notes:

[12] - Non Inferiority criterion used: Upper Limit (UL) of the 95% CI for each individual pneumococcal conjugate serotype Opsonophagocytic Assay (OPA) GMT ratio of the Control group over the Co-Ad group had to be below 2.

Statistical analysis title	Statistical analysis 10
Statistical analysis description:	
Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-19A	
Comparison groups	Co-Ad group v Control group
Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.4

Notes:

[13] - Non Inferiority criterion used: Upper Limit (UL) of the 95% CI for each individual pneumococcal conjugate serotype Opsonophagocytic Assay (OPA) GMT ratio of the Control group over the Co-Ad group had to be below 2.

Statistical analysis title	Statistical analysis 11
Statistical analysis description:	
Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-19F	
Comparison groups	Co-Ad group v Control group
Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.25

Notes:

[14] - Non Inferiority criterion used: Upper Limit (UL) of the 95% CI for each individual pneumococcal conjugate serotype Opsonophagocytic Assay (OPA) GMT ratio of the Control group over the Co-Ad group had to be below 2.

Statistical analysis title	Statistical analysis 12
Statistical analysis description:	
Adjusted ratios of GMTs between groups (Control group and Co-Ad group) for MOPA-23F	
Comparison groups	Co-Ad group v Control group

Number of subjects included in analysis	819
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.12

Notes:

[15] - Non Inferiority criterion used: Upper Limit (UL) of the 95% CI for each individual pneumococcal conjugate serotype Opsonophagocytic Assay (OPA) GMT ratio of the Control group over the Co-Ad group had to be below 2.

Primary: Adjusted GMCs between groups

End point title	Adjusted GMCs between groups

End point description:

The Adjusted ratios of GMCs between groups (Control group and Co-Ad group) was presented for anti-gE antibody ELISA concentrations

End point type	Primary

End point timeframe:

At 1 month after last vaccine dose

End point values	Co-Ad group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	401	402		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
mIU/mL	49569 (46641.4 to 52680.4)	50474.5 (47497.4 to 53638.2)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Adjusted ratios of GMCs between groups (Control group and Co-Ad group) for anti-gE antibody ELISA concentrations

Comparison groups	Co-Ad group v Control group
Number of subjects included in analysis	803
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Method	ANCOVA
Parameter estimate	Adjusted GMT
Point estimate	1.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.11

Notes:

[16] - Non Inferiority criterion used: UL of the 95% CI for the anti-gE antibodies GMC ratio between the Control group and the Co-Ad group had to be below 1.5

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, 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. The Co-Ad Group received only 2 vaccine doses.

End point type	Secondary

End point timeframe:

Within 7 days (Days 0 - 6) after each vaccination

End point values	Co-Ad group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	429	431		
Units: Subjects				
Any Pain, Dose 1 [N=428, 431]	344	168		
Grade 3 Pain, Dose 1 [N=428, 431]	46	5		
Any Redness, Dose 1 [N=428, 431]	182	30		
Grade 3 Redness, Dose 1 [N=428, 431]	15	2		
Any Swelling, Dose 1 [N=428, 431]	99	18		
Grade 3 Swelling, Dose 1 [N=428, 431]	4	1		
Any Pain, Dose 2 [N=416, 422]	298	289		
Grade 3 Pain, Dose 2 [N=416, 422]	35	28		
Any Redness, Dose 2 [N=416, 422]	144	128		
Grade 3 Redness, Dose 2 [N=416, 422]	15	4		
Any Swelling, Dose 2 [N=416, 422]	77	64		
Grade 3 Swelling, Dose 2 [N=416, 422]	4	2		
Any Pain, Dose 3 [N=0, 419]	0	293		
Grade 3 Pain, Dose 3 [N=0, 419]	0	32		
Any Redness, Dose 3 [N=0, 419]	0	136		
Grade 3 Redness, Dose 3 [N=0, 419]	0	8		
Any Swelling, Dose 3 [N=0, 419]	0	74		
Grade 3 Swelling, Dose 3 [N=0, 419]	0	3		
Any Pain, Across Doses [N=429, 431]	372	356		
Grade 3 Pain, Across Doses [N=429, 431]	68	49		
Any Redness, Across Doses [N=429, 431]	232	192		
Grade 3 Redness, Across Doses [N=429, 431]	27	12		

Any Swelling, Across Doses [N=429, 431]	135	111		
Grade 3 Swelling, Across Doses [N=429, 431]	7	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms, across doses, by vaccine

End point title	Number of subjects with solicited local symptoms, across doses, by vaccine

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	Secondary

End point timeframe:

Within 7 days (Days 0 - 6) after vaccination

End point values	Co-Ad group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	429	431		
Units: Subjects				
Any Pain, GSK1437173A, Across Doses [N=429, 426]	369	343		
Any Pain, Pneumovax 23, Across Doses [N=428, 431]	223	169		
Any Redness, GSK1437173A, Across Doses [N=429,431]	223	186		
Any Redness,Pneumovax 23,Across Doses [N=428,431]	69	31		
Any Swelling,GSK1437173A,Across Doses [N=429,426]	129	108		
Any Swelling,Pneumovax 23,Across Doses [N=428,431]	36	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with any solicited local and general symptoms

End point title	Number of days with any solicited local and general symptoms

End point description:

The Co-Ad Group received only 2 vaccine doses. Gastrointestinal symptoms included nausea, vomiting, diarrhoea and/or abdominal pain.

End point type	Secondary

End point timeframe:

Within 7 days (Days 0 - 6) after each vaccination

End point values	Co-Ad group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	293		
Units: days				
median (inter-quartile range (Q1-Q3))				
Any Pain, Dose 1 [N=344, 169]	3 (2 to 4)	2 (1 to 3)		
Any Pain, Dose 2 [N=298, 290]	3 (2 to 4)	3 (2 to 4)		
Any Pain, Dose 3 [N=0, 293]	0 (0 to 0)	3 (2 to 4)		
Any Redness, Dose 1 [N=182, 31]	3 (2 to 5)	2 (1 to 3)		
Any Redness, Dose 2 [N=146, 129]	3 (2 to 4)	3 (2 to 5)		
Any Redness, Dose 3 [N=0, 136]	0 (0 to 0)	3 (2 to 4)		
Any Swelling, Dose 1 [N=99, 21]	3 (2 to 5)	2 (1 to 3)		
Any Swelling, Dose 2 [N=79, 67]	3 (2 to 4)	4 (2 to 5)		
Any Swelling, Dose 3 [N=0, 74]	0 (0 to 0)	3 (2 to 5)		
Any Fatigue, Dose 1 [N=194, 87]	2 (1 to 4)	2 (1 to 4)		
Any Fatigue, Dose 2 [N=191, 124]	2 (1 to 3)	2 (1 to 3)		
Any Fatigue, Dose 3 [N=0, 174]	0 (0 to 0)	2 (1 to 3)		
Any Gastrointestinal, Dose 1 [N=76, 31]	2 (1 to 2.5)	2 (1 to 3)		
Any Gastrointestinal, Dose 2 [N=61, 38]	2 (1 to 3)	2 (1 to 3)		
Any Gastrointestinal, Dose 3 [N=0, 47]	0 (0 to 0)	1 (1 to 2)		
Any Headache, Dose 1 [N=156, 72]	2 (1 to 3)	2 (1 to 2)		
Any Headache, Dose 2 [N=141, 104]	2 (1 to 3)	2 (1 to 2.5)		
Any Headache, Dose 3 [N=0, 144]	0 (0 to 0)	2 (1 to 2)		
Any Myalgia, Dose 1 [N=187, 87]	2 (2 to 4)	2 (1 to 3)		
Any Myalgia, Dose 2 [N=182, 124]	2 (1 to 3)	2 (1 to 3.5)		
Any Myalgia, Dose 3 [N=0, 162]	0 (0 to 0)	2 (2 to 3)		
Any Shivering, Dose 1 [N=91, 27]	1 (1 to 2)	2 (1 to 2)		
Any Shivering, Dose 2 [N=83, 30]	1 (1 to 2)	1 (1 to 2)		
Any Shivering, Dose 3 [N=0, 72]	0 (0 to 0)	1 (1 to 2)		
Any Temperature (Oral), Dose 1 [N=69, 12]	1 (1 to 2)	1 (1 to 2)		
Any Temperature (Oral), Dose 2 [N=67, 30]	1 (1 to 2)	1 (1 to 2)		
Any Temperature (Oral), Dose 3 [N=0, 67]	0 (0 to 0)	1 (1 to 2)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

From the first dose up to 30 days post last vaccination period

End point values	Co-Ad group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	432	433		
Units: Subjects				
Subjects with any AE(s)	132	140		
Subjects with grade 3 AE(s)	16	28		
Subjects with related AE(s)	34	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) [from the first dose up to 30 days post last vaccination period]

End point title	Number of subjects with serious adverse events (SAEs) [from the first dose up to 30 days post last vaccination period]

End point description:

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

End point type	Secondary

End point timeframe:

From the first dose up to 30 days post last vaccination period

End point values	Co-Ad group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	432	433		
Units: Subjects				
Subjects with any SAE(s)	7	9		
Fatal SAEs	0	0		
Related SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with potential Immune Mediated Diseases (pIMDs) [from first vaccination up to 30 days post last vaccination]

End point title	Number of subjects with potential Immune Mediated Diseases (pIMDs) [from first vaccination up to 30 days post last vaccination]

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 up to 30 days post last vaccination (Month 0 – Month 3 for the Co-Ad Group; Month 0 – 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	432	433		
Units: Subjects				
Any pIMDs	0	1		
Related pIMDs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with potential Immune Mediated Diseases (pIMDs) [during the period starting after 30 days post last vaccination up to study end]

End point title	Number of subjects with potential Immune Mediated Diseases (pIMDs) [during the period starting after 30 days post last vaccination up to study end]

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:

During the period starting after 30 days post last vaccination up to study end (Month 3 – Month 14 for the Co-Ad Group; Month 5 – 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	432	433		
Units: Subjects				
Subjects	1	0		

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 arthralgia, fatigue, fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)], headache, myalgia, shivering and sweating. Any = occurrence of the symptom regardless of intensity grade. Grade 3 (G3) symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.0 °C. Related (Rel) = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

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

End point values	Co-Ad group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	429	431		
Units: Subjects				
Any Fatigue, Dose 1 (N=427,430)	194	87		
G3 Fatigue, Dose 1 (N=427,430)	27	3		
Rel Fatigue, Dose 1 (N=427,430)	175	81		
Any Gastrointestinal symptoms, Dose 1 (N=427,430)	76	31		
G3 Gastrointestinal symptoms, Dose 1 (N=427,430)	6	1		
Rel Gastrointestinal symptoms, Dose 1 (N=427,430)	67	28		
Any Headache, Dose 1 (N=427,430)	156	72		
G3 Headache, Dose 1 (N=427,430)	15	3		
Rel Headache, Dose 1 (N=427,430)	141	64		
Any Myalgia, Dose 1 (N=427,430)	187	87		
G3 Myalgia, Dose 1 (N=427,430)	29	5		
Rel Myalgia, Dose 1 (N=427,430)	177	82		
Any Shivering, Dose 1 (N=427,430)	91	27		
G3 Shivering, Dose 1 (N=427,430)	27	1		
Rel Shivering, Dose 1 (N=427,430)	86	26		
Any Temperature, Dose 1 (N=427,430)	69	12		
G3 Temperature, Dose 1 (N=427,430)	1	1		

Rel Temperature, Dose 1 (N=427,430)	67	11		
Any Fatigue, Dose 2 (N=415,421)	191	124		
G3 Fatigue, Dose 2 (N=415,421)	29	11		
Rel Fatigue, Dose 2 (N=415,421)	174	109		
Any Gastrointestinal symptoms, Dose 2 (N=415,421)	61	38		
G3 Gastrointestinal symptoms, Dose 2 (N=415,421)	6	4		
Rel Gastrointestinal symptoms, Dose 2 (N=415,421)	52	29		
Any Headache, Dose 2 (N=415,421)	141	104		
G3 Headache, Dose 2 (N=415,421)	19	9		
Rel Headache, Dose 2 (N=415,421)	124	85		
Any Myalgia, Dose 2 (N=415,421)	182	124		
G3 Myalgia, Dose 2 (N=415,421)	25	11		
Rel Myalgia, Dose 2 (N=415,421)	171	119		
Any Shivering, Dose 2 (N=415,421)	83	30		
G3 Shivering, Dose 2 (N=415,421)	14	3		
Rel Shivering, Dose 2 (N=415,421)	78	25		
Any Temperature, Dose 2 (N=415,421)	67	30		
G3 Temperature, Dose 2 (N=415,421)	0	0		
Rel Temperature, Dose 2 (N=415,421)	63	26		
Any Fatigue, Dose 3 (N=0, 419)	0	174		
G3 Fatigue, Dose 3 (N=0, 419)	0	22		
Rel Fatigue, Dose 3 (N=0, 419)	0	166		
Any Gastrointestinal symptoms, Dose 3 (N=0, 419)	0	47		
G3 Gastrointestinal symptoms, Dose 3 (N=0, 419)	0	3		
Rel Gastrointestinal symptoms, Dose 3 (N=0, 419)	0	46		
Any Headache, Dose 3 (N=0, 419)	0	144		
G3 Headache, Dose 3 (N=0, 419)	0	13		
Rel Headache, Dose 3 (N=0, 419)	0	135		
Any Myalgia, Dose 3 (N=0, 419)	0	162		
G3 Myalgia, Dose 3 (N=0, 419)	0	26		
Rel Myalgia, Dose 3 (N=0, 419)	0	157		
Any Shivering, Dose 3 (N=0, 419)	0	72		
G3 Shivering, Dose 3 (N=0, 419)	0	11		
Rel Shivering, Dose 3 (N=0, 419)	0	69		
Any Temperature, Dose 3 (N=0, 419)	0	67		
G3 Temperature, Dose 3 (N=0, 419)	0	2		
Rel Temperature, Dose 3 (N=0, 419)	0	66		
Any Fatigue, Across doses (N=429,431)	253	228		
G3 Fatigue, Across doses (N=429,431)	47	31		
Rel Fatigue, Across doses (N=429,431)	236	216		
Any Gastrointestinal sympt,Across doses(N=429,431)	114	84		
G3 Gastrointestinal sympt, Across doses(N=429,431)	12	7		
Rel Gastrointestinal sympt,Across doses(N=429,431)	100	77		
Any Headache, Across doses (N=429,431)	209	208		

G3 Headache, Across doses (N=429,431)	29	24		
Rel Headache, Across doses (N=429,431)	195	193		
Any Myalgia, Across doses (N=429,431)	257	225		
G3 Myalgia, Across doses (N=429,431)	46	37		
Rel Myalgia, Across doses (N=429,431)	245	218		
Any Shivering, Across doses (N=429,431)	137	99		
G3 Shivering, Across doses (N=429,431)	25	15		
Rel Shivering, Across doses (N=429,431)	131	95		
Any Temperature, Across doses (N=429,431)	112	96		
G3 Temperature, Across doses (N=429,431)	1	3		
Rel Temperature, Across doses (N=429,431)	108	91		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) [from 30 days post last vaccination up to study end]

End point title	Number of subjects with serious adverse events (SAEs) [from 30 days post last vaccination up to study end]

End point description:

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

End point type	Secondary

End point timeframe:

From 30 days post last vaccination up to study end

End point values	Co-Ad group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	432	433		
Units: Subjects				
Subjects with any SAE(s)	10	10		
Fatal SAE(s)	2	2		
Related SAE(s)	2	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms during the 7-day post-vaccination period, Unsolicited AEs during the 30-day post-vaccination period. SAE(s) were collected during the entire study period (Month 0 to Month 16)

Adverse event reporting additional description:

Individual SAEs remain blinded as long as the study is ongoing.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Control Group

Reporting group description:

Subjects received one dose of the Pneumovax™ 23 vaccine at Day 0, one dose of the GSK1437173A study vaccine at Month 2 and a second dose of the GSK1437173A study vaccine at Month 4. GSK1437173A vaccine was administered intramuscularly, in the deltoid region of the non-dominant arm. Pneumovax™ 23 was administered intramuscularly, in the deltoid region of the dominant arm.

Reporting group title	Co-Ad Group

Reporting group description:

Subjects received one dose of the GSK1437173A study vaccine and one dose of the Pneumovax™ 23 vaccine at Day 0 and a second dose of GSK1437173A study vaccine at Month 2. GSK1437173A vaccine was administered intramuscularly, in the deltoid region of the non-dominant arm. Pneumovax™ 23 was administered intramuscularly, in the deltoid region of the dominant arm.

Serious adverse events	Control Group	Co-Ad Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 433 (4.39%)	17 / 432 (3.94%)	
number of deaths (all causes)	2	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Angiomyolipoma			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma stage iv			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			

subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma multiforme			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteriosclerosis			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chest pain			
subjects affected / exposed	2 / 433 (0.46%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Sarcoidosis			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Limb traumatic amputation			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
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 / 433 (0.23%)	3 / 432 (0.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 433 (0.23%)	2 / 432 (0.46%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	2 / 433 (0.46%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	2 / 433 (0.46%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			

subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbosacral radiculopathy			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (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	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral artery dissection			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (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			
Leukocytosis			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Calculus urinary			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (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			
Osteoarthritis			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (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	3 / 433 (0.69%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	

Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 433 (0.00%)	1 / 432 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperlipidaemia			
subjects affected / exposed	1 / 433 (0.23%)	0 / 432 (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	Control Group	Co-Ad Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	393 / 433 (90.76%)	400 / 432 (92.59%)	
Nervous system disorders			
Headache			
subjects affected / exposed	209 / 433 (48.27%)	210 / 432 (48.61%)	
occurrences (all)	331	306	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	228 / 433 (52.66%)	253 / 432 (58.56%)	
occurrences (all)	385	385	
Pain			
subjects affected / exposed	357 / 433 (82.45%)	372 / 432 (86.11%)	
occurrences (all)	754	642	
Pyrexia			
subjects affected / exposed	97 / 433 (22.40%)	112 / 432 (25.93%)	
occurrences (all)	110	138	
Swelling			
subjects affected / exposed	115 / 433 (26.56%)	137 / 432 (31.71%)	
occurrences (all)	162	178	
Erythema			
subjects affected / exposed	194 / 433 (44.80%)	234 / 432 (54.17%)	
occurrences (all)	297	330	
Gastrointestinal disorders			

Gastrointestinal disorder			
subjects affected / exposed	84 / 433 (19.40%)	114 / 432 (26.39%)	
occurrences (all)	116	137	
Chills			
subjects affected / exposed	99 / 433 (22.86%)	137 / 432 (31.71%)	
occurrences (all)	130	176	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	227 / 433 (52.42%)	257 / 432 (59.49%)	
occurrences (all)	376	370	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported