Clinical trial results:
A Phase IIB, randomised, observer-blind, placebo-controlled, multi-centre study to evaluate the efficacy, safety, reactogenicity and immunogenicity of the GSK Biologicals' investigational vaccine GSK3277511A when administered intramuscularly according to a 0, 2 month schedule in COPD patients aged 40 to 80 years with a previous history of acute exacerbation (AECOPD)

Summary

EudraCT number	2017-000880-34
Trial protocol	GB BE ES DE FR IT
Global end of trial date	12 June 2020

Results information

Result version number	v2 (current)
This version publication date	04 March 2021
First version publication date	03 December 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	207489

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03281876
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	06 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 March 2020
Global end of trial reached?	Yes
Global end of trial date	12 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess efficacy of the investigational vaccine as compared to the placebo control with respect to the rate of moderate and severe AECOPDs

Protection of trial subjects:

All subjects were supervised for 60 min after vaccination with appropriate medical treatment available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccine. Subjects were called by the investigator or a medically trained delegate one week after the vaccination. If the subject experienced an acute exacerbation, he/she was invited to visit the study site for follow-up.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 November 2017
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	Belgium: 34
Country: Number of subjects enrolled	Canada: 93
Country: Number of subjects enrolled	France: 42
Country: Number of subjects enrolled	Germany: 118
Country: Number of subjects enrolled	Italy: 37
Country: Number of subjects enrolled	Spain: 55
Country: Number of subjects enrolled	United Kingdom: 67
Country: Number of subjects enrolled	United States: 160
Worldwide total number of subjects	606
EEA total number of subjects	286

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	241
From 65 to 84 years	365
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All enrolled subjects received the study intervention

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

This is an observer blind study

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK3277511A Group

Arm description:

Healthy males and females, 40 to 80 years of age, who received two doses of the adjuvanted GSK3277511A investigational vaccine containing surface protein D (PD), protein E- type IV pilus assembly protein (PE-PilA,) and ubiquitous surface protein A2 (UspA2), administered at Day 1 and Day 61

Arm type	Experimental
Investigational medicinal product name	NTHi Mcat investigational vaccine (GSK3277511A)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses administered in the non-dominant arm

Arm title	Control Group

Arm description:

Healthy males and females, 40 to 80 years of age, who received two doses of placebo, administered at Day 1 and Day 61.

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

Dosage and administration details:

2 doses administered in the non-dominant arm

Number of subjects in period 1	GSK3277511A Group	Control Group
Started	304	302
Completed	281	263
Not completed	23	39
OTHER	5	5
Adverse event, non-fatal	4	15
MIGRATED / MOVED FROM THE STUDY AREA	2	-
Consent withdrawn by subject	11	15
Lost to follow-up	1	4

Baseline characteristics

Reporting groups	
Reporting group title	GSK3277511A Group
Reporting group description:	
Healthy males and females, 40 to 80 years of age, who received two doses of the adjuvanted GSK3277511A investigational vaccine containing surface protein D (PD), protein E- type IV pilus assembly protein (PE-PilA,) and ubiquitous surface protein A2 (UspA2), administered at Day 1 and Day 61	
Reporting group title	Control Group
Reporting group description:	
Healthy males and females, 40 to 80 years of age, who received two doses of placebo, administered at Day 1 and Day 61.	

Reporting group values	GSK3277511A Group	Control Group	Total
Number of subjects	304	302	606
Age categorical Units: Subjects			
Adults (18-64 years)	127	114	241
From 65-84 years	177	188	365
Age continuous Units: years			
arithmetic mean	65.7	66.3	
standard deviation	± 7.5	± 7.3	-
Sex: Female, Male Units: Participants			
Female	120	125	245
Male	184	177	361
Race/Ethnicity, Customized Units: Subjects			
American Indian Or Alaska Native	0	1	1
Asian - Central / South Asian Heritage	2	0	2
Asian - South East Asian Heritage	0	1	1
Black Or African American	5	4	9
Other	1	0	1
White - Arabic / North African Heritage	2	0	2
White - Caucasian / European Heritage	294	296	590

End points

End points reporting groups

Reporting group title	GSK3277511A Group

Reporting group description:

Healthy males and females, 40 to 80 years of age, who received two doses of the adjuvanted GSK3277511A investigational vaccine containing surface protein D (PD), protein E- type IV pilus assembly protein (PE-PilA,) and ubiquitous surface protein A2 (UspA2), administered at Day 1 and Day 61

Reporting group title	Control Group

Reporting group description:

Healthy males and females, 40 to 80 years of age, who received two doses of placebo, administered at Day 1 and Day 61.

Primary: Rate of moderate and severe AECOPD (any cause)-analysis (87% Confidence Interval [CI]), post-dose 2 and lasting for 1 year

End point title	Rate of moderate and severe AECOPD (any cause)-analysis (87% Confidence Interval [CI]), post-dose 2 and lasting for 1 year

End point description:

Efficacy of the investigational vaccine was measured by the rate of moderate and severe AECOPD from 1-month post dose 2 up to study end (i.e. rate expressed per year and calculated as the total number of events over the follow-up exposure time). The CIs of the rate is computed using a model which accounts for repeated events. Anthonisen criteria used to detect potential AECOPD: Worsening of 2 or more of the following major symptoms for at least 2 consecutive days: dyspnoea, sputum volume, sputum purulence, OR Worsening of any major symptom together with any of the following minor symptoms for at least 2 consecutive days: sore throat, cold, fever without other cause, increased cough, increased wheeze. Moderate AECOPD requires treatment with systemic corticosteroids and/ or antibiotics. Severe AECOPD requires hospitalization. Confirmation of AECOPD was as per investigator's judgement.

End point type	Primary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: exacerbations per person-year				
number (confidence interval 87%)	1.22 (1.09 to 1.36)	1.17 (1.06 to 1.3)		

Statistical analyses

Statistical analysis title	Vaccine efficacy-87%

Statistical analysis description:

To assess efficacy of the investigational vaccine as compared to the placebo control with respect to the rate of moderate and severe AECOPDs

Comparison groups	GSK3277511A Group v Control Group

Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8157
Method	Negative Binomial regression
Parameter estimate	Other: Vaccine Efficacy rate
Point estimate	-2.26
Confidence interval	
level	Other: 87 %
sides	2-sided
lower limit	-18.27
upper limit	11.58

Primary: Rate of moderate and severe AECOPD (any cause) -Analysis (95% CI), post-dose 2 and lasting for 1 year

End point title	Rate of moderate and severe AECOPD (any cause) -Analysis (95% CI), post-dose 2 and lasting for 1 year

End point description:

Efficacy of the investigational vaccine was measured by the rate of moderate and severe AECOPD from 1-month post dose 2 up to study end (i.e. rate expressed per year and calculated as the total number of events over the follow-up exposure time). The CIs of the rate is computed using a model which accounts for repeated events. Anthonisen criteria used to detect potential AECOPD: Worsening of 2 or more of the following major symptoms for at least 2 consecutive days: dyspnoea, sputum volume, sputum purulence, OR Worsening of any major symptom together with any of the following minor symptoms for at least 2 consecutive days: sore throat, cold, fever without other cause, increased cough, increased wheeze. Moderate AECOPD requires treatment with systemic corticosteroids and/ or antibiotics. Severe AECOPD requires hospitalization. Confirmation of AECOPD was as per investigator's judgement.

End point type	Primary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: exacerbations per person-year				
number (confidence interval 95%)	1.22 (1.05 to 1.41)	1.17 (1.02 to 1.34)		

Statistical analyses

Statistical analysis title	Vaccine efficacy-95%

Statistical analysis description:

To assess efficacy of the investigational vaccine as compared to the placebo control with respect to the rate of moderate and severe AECOPDs

Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified

Analysis type	
P-value	= 0.8157
Method	Negative Binomial regression
Parameter estimate	Other: Vaccine Efficacy rate
Point estimate	-2.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.45
upper limit	15.29

Secondary: Number of subjects reported with each solicited local Adverse Event (AE)

End point title	Number of subjects reported with each solicited local Adverse Event (AE)

End point description:

Assessed solicited local symptoms were pain, redness and swelling

End point type	Secondary

End point timeframe:

During the 7-day follow-up period (the day of vaccination + 6 days) after each vaccination administered approximately at Day 1 and Day 61

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	291		
Units: Participants				
Pain, Dose 1(N-292,291)	153	16		
Pain, Dose 2(N-265,273)	163	13		
Redness (mm), Dose 1(N-292,291)	18	1		
Redness (mm), Dose 2(N-265,273)	37	0		
Swelling (mm), Dose 1(N-292,291)	13	2		
Swelling (mm), Dose 2(N-265,273)	31	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with each solicited general AE

End point title	Number of subjects reported with each solicited general AE

End point description:

Assessed solicited general symptoms were Chills, fatigue, fever [defined as (oral cavity or axillary) temperature equal to or above (≥) 37.5 degrees Celsius (°C)], gastrointestinal symptoms [nausea, vomiting, diarrhoea and/or abdominal pain], headache and myalgia.

End point type	Secondary

End point timeframe:

During the 7-day follow-up period (the day of vaccination + 6 days) after each vaccination administered approximately at Day 1 and Day 61

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292	291		
Units: Participants				
Chills, Dose 1(N-292,291)	29	35		
Chills, Dose 2(N-265,273)	35	28		
Fatigue, Dose 1(N-292,291)	157	167		
Fatigue, Dose 2(N-265,273)	136	130		
Fever, Dose 1(N-292,291)	24	25		
Fever, Dose 2(N-265,273)	18	11		
Gastrointestinal, Dose 1(N-292,291)	47	54		
Gastrointestinal, Dose 2(N-265,273)	39	35		
Headache, Dose 1(N-292,291)	98	76		
Headache, Dose 2(N-265,273)	75	64		
Myalgia, Dose 1(N-292,291)	78	72		
Myalgia, Dose 2(N-265,273)	74	43		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with any unsolicited adverse event (AE)

End point title	Number of subjects reported with any unsolicited adverse event (AE)

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 any solicited symptoms.

End point type	Secondary

End point timeframe:

During the 30-day follow-up period (the day of vaccination + 29 days) after each vaccination administered approximately at Day 1 and Day 61

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	302		
Units: Participants	110	103		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reported with any potential immune-mediated diseases (pIMDs)

End point description:

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 (Day 1) up to Study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	302		
Units: Participants	6	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with any Serious Adverse Event (SAE)

End point title	Number of subjects reported with any Serious Adverse Event (SAE)

End point description:

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 first vaccination (Day 1) up to Study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	302		
Units: Participants	89	99		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of moderate and severe AECOPD in vaccinated and control subjects, one year follow up starting 1 month post dose 2, by 3 months period

End point title	Rate of moderate and severe AECOPD in vaccinated and control subjects, one year follow up starting 1 month post dose 2, by 3 months period

End point description:

The rates of AECOPD were expressed per year and calculated as the total number of events over the follow-up exposure time. The CIs of the rate was computed using a model which accounts for repeated events. The severity of AECOPD can be graded according to the intensity of medical intervention required. Moderate AECOPD= requires treatment with systemic corticosteroids and/or antibiotics. Severe AECOPD= requires hospitalization. The intention of the analysis of the Rate during 3, 6 and 9 months observation starting 1 month post-Dose 2 was to report the rate by 3 months period, so for the periods: 0-3, 3-6, 6-9, 9-12 months.

End point type	Secondary

End point timeframe:

During following periods: from 0 to 3 months, from 3 to 6 months, from 6 to 9 months, from 9 to 12 months (observation starting 1 month post-Dose 2)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: exacerbations per person-year				
number (confidence interval 95%)				
FROM 0 TO 3 MONTHS(N-278,292)	1.35 (1.1 to 1.66)	1.15 (0.92 to 1.43)		
FROM 3 TO 6 MONTHS(N-274,288)	1.33 (1.08 to 1.63)	1.44 (1.19 to 1.75)		
FROM 6 TO 9 MONTHS(N-272,280)	1.36 (1.11 to 1.67)	1.19 (0.96 to 1.48)		
FROM 9 TO 12 MONTHS(N-271,272)	0.87 (0.69 to 1.11)	0.9 (0.71 to 1.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of any AECOPD case in vaccinated and control subjects, one year follow up starting 1 month post dose 2, by 3 months period

End point title	Rate of any AECOPD case in vaccinated and control subjects, one year follow up starting 1 month post dose 2, by 3 months period

End point description:

The rates of any AECOPD were expressed per year and calculated as the total number of events over the follow-up exposure time. The CIs of the rate was computed using a model which accounts for repeated events. The intention of the analysis of the Rate during 3, 6, 9 and 12 months observation starting 1 month post-Dose 2 was to report the rate by 3 months period, so for the periods: 0-3, 3-6, 6-9, 9-12, 0-12 months.

End point type	Secondary

End point timeframe:

During following periods: from 0 to 3 months, from 3 to 6 months, from 6 to 9 months, from 9 to 12 months and 0-12 months (observation starting 1 month post-Dose 2)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: exacerbations per person-year				
number (confidence interval 95%)				
FROM 0 TO 3 MONTHS(N-278,292)	1.47 (1.21 to 1.79)	1.33 (1.09 to 1.63)		
FROM 3 TO 6 MONTHS(N-274,288)	1.56 (1.29 to 1.89)	1.56 (1.29 to 1.88)		
FROM 6 TO 9 MONTHS(N-272,280)	1.49 (1.23 to 1.82)	1.29 (1.05 to 1.59)		
FROM 9 TO 12 MONTHS(N-271,272)	0.98 (0.78 to 1.22)	1.04 (0.84 to 1.3)		
FROM 0 TO 12 MONTHS	1.36 (1.19 to 1.57)	1.31 (1.15 to 1.48)		

Statistical analyses

Statistical analysis title	Vaccine efficacy- Any AECOPD, any severity

Statistical analysis description:

To assess efficacy of the investigational vaccine as compared to the placebo control with respect to the rate of AECOPDs of any severity- upto 12 months follow up period

Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.77
Method	Negative Binomial regression
Parameter estimate	Vaccine efficacy rate
Point estimate	-2.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.95
upper limit	14.19

Notes:

[1] - Vaccine Efficacy is defined as 1 minus the risk ratio (Rvacc / Rcon) based on the number of moderate and severe AECOPD observed in 1 year , with Rvacc = average yearly incidence rate of AECOPD events per subject in the GSK3277511A Group and Rcon = average yearly incidence rate of AECOPD events per subject in the control group.

Secondary: Exacerbation rate of any AECOPD cases, classified by severity, one year follow up starting 1 month post dose 2, by 3 months period

End point title	Exacerbation rate of any AECOPD cases, classified by severity, one year follow up starting 1 month post dose 2, by 3 months period

End point description:

The exacerbation rate of any AECOPD by severity is the average number of exacerbations for each subject: It is calculated proportionally to the follow-up time per subject and then scaled to the period considered. Mean and standard deviation of the exacerbation rate are given for each period considered. The severity of AECOPD can be graded according to the intensity of medical intervention required. Mild = can be controlled with an increase in dosage of regular medications. Moderate AECOPD= requires treatment with systemic corticosteroids and/or antibiotics. Severe AECOPD= requires hospitalization. The intention of the analysis of the Rate during 3, 6 and 9 months observation starting 1 month post-Dose 2 was to report the rate by 3 months period, so for the periods: 0-3, 3-6, 6-9, 9-12 months.

End point type	Secondary

End point timeframe:

During following periods: from 0 to 3 months, from 3 to 6 months, from 6 to 9 months, from 9 to 12 months (observation starting 1 month post-Dose 2)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: exacerbations per person				
arithmetic mean (standard deviation)				
MILD, FROM 0 TO 3 MONTHS(N-278,292)	0.02 (± 0.15)	0.03 (± 0.20)		
MILD, FROM 3 TO 6 MONTHS(N-274,288)	0.05 (± 0.24)	0.02 (± 0.14)		
MILD, FROM 6 TO 9 MONTHS(N-272,280)	0.03 (± 0.19)	0.03 (± 0.18)		
MILD, FROM 9 TO 12 MONTHS(N-271,272)	0.03 (± 0.17)	0.03 (± 0.16)		
MODERATE, FROM 0 TO 3 MONTHS(N-278,292)	0.29 (± 0.62)	0.23 (± 0.48)		
MODERATE, FROM 3 TO 6 MONTHS(N-274,288)	0.27 (± 0.51)	0.3 (± 0.57)		
MODERATE, FROM 6 TO 9 MONTHS(N-272,280)	0.3 (± 0.56)	0.25 (± 0.51)		
MODERATE, FROM 9 TO 12 MONTHS(N-271,272)	0.2 (± 0.44)	0.17 (± 0.42)		
SEVERE, FROM 0 TO 3 MONTHS(N-278,292)	0.04 (± 0.24)	0.05 (± 0.23)		
SEVERE, FROM 3 TO 6 MONTHS(N-274,288)	0.05 (± 0.22)	0.06 (± 0.29)		
SEVERE, FROM 6 TO 9 MONTHS(N-272,280)	0.05 (± 0.29)	0.05 (± 0.24)		
SEVERE, FROM 9 TO 12 MONTHS(N-271,272)	0.01 (± 0.11)	0.05 (± 0.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first moderate or severe AECOPD

End point title	Number of subjects with first moderate or severe AECOPD

End point description:

Number of subjects with first occurrence of moderate or severe episode of AECOPD was reported, in order to compute time to first occurrence and derive the hazard rate using Cox's proportional hazard regression model.

End point type	Secondary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: Participants	158	176		

Statistical analyses

Statistical analysis title	Hazard ratio-Moderate or severe AECOPD

Statistical analysis description:

Hazard rate for moderate or severe AECOPDs, one year follow-up starting 1 month post dose 2

Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5751
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.758
upper limit	1.166

Secondary: Number of subjects with first AECOPD of any severity

End point title	Number of subjects with first AECOPD of any severity

End point description:

Number of subjects with first occurrence of any episode of AECOPD of any severity was reported, in order to compute time to first occurrence and derive the hazard rate using Cox's proportional hazard regression model.

End point type	Secondary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: Participants	168	188		

Statistical analyses

Statistical analysis title	Hazard rate- Any AECOPD

Statistical analysis description:

Hazard rate for any AECOPDs, one year follow-up starting 1 month post dose 2

Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5194
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.934
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.758
upper limit	1.15

Secondary: Number of subjects with first AECOPD classified by severity

End point title	Number of subjects with first AECOPD classified by severity

End point description:

Number of subjects with first occurrence of any episode of AECOPD classified by severity was reported, in order to compute time to first occurrence and derive the hazard rate using Cox's proportional hazard regression model.

End point type	Secondary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: Participants				
AFTER 1 MONTH POST DOSE 2, MILD	27	27		
AFTER 1 MONTH POST DOSE 2, MODERATE	144	154		
AFTER 1 MONTH POST DOSE 2, SEVERE	30	41		

Statistical analyses

Statistical analysis title	Hazard rate-Mild AECOPD
Statistical analysis description:	
Hazard rate for mild AECOPDs, one year follow-up starting 1 month post dose 2	
Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8581
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.616
upper limit	1.791

Statistical analysis title	Hazard rate-Moderate AECOPD
Statistical analysis description:	
Hazard rate for moderate AECOPDs, one year follow-up starting 1 month post dose 2	
Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9634
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.995
Confidence interval	
level	95 %

sides	2-sided
lower limit	0.792
upper limit	1.249

Statistical analysis title	Hazard rate-Severe AECOPD
Statistical analysis description:	
Hazard rate for severe AECOPDs, one year follow-up starting 1 month post dose 2	
Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1755
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.722
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.157

Secondary: Number of days with moderate and severe AECOPDs

End point title	Number of days with moderate and severe AECOPDs
End point description:	
The length of each AECOPD was tabulated and presented via descriptive statistics (mean, Standard Deviation) and expressed in Days.	
End point type	Secondary
End point timeframe:	
From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)	

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	292		
Units: Days				
arithmetic mean (standard deviation)	16.6 (± 14.29)	15.6 (± 13.93)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with AECOPDs of any severity

End point title	Number of days with AECOPDs of any severity

End point description:

The length of each AECOPDs was tabulated and presented via descriptive statistics (mean, Standard Deviation).

End point type	Secondary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	292		
Units: Days				
arithmetic mean (standard deviation)	15.9 (± 13.79)	15.3 (± 13.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with AECOPDs classified by severity

End point title	Number of days with AECOPDs classified by severity

End point description:

The length of each AECOPDs by severity was tabulated and presented via descriptive statistics (mean, Standard Deviation).

End point type	Secondary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	292		
Units: Days				
arithmetic mean (standard deviation)				
MILD, AFTER 1 MONTH POST DOSE 2	8.9 (± 3.56)	12.3 (± 9.11)		
MODERATE, AFTER 1 MONTH POST DOSE 2	16.1 (± 13.90)	14.5 (± 10.50)		
SEVERE, AFTER 1 MONTH POST DOSE 2	20.4 (± 16.78)	21.2 (± 23.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Non-Typeable Haemophilus influenzae (NTHi)-associated and/ or Moraxella catarrhalis (Mcat)-associated moderate and severe AECOPD

End point title	Rate of Non-Typeable Haemophilus influenzae (NTHi)-associated and/ or Moraxella catarrhalis (Mcat)-associated moderate and severe AECOPD

End point description:

The rates of AECOPD were expressed per year and calculated as the total number of events over the follow-up exposure time. The CIs of the rate was computed using a model which accounts for repeated events. Respiratory pathogens NTHi and Mcat was determined by Polymerase chain reaction (PCR) analysis in sputum samples.

End point type	Secondary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: exacerbations per person-year				
number (confidence interval 95%)	0.32 (0.25 to 0.42)	0.32 (0.24 to 0.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of NTHi-associated and/ or Mcat-associated AECOPD of any severity

End point title	Rate of NTHi-associated and/ or Mcat-associated AECOPD of any severity

End point description:

The rates of AECOPD of any severity were expressed per year and calculated as the total number of events over the follow-up exposure time. The CIs of the rate was computed using a model which accounts for repeated events. Respiratory pathogens NTHi and Mcat was determined by polymerase chain reaction (PCR) analysis in sputum samples.

End point type	Secondary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: exacerbation per person-year				
number (confidence interval 95%)	0.39 (0.30 to 0.50)	0.35 (0.27 to 0.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Exacerbation rate of any NTHi-associated and/ or Mcat-associated AECOPD cases, classified by severity

End point title	Exacerbation rate of any NTHi-associated and/ or Mcat-associated AECOPD cases, classified by severity

End point description:

The exacerbation rate of any AECOPD by severity is the average number of exacerbations for each subject: it is calculated proportionally to the follow-up time per subject, and then scaled to the period considered. Mean and standard deviation of the exacerbation rate are given for the period considered. Respiratory pathogens NTHi and Mcat was determined PCR analysis in sputum samples

End point type	Secondary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: exacerbations per person				
arithmetic mean (standard deviation)				
MILD, AFTER 1 MONTH POST DOSE 2	0.06 (± 0.28)	0.03 (± 0.21)		
MODERATE, AFTER 1 MONTH POST DOSE 2	0.3 (± 0.67)	0.31 (± 0.74)		
SEVERE, AFTER 1 MONTH POST DOSE 2	0.02 (± 0.18)	0.01 (± 0.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first moderate or severe NTHi-associated and/or Mcat-associated AECOPD

End point title	Number of subjects with first moderate or severe NTHi-associated and/or Mcat-associated AECOPD

End point description:

Number of subjects with first occurrence of moderate or severe NTHI-associated and/or Mcat-associated AECOPD was reported,in order to compute time to first occurrence and derive the hazard rate using Cox’s proportional hazard regression model. Respiratory pathogens NTHi and Mcat was determined PCR analysis in sputum samples.

End point type	Secondary

End point timeframe:

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: Participants	62	62		

Statistical analyses

Statistical analysis title	Hazard rate-Moderate or Severe AECOPD
Statistical analysis description:	
Hazard rate for moderate or severe NTHi-associated and/or Mcat-associated AECOPDs, one year follow-up starting 1 month post dose 2	
Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9463
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.038
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.477

Secondary: Number of subjects with first NTHi-associated and/or Mcat-associated AECOPD of any severity

End point title	Number of subjects with first NTHi-associated and/or Mcat-associated AECOPD of any severity
End point description:	
Number of subjects with first occurrence of NTHI-associated and/or Mcat-associated AECOPD of any severity was reported,in order to compute time to first occurrence and derive the hazard rate using Cox’s proportional hazard regression model. Respiratory pathogens NTHi and Mcat was determined PCR analysis in sputum samples.	
End point type	Secondary
End point timeframe:	
From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)	

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: Participants	70	67		

Statistical analyses

Statistical analysis title	Hazard rate- Any AECOPD

Statistical analysis description:

Hazard rate for any NTHi-associated and/or Mcat-associated AECOPDs, one year follow-up starting 1 month post dose 2

Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6042
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.093
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.782
upper limit	1.528

Secondary: Number of subjects with first NTHi-associated and/or Mcat-associated AECOPD, classified by severity

End point title	Number of subjects with first NTHi-associated and/or Mcat-associated AECOPD, classified by severity

End point description:

Number of subjects with first occurrence of NTHI-associated and/or Mcat-associated AECOPD classified by severity was reported, in order to compute time to first occurrence and derive the hazard rate using Cox's proportional hazard regression model. Respiratory pathogens NTHi and Mcat was determined PCR analysis in sputum samples.

End point type	Secondary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	292		
Units: Participants				
AFTER 1 MONTH POST DOSE 2, MILD	15	7		

AFTER 1 MONTH POST DOSE 2, MODERATE	58	59		
AFTER 1 MONTH POST DOSE 2, SEVERE	4	4		

Statistical analyses

Statistical analysis title	Hazard rate-Mid AECOPD
Statistical analysis description:	
Hazard rate for mild NTHi-associated and/or Mcat-associated AECOPDs, one year follow-up starting 1 month post dose 2	
Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0777
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	2.243
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.914
upper limit	5.504

Statistical analysis title	Hazard rate-Moderate AECOPD
Statistical analysis description:	
Hazard rate for moderate NTHi-associated and/or Mcat-associated AECOPDs, one year follow-up starting 1 month post dose 2	
Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9121
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.021
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.467

Statistical analysis title	Hazard rate-Severe AECOPD
Statistical analysis description:	
Hazard rate for severe NTHi-associated and/or Mcat-associated AECOPDs, one year follow-up starting 1	

month post dose 2

Comparison groups	GSK3277511A Group v Control Group
Number of subjects included in analysis	570
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8737
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.278
upper limit	4.502

Secondary: Number of days with moderate and severe NTHi-associated and Mcat-associated AECOPD

End point title	Number of days with moderate and severe NTHi-associated and Mcat-associated AECOPD

End point description:

The length of each NTHi associated and/or Mcat associated AECOPDs was tabulated and presented via descriptive statistics (mean, Standard Deviation).

End point type	Secondary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	292		
Units: Days				
arithmetic mean (standard deviation)	14 (± 10.43)	12.3 (± 5.59)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with NTHi-associated and/or Mcat-associated AECOPDs of any severity

End point title	Number of days with NTHi-associated and/or Mcat-associated AECOPDs of any severity

End point description:

The length of each NTHi associated and/or Mcat associated AECOPDs was tabulated and presented via descriptive statistics (mean, Standard Deviation).

End point type	Secondary

End point timeframe:

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	292		
Units: Days				
arithmetic mean (standard deviation)	13.3 (± 9.76)	12.1 (± 5.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days with NTHi-associated and/or Mcat-associated AECOPD, classified by severity

End point title	Number of days with NTHi-associated and/or Mcat-associated AECOPD, classified by severity

End point description:

The length of each NTHi associated and/or Mcat associated AECOPDs was tabulated and presented via descriptive statistics (mean, Standard Deviation).

End point type	Secondary

End point timeframe:

From 1-month post-Dose 2 (at Day 91) up to study end (at Day 451)

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	292		
Units: Days				
arithmetic mean (standard deviation)				
AFTER 1 MONTH POST DOSE 2, MILD	9.5 (± 3.54)	9.9 (± 6.83)		
AFTER 1 MONTH POST DOSE 2, MODERATE	13.8 (± 10.41)	12.5 (± 5.62)		
AFTER 1 MONTH POST DOSE 2, SEVERE	17.3 (± 11.02)	7.5 (± 1.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PD antibody concentrations as measured by the Enzyme-Linked Immunosorbent Assay (ELISA)

End point title	Anti-PD antibody concentrations as measured by the Enzyme-Linked Immunosorbent Assay (ELISA)

End point description:

Anti–Protein D (PD) antibody concentrations as determined by ELISA, and expressed as geometric mean concentrations (GMCs) in ELISA unit per milliliter (EU/mL). For anti-PD antibodies, the cut-off of the assay is 153 ELISA Units per millilitre (EU/mL.)

End point type	Secondary

End point timeframe:

At Day 1, Day 31, Day 61, Day 91, Day 271 and at Day 451

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	247	256		
Units: EU/mL.				
geometric mean (confidence interval 95%)				
Day 1(N-247,256)	103.7 (93.8 to 114.7)	95.4 (86.3 to 105.4)		
Day 31(N-232,243)	1048.1 (910.2 to 1206.8)	98.2 (85.3 to 113.1)		
Day 61(N-239,253)	654.6 (572.3 to 748.9)	95.5 (83.6 to 109.1)		
Day 91(N-208,211)	1521.4 (1357.6 to 1704.9)	90.3 (80.6 to 101.3)		
Day 271(N-210,223)	546 (480.3 to 620.8)	94.8 (83.6 to 107.4)		
Day 451(N-221,216)	444.1 (390.2 to 505.4)	97.9 (85.9 to 111.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PE antibody concentrations as measured by ELISA

End point title	Anti-PE antibody concentrations as measured by ELISA

End point description:

Anti–Protein E (PE) antibody concentrations as determined by ELISA and expressed as GMCs in EU/mL For Anti-PE antibodies, the cut-off of the assay is 16 EU/mL.

End point type	Secondary

End point timeframe:

At Day 1, Day 31, Day 61, Day 91, Day 271 and at Day 451

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	256		
Units: EU/mL.				
geometric mean (confidence interval 95%)				
Day 1(N-246,256)	20.9 (17.6 to 24.8)	21.6 (18.2 to 25.7)		
Day 31(N-232,244)	1108.1 (921.5 to 1332.5)	20.7 (17.2 to 24.9)		
Day 61(N-239,251)	872.8 (726.6 to 1048.3)	20.5 (17.1 to 24.6)		
Day 91(N-208,211)	6020 (5181.2 to 6994.7)	20.1 (17.3 to 23.4)		
Day 271(N-210,223)	1254.9 (1069.5 to 1472.5)	19.3 (16.5 to 22.5)		
Day 451(N-221,215)	835.2 (715.0 to 975.6)	19.7 (16.8 to 23.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PilA antibody concentrations as measured by ELISA

End point title	Anti-PilA antibody concentrations as measured by ELISA

End point description:

Anti-Type IV pilus assembly protein (PilA) antibody concentrations as determined by ELISA, and expressed as GMCs in EU/mL. For Anti-PilA antibodies, the cut-off of the assay is 8 EU/mL.

End point type	Secondary

End point timeframe:

At Day 1, Day 31, Day 61, Day 91, Day 271 and at Day 451

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	247	256		
Units: EU/mL.				
geometric mean (confidence interval 95%)				
Day 1(N-247,256)	8.3 (6.9 to 9.8)	8.5 (7.1 to 10.1)		
Day 31(N-231,243)	153 (124.2 to 188.6)	9.2 (7.5 to 11.4)		
Day 61(N-238,251)	134.2 (109.7 to 164.2)	8.8 (7.2 to 10.8)		
Day 91(N-208,211)	913.5 (770.5 to 1082.9)	8.9 (7.5 to 10.5)		
Day 271(N-210,223)	189.6 (159.2 to 225.7)	8 (6.8 to 9.5)		

Day 451(N-221,216)	126.5 (106.1 to 150.8)	8.3 (6.9 to 9.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-UspA2 antibody concentrations as measured by ELISA

End point title	Anti-UspA2 antibody concentrations as measured by ELISA

End point description:

Anti–ubiquitous surface protein A2 of Moraxella catarrhalis (UspA2) aantibody concentrations as determined by ELISA, and expressed as GMCs in EU/mL. For Anti-UspA2 antibodies, the cut-off of the assay is 28 EU/mL.

End point type	Secondary

End point timeframe:

At Day 1, Day 31, Day 61, Day 91, Day 271 and at Day 451

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	255		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Day 1(N-246,255)	540.3 (452.6 to 645.0)	604.7 (507.2 to 721.0)		
Day 31(N-232,242)	1092.1 (997.5 to 1195.5)	485.2 (442.9 to 531.6)		
Day 61(N-238,251)	848.7 (781.5 to 921.5)	473.5 (436.2 to 513.9)		
Day 91(N-208,211)	1223.7 (1110.8 to 1348.0)	446 (404.5 to 491.8)		
Day 271(N-210,222)	645.1 (582.1 to 714.8)	445.4 (402.7 to 492.6)		
Day 451(N-221,215)	575.9 (512.9 to 646.7)	468.5 (416.5 to 527.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of PD specific cluster of differentiation (CD)4+ T-cells expressing at least 2 markers among CD40L, IL2, TNF-Alpha, IFN-Gamma, IL-13 and IL-17 using background reduced frequency data

End point title	Frequency of PD specific cluster of differentiation (CD)4+ T-cells expressing at least 2 markers among CD40L, IL2, TNF-

	Alpha, IFN-Gamma, IL-13 and IL-17 using background reduced frequency data

End point description:

The ICS staining assay was used to assess cell-mediated immunogenicity (CMI) responses. After Peripheral blood mononuclear cell (PBMC) stimulation with the relevant antigen, the frequency of PD specific CD4+ T-cells expressing selected combination of cytokines such as interleukine-2, 13, 17 (IL-2, IL-13, IL-17), interferon-gamma (IFN-γ), tumour necrosis factor-alpha (TNF-α) and cluster of differentiation 40 ligand (CD40L) are evaluated by flow cytometry and expressed as mean and standard deviation. The analysis was performed on the Per-Protocol CMI set for analysis of immunogenicity cohort which includes all vaccinated subjects who were complied with the vaccination schedule and who have CMI data for the specified timepoints.

End point type	Secondary

End point timeframe:

At Day 1, Day 91, Day 271 and at Day 451

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: T cells/million cells				
arithmetic mean (standard deviation)				
Day 1(N-47,41)	56.6 (± 125.7)	59.7 (± 118.2)		
Day 91(N-42,36)	890.2 (± 988.8)	55.8 (± 88.2)		
Day 271(N-42,41)	364.6 (± 363.9)	51.8 (± 90.9)		
Day 451(N-42,36)	267 (± 282.6)	46.7 (± 101.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of PE specific (CD)4+ T-cells expressing at least 2 markers among CD40L, IL2, TNF-Alpha, IFN-Gamma, IL-13 and IL-17 using background reduced frequency data

End point title	Frequency of PE specific (CD)4+ T-cells expressing at least 2 markers among CD40L, IL2, TNF-Alpha, IFN-Gamma, IL-13 and IL-17 using background reduced frequency data

End point description:

The ICS staining assay was used to assess CMI responses. After PBMC stimulation with the relevant antigen, the frequency of PE specific CD4+ T-cells expressing selected combination of cytokines such as (IL-2, IL-13, IL-17), IFN-γ, TNF-α and CD40L are evaluated by flow cytometry and expressed as mean and standard deviation. The analysis was performed on the Per-Protocol CMI set for analysis of immunogenicity cohort which includes all vaccinated subjects who were complied with the vaccination schedule and who have CMI data for the specified timepoints.

End point type	Secondary

End point timeframe:

At Day 1, Day 91, Day 271 and at Day 451

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: T cells/million cells				
arithmetic mean (standard deviation)				
Day 1(N-47,41)	63.1 (± 211.4)	92.9 (± 266.0)		
Day 91(N-42,36)	797 (± 1082.9)	76.2 (± 195.0)		
Day 271(N-42,41)	384.8 (± 539.9)	61.4 (± 207.2)		
Day 451(N-42,36)	335.7 (± 493.7)	81.2 (± 258.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of PilA specific CD4+ T-cells expressing at least 2 markers among CD40L, IL2, TNF-Alpha, IFN-Gamma, IL-13 and IL-17 using background reduced frequency data

End point title	Frequency of PilA specific CD4+ T-cells expressing at least 2 markers among CD40L, IL2, TNF-Alpha, IFN-Gamma, IL-13 and IL-17 using background reduced frequency data

End point description:

The ICS staining assay was used to assess CMI responses. After PBMC stimulation with the relevant antigen, the frequency of PilA specific CD4+ T-cells expressing selected combination of cytokines such as IL-2, IL-13, IL-17, IFN-γ, TNF-α and CD40L are evaluated by flow cytometry and expressed as mean and standard deviation. The analysis was performed on the Per-Protocol CMI set for analysis of immunogenicity cohort which includes all vaccinated subjects who were complied with the vaccination schedule and who have CMI data for the specified timepoints.

End point type	Secondary

End point timeframe:

At Day 1, Day 91, Day 271 and at Day 451

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: T cells/million cells				
arithmetic mean (standard deviation)				
Day 1(N-47,40)	26.2 (± 45.4)	53.3 (± 95.9)		
Day 91(N-42,36)	305.8 (± 321.7)	44.6 (± 114.8)		
Day 271(N-42,41)	137.3 (± 163.2)	42.1 (± 78.2)		
Day 451(N-42,36)	141 (± 147.1)	42.4 (± 95.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of UspA2 specific CD4 + T-cells expressing at least 2 markers among CD40L, IL2, TNF-Alpha, IFN-Gamma, IL-13 and IL-17 using background reduced frequency data

End point title	Frequency of UspA2 specific CD4 + T-cells expressing at least 2 markers among CD40L, IL2, TNF-Alpha, IFN-Gamma, IL-13 and IL-17 using background reduced frequency data

End point description:

The ICS staining assay was used to assess CMI responses. After PBMC stimulation with the relevant antigen, the frequency of UspA2 specific CD4+ T-cells expressing selected combination of cytokines such as IL-2, IL-13, IL-17, IFN-γ, TNF-α and CD40L are evaluated by flow cytometry and expressed as mean and standard deviation. The analysis was performed on the Per-Protocol CMI set for analysis of immunogenicity cohort which includes all vaccinated subjects who were complied with the vaccination schedule and who have CMI data for the specified timepoints.

End point type	Secondary

End point timeframe:

At Day 1, Day 91, Day 271 and at Day 451

End point values	GSK3277511A Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	41		
Units: T cells/million cells				
arithmetic mean (standard deviation)				
Day 1(N-47,40)	66.1 (± 177.1)	47.2 (± 85.8)		
Day 91(N-42,36)	646.3 (± 545.2)	70.3 (± 94.6)		
Day 271(N-42,41)	330.5 (± 278.5)	60.8 (± 80.0)		
Day 451(N-42,35)	331.3 (± 310.4)	61.5 (± 89.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs reported during the 7-day follow-up period and Unsolicited AEs reported during the 30-day follow-up period after any vaccination. SAEs reported from first vaccination (Day 1) up to Study end (at Day 451 - an average of 15 months).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	GSK3277511A Group

Reporting group description:

Healthy males and females, 40 to 80 years of age, who received two doses of the adjuvanted GSK3277511A investigational vaccine containing surface protein D (PD), protein E- type IV pilus assembly protein (PE-PilA,) and ubiquitous surface protein A2 (UspA2), administered at Day 1 and Day 61

Reporting group title	Control Group

Reporting group description:

Healthy males and females, 40 to 80 years of age, who received two doses of placebo, administered at Day 1 and Day 61.

Serious adverse events	GSK3277511A Group	Control Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	89 / 304 (29.28%)	99 / 302 (32.78%)	
number of deaths (all causes)	1	10	
number of deaths resulting from adverse events			
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral artery aneurysm			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Peripheral artery aneurysm			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vein occlusion			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colon cancer			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypopharyngeal cancer stage IV			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Laryngeal cancer			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Leukaemia			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic gastric cancer			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penile cancer			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	2 / 304 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	

occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Condition aggravated			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug withdrawal syndrome			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol withdrawal syndrome			

subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal inflammation			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
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			
Abdominal wound dehiscence			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol poisoning			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic complication			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Drain site complication			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Exposure to toxic agent			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal procedural complication			

subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pneumothorax			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Oxygen saturation decreased			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Acute left ventricular failure			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	2 / 304 (0.66%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
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	4 / 304 (1.32%)	2 / 302 (0.66%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 304 (0.33%)	2 / 302 (0.66%)	

occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery insufficiency			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
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	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trifascicular block			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
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			
Acute pulmonary oedema			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	7 / 304 (2.30%)	7 / 302 (2.32%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atelectasis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	2 / 304 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	41 / 304 (13.49%)	53 / 302 (17.55%)	
occurrences causally related to treatment / all	0 / 55	0 / 83	
deaths causally related to treatment / all	0 / 0	0 / 3	
Dyspnoea			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	

deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 304 (0.66%)	4 / 302 (1.32%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Nervous system disorders			
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
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 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegic migraine			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ruptured cerebral aneurysm			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Transient ischaemic attack			
subjects affected / exposed	3 / 304 (0.99%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyschezia			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovesical fistula			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ileus paralytic			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intestinal pseudo-obstruction			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			

subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cirrhosis alcoholic			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device loosening			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
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			
Arthritis			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intervertebral disc protrusion			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

CNS ventriculitis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterococcal infection			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis viral			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft infection			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 304 (0.33%)	4 / 302 (1.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Influenza			
subjects affected / exposed	4 / 304 (1.32%)	2 / 302 (0.66%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus infection			

subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (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	5 / 304 (1.64%)	15 / 302 (4.97%)	
occurrences causally related to treatment / all	0 / 5	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia pneumococcal			
subjects affected / exposed	2 / 304 (0.66%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pseudomonal			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyelonephritis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
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 / 304 (0.00%)	1 / 302 (0.33%)	

occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septic shock			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 304 (0.00%)	3 / 302 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound abscess			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GSK3277511A Group	Control Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	276 / 304 (90.79%)	247 / 302 (81.79%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
Hypotension			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	

occurrences (all)	0	1	
Peripheral venous disease			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Chest discomfort			
subjects affected / exposed	2 / 304 (0.66%)	2 / 302 (0.66%)	
occurrences (all)	2	2	
Chills			
subjects affected / exposed	52 / 304 (17.11%)	52 / 302 (17.22%)	
occurrences (all)	64	65	
Drug intolerance			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	195 / 304 (64.14%)	197 / 302 (65.23%)	
occurrences (all)	297	299	
Feeling hot			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Injection site bruising			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Injection site erythema			
subjects affected / exposed	43 / 304 (14.14%)	1 / 302 (0.33%)	

occurrences (all)	55	1	
Injection site pain			
subjects affected / exposed	213 / 304 (70.07%)	30 / 302 (9.93%)	
occurrences (all)	324	31	
Injection site reaction			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Injection site swelling			
subjects affected / exposed	35 / 304 (11.51%)	3 / 302 (0.99%)	
occurrences (all)	45	3	
Malaise			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	5 / 304 (1.64%)	0 / 302 (0.00%)	
occurrences (all)	5	0	
Pyrexia			
subjects affected / exposed	39 / 304 (12.83%)	32 / 302 (10.60%)	
occurrences (all)	42	36	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 304 (0.66%)	2 / 302 (0.66%)	
occurrences (all)	2	2	
Depression			
subjects affected / exposed	2 / 304 (0.66%)	0 / 302 (0.00%)	
occurrences (all)	2	0	
Panic attack			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Bartholin's cyst			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	

Scrotal pain			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Scrotal swelling			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Chest injury			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
Contusion			
subjects affected / exposed	2 / 304 (0.66%)	0 / 302 (0.00%)	
occurrences (all)	2	0	
Fall			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Joint injury			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Meniscus injury			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Rib fracture			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Skin laceration			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Thermal burn			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Investigations			

Weight increased			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 304 (0.66%)	0 / 302 (0.00%)	
occurrences (all)	2	0	
Cardiac failure			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Mitral valve prolapse			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
Cough			
subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences (all)	0	2	
Dyspnoea			
subjects affected / exposed	5 / 304 (1.64%)	3 / 302 (0.99%)	
occurrences (all)	5	3	
Epistaxis			
subjects affected / exposed	2 / 304 (0.66%)	0 / 302 (0.00%)	
occurrences (all)	2	0	
Haemoptysis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Increased upper airway secretion			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			

subjects affected / exposed	3 / 304 (0.99%)	0 / 302 (0.00%)	
occurrences (all)	3	0	
Nasal polyps			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	1 / 304 (0.33%)	2 / 302 (0.66%)	
occurrences (all)	1	2	
Paranasal sinus discomfort			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Pharyngeal erythema			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Pleuritic pain			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Pulmonary fibrosis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Pulmonary mass			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Sinus congestion			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Sputum discoloured			

subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Sputum increased			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 304 (0.33%)	2 / 302 (0.66%)	
occurrences (all)	1	2	
Epilepsy			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Focal dyscognitive seizures			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	127 / 304 (41.78%)	111 / 302 (36.75%)	
occurrences (all)	178	145	
Paraesthesia			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Post herpetic neuralgia			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Post polio syndrome			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	2 / 304 (0.66%)	0 / 302 (0.00%)	
occurrences (all)	2	0	
Tension headache			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	

occurrences (all)	1	0	
Tremor			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Dermatochalasis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Ocular hyperaemia			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Retinoschisis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Vitreous detachment			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Ear pain			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
Vertigo			
subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	

Abdominal pain			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Abdominal pain lower			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Dental caries			
subjects affected / exposed	2 / 304 (0.66%)	0 / 302 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	3 / 304 (0.99%)	9 / 302 (2.98%)	
occurrences (all)	3	9	
Faecaloma			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Gastrointestinal disorder			
subjects affected / exposed	71 / 304 (23.36%)	77 / 302 (25.50%)	
occurrences (all)	86	90	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
Inguinal hernia			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Intestinal polyp			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	1 / 304 (0.33%)	3 / 302 (0.99%)	
occurrences (all)	1	3	
Pancreatic disorder			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	2 / 304 (0.66%)	0 / 302 (0.00%)	
occurrences (all)	2	0	

Vomiting			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Urine odour abnormal			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Dandruff			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Dermal cyst			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences (all)	0	2	
Eczema			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Photosensitivity reaction			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Pruritus allergic			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Psoriasis			

subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Skin lesion			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
Costochondritis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	2 / 304 (0.66%)	1 / 302 (0.33%)	
occurrences (all)	2	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	115 / 304 (37.83%)	94 / 302 (31.13%)	
occurrences (all)	153	116	
Osteoarthritis			
subjects affected / exposed	2 / 304 (0.66%)	2 / 302 (0.66%)	
occurrences (all)	2	2	
Pain in extremity			
subjects affected / exposed	1 / 304 (0.33%)	4 / 302 (1.32%)	
occurrences (all)	1	5	
Rotator cuff syndrome			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	

Spinal osteoarthritis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Synovial cyst			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Tendon disorder			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Tenosynovitis			
subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences (all)	0	2	
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	2	0	
Hyperinsulinaemic hypoglycaemia			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
Vitamin D deficiency			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	

Bronchitis			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
Chronic sinusitis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	3 / 304 (0.99%)	1 / 302 (0.33%)	
occurrences (all)	3	1	
Ear infection			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Erysipelas			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Fungal infection			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 304 (0.33%)	3 / 302 (0.99%)	
occurrences (all)	1	3	
Gastroenteritis viral			
subjects affected / exposed	0 / 304 (0.00%)	2 / 302 (0.66%)	
occurrences (all)	0	2	
Gingivitis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Infection			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	

Influenza			
subjects affected / exposed	2 / 304 (0.66%)	3 / 302 (0.99%)	
occurrences (all)	2	3	
Kidney infection			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Labyrinthitis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Laryngitis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Localised infection			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	13 / 304 (4.28%)	13 / 302 (4.30%)	
occurrences (all)	13	15	
Oral candidiasis			
subjects affected / exposed	2 / 304 (0.66%)	1 / 302 (0.33%)	
occurrences (all)	2	1	
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Otitis media acute			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Paronychia			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	

Pneumonia			
subjects affected / exposed	0 / 304 (0.00%)	3 / 302 (0.99%)	
occurrences (all)	0	3	
Respiratory tract infection			
subjects affected / exposed	1 / 304 (0.33%)	1 / 302 (0.33%)	
occurrences (all)	1	1	
Rhinitis			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	0 / 304 (0.00%)	4 / 302 (1.32%)	
occurrences (all)	0	4	
Sweat gland infection			
subjects affected / exposed	1 / 304 (0.33%)	0 / 302 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	4 / 304 (1.32%)	3 / 302 (0.99%)	
occurrences (all)	4	3	
Urinary tract infection			
subjects affected / exposed	1 / 304 (0.33%)	4 / 302 (1.32%)	
occurrences (all)	1	5	
Viral infection			
subjects affected / exposed	0 / 304 (0.00%)	1 / 302 (0.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2017	CD8+ T cell component removed from secondary endpoint, exclusion criteria was updated, cut-off values were updated for anti-PD, anti-PE, anti-PilA and anti-UspA2 antibody ELISA

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported