



Clinical trial results:

A Phase 2, randomised, observer-blind, multi-centre study to evaluate the safety, reactogenicity and immunogenicity of GSK Biologicals' GSK3277511A investigational vaccine when administered intramuscularly according to two different vaccine schedules in adults aged 40 to 80 years old

Summary

EudraCT number	2017-002941-31
Trial protocol	DE GB
Global end of trial date	13 November 2020

Results information

Result version number	v2 (current)
This version publication date	20 August 2021
First version publication date	30 September 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	207759
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03443427
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	05 February 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and reactogenicity profile of the NTHi-Mcat vaccine administered according to two vaccination schedules

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 March 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 100
Country: Number of subjects enrolled	Germany: 50
Country: Number of subjects enrolled	United Kingdom: 50
Worldwide total number of subjects	200
EEA total number of subjects	50

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	133
From 65 to 84 years	67

85 years and over	0
-------------------	---

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All subjects enrolled were included for analysis in this study

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, Carer, Data analyst, Assessor

Blinding implementation details:

This is an observer blind study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Schedule 0-2-6 Group

Arm description:

Subjects between, and including, 40 and 80 years of age at the time of the first vaccination, receiving three doses of the GSK3277511A investigational vaccine at Day 1 (Month 0), Day 61 (Month 2) and Day 181 (Month 6) and one dose of placebo at Day 361 (Month 12).

Arm type	Experimental
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:

One dose administered intramuscularly in the deltoid of the non-dominant arm

Investigational medicinal product name	NTHi Mcat investigational vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses administered intramuscularly in the deltoid of the non-dominant arm

Arm title	Schedule 0-2-12 Group
------------------	-----------------------

Arm description:

Subjects between, and including, 40 and 80 years of age at the time of the first vaccination, receiving three doses of the GSK3277511A investigational vaccine at Day 1 (Month 0), Day 61 (Month 2) and Day 361 (Month 12) and one dose of placebo at Day 181 (Month 6).

Arm type	Experimental
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:

One dose administered intramuscularly in the deltoid of the non-dominant arm

Investigational medicinal product name	NTHi Mcat investigational vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses administered intramuscularly in the deltoid of the non-dominant arm

Number of subjects in period 1	Schedule 0-2-6 Group	Schedule 0-2-12 Group
Started	100	100
Completed	88	89
Not completed	12	11
Adverse event, non-fatal	2	3
Unspecified	4	6
CONSENT WITHDRAWAL NOT DUE TO ADV. EVENT	6	2

Baseline characteristics

Reporting groups

Reporting group title	Schedule 0-2-6 Group
-----------------------	----------------------

Reporting group description:

Subjects between, and including, 40 and 80 years of age at the time of the first vaccination, receiving three doses of the GSK3277511A investigational vaccine at Day 1 (Month 0), Day 61 (Month 2) and Day 181 (Month 6) and one dose of placebo at Day 361 (Month 12).

Reporting group title	Schedule 0-2-12 Group
-----------------------	-----------------------

Reporting group description:

Subjects between, and including, 40 and 80 years of age at the time of the first vaccination, receiving three doses of the GSK3277511A investigational vaccine at Day 1 (Month 0), Day 61 (Month 2) and Day 361 (Month 12) and one dose of placebo at Day 181 (Month 6).

Reporting group values	Schedule 0-2-6 Group	Schedule 0-2-12 Group	Total
Number of subjects	100	100	200
Age categorical			
Units: Subjects			
Adults (18-64 years)	68	65	133
From 65-84 years	32	35	67
Age continuous			
Units: years			
arithmetic mean	58.4	59.8	
standard deviation	± 10.3	± 10.1	-
Sex: Female, Male			
Units: Participants			
FEMALE	46	43	89
MALE	54	57	111
Race/Ethnicity, Customized			
Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	0	1	1
WHITE	100	99	199

End points

End points reporting groups

Reporting group title	Schedule 0-2-6 Group
Reporting group description:	
Subjects between, and including, 40 and 80 years of age at the time of the first vaccination, receiving three doses of the GSK3277511A investigational vaccine at Day 1 (Month 0), Day 61 (Month 2) and Day 181 (Month 6) and one dose of placebo at Day 361 (Month 12).	
Reporting group title	Schedule 0-2-12 Group
Reporting group description:	
Subjects between, and including, 40 and 80 years of age at the time of the first vaccination, receiving three doses of the GSK3277511A investigational vaccine at Day 1 (Month 0), Day 61 (Month 2) and Day 361 (Month 12) and one dose of placebo at Day 181 (Month 6).	

Primary: Number of subjects reported with each solicited local adverse event (AE) (any and grade 3) within each vaccination schedule

End point title	Number of subjects reported with each solicited local adverse event (AE) (any and grade 3) within each vaccination schedule ^[1]
End point description:	
Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) injection site. Analysis was performed on the Exposed set which included all eligible subjects, enrolled in this study, who provided informed consent, had at least one vaccine dose administered and who provided solicited safety data.	
End point type	Primary
End point timeframe:	
During the 7-day follow-up period (the day of vaccination + 6 days) after each vaccination administered at Day 1, Day 61, Day 181 and Day 361	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	100		
Units: Participants				
Pain, Any, Dose 1 (N-100,100)	64	64		
Pain, Grade 3, Dose 1 (N-100,100)	2	1		
Pain, Any, Dose 2(N-92,97)	72	69		
Pain, Grade 3, Dose 2(N-92,97)	13	3		
Pain, Any, Dose 3(N-89,97)	67	4		
Pain, Grade 3, Dose 3(N-89,97)	12	0		
Pain, Any, Dose 4(N-84,93)	9	73		
Pain, Grade 3, Dose 4(N-84,93)	0	8		
Redness, Any, Dose 1 (N-100,100)	9	18		
Redness, Grade 3, Dose 1 (N-100,100)	0	0		
Redness, Any, Dose 2(N-92,97)	12	11		
Redness, Grade 3, Dose 2(N-92,97)	0	0		
Redness, Any, Dose 3(N-89,97)	13	0		

Redness, Grade 3, Dose 3(N-89,97)	1	0		
Redness, Any, Dose 4(N-84,93)	1	12		
Redness, Grade 3, Dose 4(N-84,93)	0	1		
Swelling, Any, Dose 1(N-100,100)	8	10		
Swelling, Grade 3, Dose 1(N-100,100)	0	0		
Swelling, Any, Dose 2(N-92,97)	7	7		
Swelling, Grade 3, Dose 2(N-92,97)	0	0		
Swelling, Any, Dose 3(N-89,97)	9	0		
Swelling, Grade 3, Dose 3(N-89,97)	1	0		
Swelling, Any, Dose 4(N-84,93)	1	10		
Swelling, Grade 3, Dose 4(N-84,93)	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reported with each solicited general adverse event (AE) (any and grade 3) within each vaccination schedule

End point title	Number of subjects reported with each solicited general adverse event (AE) (any and grade 3) within each vaccination schedule ^[2]
-----------------	--

End point description:

Assessed solicited general symptoms were chills, gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain), fatigue, myalgia, headache and fever [defined Oral cavity or axillary temperature equal to or above ($\geq$) 37.5 degrees Celsius ($^{\circ}$ C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever $\geq$ 39.0 $^{\circ}$ C. Analysis was performed on the Exposed set which included all eligible subjects, enrolled in this study, who provided informed consent, had at least one vaccine dose administered and who provided solicited safety data.

End point type	Primary
----------------	---------

End point timeframe:

During the 7-day follow-up period (the day of vaccination + 6 days) after each vaccination administered at Day 1, Day 61, Day 181 and Day 361

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	100		
Units: Participants				
Chills, Any, Dose 1 (N-100,100)	6	5		
Chills, Grade 3, Dose 1(N-100,100)	0	0		
Chills, Any, Dose 2(N-92,97)	13	8		
Chills, Grade 3, Dose 2(N-92,97)	4	1		
Chills, Any, Dose 3(N-89,97)	12	2		
Chills, Grade 3, Dose 3(N-89,97)	4	0		
Chills, Any, Dose 4(N-84,93)	2	18		
Chills, Grade 3, Dose 4(N-84,93)	1	1		

Gastrointestinal symptoms,Any,Dose 1(N-100,100)	11	7		
Gastrointestinal symptoms,Grade3,Dose 1(N-100,100)	0	0		
Gastrointestinal symptoms,Any,Dose 2(N-92,97)	11	10		
Gastrointestinal symptoms,Grade3,Dose 2(N-92,97)	1	1		
Gastrointestinal symptoms, Any, Dose 3(N-89,97)	9	7		
Gastrointestinal symptoms,Grade3,Dose 3(N-89,97)	0	0		
Gastrointestinal symptoms, Any,Dose 4(N-84,93)	3	15		
Gastrointestinal symptoms,Grade3,Dose 4(N-84,93)	1	1		
Fatigue, Any, Dose 1(N-100,100)	22	16		
Fatigue, Grade 3, Dose 1(N-100,100)	0	1		
Fatigue, Any, Dose 2(N-92,97)	28	32		
Fatigue, Grade 3, Dose 2(N-92,97)	9	1		
Fatigue, Any, Dose 3(N-89,97)	20	13		
Fatigue, Grade 3, Dose 3(N-89,97)	4	0		
Fatigue, Any, Dose 4(N-84,93)	8	35		
Fatigue, Grade 3, Dose 4(N-84,93)	3	5		
Myalgia, Any, Dose 1(N-100,100)	17	16		
Myalgia, Grade 3, Dose 1(N-100,100)	1	0		
Myalgia, Any, Dose 2(N-92,97)	22	23		
Myalgia, Grade 3, Dose 2(N-92,97)	7	1		
Myalgia, Any, Dose 3(N-89,97)	20	3		
Myalgia, Grade 3, Dose 3(N-89,97)	6	0		
Myalgia, Any, Dose 4(N-84,93)	4	28		
Myalgia, Grade 3, Dose 4(N-84,93)	1	5		
Headache, Any, Dose 1(N-100,100)	13	15		
Headache, Grade 3, Dose 1(N-100,100)	0	1		
Headache, Any, Dose 2(N-92,97)	24	21		
Headache, Grade 3, Dose 2(N-92,97)	2	1		
Headache, Any, Dose 3(N-89,97)	24	7		
Headache, Grade 3, Dose 3(N-89,97)	4	0		
Headache, Any, Dose 4(N-84,93)	5	27		
Headache, Grade 3, Dose 4(N-84,93)	1	1		
Fever, Any, Dose 1(N-100,100)	3	3		
Fever, Grade 3, Dose 1(N-100,100)	0	0		
Fever, Any, Dose 2(N-92,97)	3	6		
Fever, Grade 3, Dose 2(N-92,97)	0	0		
Fever, Any, Dose 3(N-89,97)	4	2		
Fever, Grade 3, Dose 3(N-89,97)	0	0		
Fever, Any, Dose 4(N-84,93)	3	5		
Fever, Grade 3, Dose 4(N-84,93)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reported with any unsolicited adverse event (AE) within each vaccination schedule

End point title	Number of subjects reported with any unsolicited adverse event (AE) within each vaccination schedule ^[3]
-----------------	---

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Unsolicited AE is any AE reported in addition to those solicited during the clinical study. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event. Analysis was performed on the Exposed set which included all eligible subjects, enrolled in this study, who provided informed consent, had at least one vaccine dose administered and who provided unsolicited safety data.

End point type	Primary
----------------	---------

End point timeframe:

During the 30-day follow-up period (the day of vaccination + 29 days) after each vaccination administered at Day 1, Day 61, Day 181 and Day 361

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	100		
Units: Participants				
Dose 1 (N-100,100)	16	20		
Dose 2 (N-93,98)	15	20		
Dose 3 (N-90,97)	13	11		
Dose 4 (N-85,93)	7	9		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reported with any serious adverse event (SAE) within each vaccination schedule

End point title	Number of subjects reported with any serious adverse event (SAE) within each vaccination schedule ^[4]
-----------------	--

End point description:

An SAE is defined as any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity in a subject or was a congenital anomaly/birth defect in the offspring of a study subject. AE(s) considered as SAE(s) also include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, as per the medical or scientific judgement of the physician. Analysis was performed on the Exposed set which included all eligible subjects, enrolled in this study, who provided informed consent, had at least one vaccine dose administered and who provided safety data.

End point type	Primary
----------------	---------

End point timeframe:

From first vaccination (Day 1) up to Day 541 (an average of 18 months)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	100		
Units: Participants	12	8		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reported with any potential immune-mediated diseases (pIMDs) within each vaccination schedule

End point title	Number of subjects reported with any potential immune-mediated diseases (pIMDs) within each vaccination schedule ^[5]
-----------------	---

End point description:

Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology. Analysis was performed on the Exposed set which included all eligible subjects, enrolled in this study, who provided informed consent, had at least one vaccine dose administered and who provided safety data.

End point type	Primary
----------------	---------

End point timeframe:

From first vaccination (Day 1) up to Day 541 (an average of 18 months)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	100		
Units: Participants	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with any SAE within each vaccination schedule

End point title	Number of subjects reported with any SAE within each vaccination schedule
-----------------	---

End point description:

An SAE is defined as any untoward medical occurrence that resulted in death, was life-threatening,

required hospitalization or prolongation of hospitalization, resulted in disability/incapacity in a subject or was a congenital anomaly/birth defect in the offspring of a study subject. AE(s) considered as SAE(s) also include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, as per the medical or scientific judgement of the physician.

End point type	Secondary
End point timeframe:	
From Day 541 up to Day 721 (an average of 6 months)	

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	100		
Units: Participants				
Any SAEs (N=100, 100)	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with any pIMDs within each vaccination schedule

End point title	Number of subjects reported with any pIMDs within each vaccination schedule
-----------------	---

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 Day 541 up to Day 721 (an average of 6 months)

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	100		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Protein D (PD) antibody concentrations, as measured by ELISA, within each vaccination schedule

End point title	Anti-Protein D (PD) antibody concentrations, as measured by
-----------------	---

End point description:

Anti-Protein D (PD) antibody concentrations as determined by Enzyme-linked Immunosorbent Assay (ELISA), and expressed as geometric mean concentrations (GMCs) in ELISA unit per milliliter (EU/mL). Calculation of the GMCs are performed by taking the anti-logarithm in base 10 (anti-log₁₀) of the mean of the log₁₀ concentration transformations. Antibody concentrations below the assay cut-off (153 EU/mL) is given an arbitrary value of half the assay cut-off for the purpose of GMC calculation. Analysis was performed on the Per Protocol Set which included all eligible subjects enrolled in this study, who provided informed consent, who complied with the vaccination schedule and who provided immunogenicity data according to blood sample timings specified in the protocol.

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

End point timeframe:

At Day 1, Day 91, Day 181, Day 211, Day 361, Day 391, Day 541 and Day 721

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	87		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Day 1 (N=82,87)	88 (79.2 to 97.9)	88.1 (79.8 to 97.2)		
Day 91(N=79,82)	1365.5 (1073.0 to 1737.8)	1394.1 (1116.9 to 1740.1)		
Day 181(N=81,87)	853.4 (665.4 to 1094.6)	835.6 (665.4 to 1049.3)		
Day 211(N=81,84)	2338 (1840.1 to 2970.8)	679 (541.7 to 850.9)		
Day 361(N=82,87)	1199 (942.8 to 1524.9)	483.1 (386.4 to 603.9)		
Day 391(N=81,82)	1064.1 (829.4 to 1365.2)	2677 (2111.4 to 3394.1)		
Day 541(N=80,84)	826.5 (646.3 to 1057.0)	1346.4 (1072.1 to 1690.8)		
Day 721 (N=77,79)	679.6 (529.5 to 872.1)	900.4 (716.1 to 1132.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Protein E (PE) antibody concentrations, as measured by ELISA, within each vaccination schedule

End point title	Anti-Protein E (PE) antibody concentrations, as measured by ELISA, within each vaccination schedule
-----------------	---

End point description:

Anti-Protein E (PE) antibody concentrations as determined by ELISA, and expressed in EU/mL. Calculation of the GMCs are performed by taking the anti-logarithm in base 10 (anti-log₁₀) of the mean of the log₁₀ concentration transformations. Antibody concentrations below the assay cut-off (16 EU/mL) is given an arbitrary value of half the assay cut-off for the purpose of GMC calculation. Analysis was performed on the Per Protocol Set which included all eligible subjects enrolled in this study, who

provided informed consent, who complied with the vaccination schedule and who provided immunogenicity data according to blood sample timings specified in the protocol.

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

End point timeframe:

At Day 1, Day 91, Day 181, Day 211, Day 361, Day 391, Day 541 and Day 721

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	87		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Day 1 (N-82,87)	19.6 (15.1 to 25.5)	18.4 (14.5 to 23.5)		
Day 91(N-79,82)	5867.9 (4644.4 to 7413.8)	5896.7 (4755.2 to 7312.3)		
Day 181(N-81,87)	2649.1 (2113.3 to 3320.7)	2787.1 (2266.0 to 3428.0)		
Day 211(N-80,84)	7557.1 (6107.9 to 9350.0)	2309.9 (1892.1 to 2819.8)		
Day 361(N-82,87)	2735.3 (2196.7 to 3406.1)	1298 (1058.6 to 1591.6)		
Day 391(N-81,82)	2604.2 (2118.3 to 3201.5)	9339.4 (7670.2 to 11372.0)		
Day 541(N-80,84)	1762.2 (1443.9 to 2150.6)	3620.7 (3009.9 to 4355.4)		
Day 721 (N-77,79)	1348.3 (1085.6 to 1674.7)	1942.0 (1591.0 to 2370.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-type IV pili subunit (PilA) antibody concentrations, as measured by ELISA, within each vaccination schedule

End point title	Anti-type IV pili subunit (PilA) antibody concentrations, as measured by ELISA, within each vaccination schedule
-----------------	--

End point description:

Anti-type IV pili subunit (PilA) antibody concentrations as determined by ELISA, and expressed in EU/mL. Calculation of the GMCs are performed by taking the anti-logarithm in base 10 (anti-log₁₀) of the mean of the log₁₀ concentration transformations. Antibody concentrations below the assay cut-off (8 EU/mL) is given an arbitrary value of half the assay cut-off for the purpose of GMC calculation. Analysis was performed on the Per Protocol Set which included all eligible subjects enrolled in this study, who provided informed consent, who complied with the vaccination schedule and who provided immunogenicity data according to blood sample timings specified in the protocol.

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

End point timeframe:

At Day 1, Day 91, Day 181, Day 211, Day 361, Day 391, Day 541 and Day 721

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	87		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Day 1(N-82,87)	10.9 (8.5 to 14.2)	8.3 (6.5 to 10.5)		
Day 91(N-79,82)	992.5 (747.2 to 1318.5)	893.1 (688.6 to 1158.3)		
Day 181(N-81,87)	589.3 (442.8 to 784.3)	504.2 (388.4 to 654.3)		
Day 211(N-81,84)	1191.7 (920.0 to 1543.6)	396.3 (310.9 to 505.2)		
Day 361(N-82,87)	546.6 (418.1 to 714.5)	250.3 (195.3 to 320.7)		
Day 391(N-81,82)	456.4 (360.7 to 577.6)	1163.9 (931.1 to 1454.9)		
Day 541(N-80,84)	330.4 (260.5 to 419.1)	524.3 (421.0 to 653.1)		
Day 721 (N-77,79)	242.9 (186.4 to 316.5)	305.5 (239.8 to 389.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-ubiquitous surface protein A2 of Moraxella catarrhalis (UspA2) antibody concentrations, as measured by ELISA, within each vaccination schedule

End point title	Anti-ubiquitous surface protein A2 of Moraxella catarrhalis (UspA2) antibody concentrations, as measured by ELISA, within each vaccination schedule
-----------------	---

End point description:

Anti-ubiquitous surface protein A2 of Moraxella catarrhalis (UspA2) antibody concentrations as determined by ELISA, and expressed in EU/mL. Calculation of the GMCs are performed by taking the anti-logarithm in base 10 (anti-log₁₀) of the mean of the log₁₀ concentration transformations. Antibody concentrations below the assay cut-off (28 EU/mL) is given an arbitrary value of half the assay cut-off for the purpose of GMC calculation. Analysis was performed on the Per Protocol Set which included all eligible subjects enrolled in this study, who provided informed consent, who complied with the vaccination schedule and who provided immunogenicity data according to blood sample timings specified in the protocol.

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

End point timeframe:

At Day 1, Day 91, Day 181, Day 211, Day 361, Day 391, Day 541 and Day 721

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	87		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Day 1(N-82,87)	682.4 (544.4 to 855.4)	544.9 (441.8 to 672.1)		
Day 91(N-79,82)	1364.5 (1217.6 to 1529.1)	1159.7 (1044.8 to 1287.2)		
Day 181(N-81,87)	1019.7 (920.9 to 1129.0)	915.2 (834.1 to 1004.3)		
Day 211(N-81,84)	1270.9 (1138.1 to 1419.2)	864.6 (779.5 to 959.1)		
Day 361(N-82,87)	885.8 (801.7 to 978.8)	730 (665.6 to 800.6)		
Day 391(N-81,82)	909.9 (818.5 to 1011.4)	1142.8 (1033.9 to 1263.3)		
Day 541(N-80,84)	898.2 (811.5 to 994.2)	847.4 (771.6 to 930.7)		
Day 721 (N-77,79)	790.6 (705.1 to 886.6)	715.2 (644.0 to 794.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-PD antibody, as measured by ELISA, within each vaccination schedule

End point title	Number of seropositive subjects for anti-PD antibody, as measured by ELISA, within each vaccination schedule
End point description: A Seropositive subject is defined as a subject whose antibody concentration is greater than or equal to the assay cut off (i.e. the ELISA lower limit of quantification = 153 EU/mL).Antibody concentrations as determined by Enzyme-linked Immunosorbent Assay (ELISA), and expressed in EU/mL. Analysis was performed on the Per Protocol Set which included all eligible subjects enrolled in this study, who provided informed consent, who complied with the vaccination schedule and who provided immunogenicity data according to blood sample timings specified in the protocol.	
End point type	Secondary
End point timeframe: At Day 1, Day 91, Day 181, Day 211, Day 361, Day 391, Day 541 and Day 721	

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	87		
Units: Participants				
Day 1(N-82,87)	7	12		
Day 91(N-79,82)	78	80		

Day 181(N-81,87)	75	80		
Day 211(N-81,84)	81	75		
Day 361(N-82,87)	78	71		
Day 391(N-81,82)	77	81		
Day 541(N-80,84)	76	79		
Day 721 (N-77,79)	72	74		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-PE antibody, as measured by ELISA, within each vaccination schedule

End point title	Number of seropositive subjects for anti-PE antibody, as measured by ELISA, within each vaccination schedule
-----------------	--

End point description:

A Seropositive subject is defined as a subject whose antibody concentration is greater than or equal to the assay cut off (i.e. the ELISA lower limit of quantification = 16 EU/mL). Antibody concentrations as determined by Enzyme-linked Immunosorbent Assay (ELISA), and expressed in EU/mL. Analysis was performed on the Per Protocol Set which included all eligible subjects enrolled in this study, who provided informed consent, who complied with the vaccination schedule and who provided immunogenicity data according to blood sample timings specified in the protocol.

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

End point timeframe:

At Day 1, Day 91, Day 181, Day 211, Day 361, Day 391, Day 541 and Day 721

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	87		
Units: Participants				
Day 1(N-82,87)	43	43		
Day 91(N-79,82)	79	82		
Day 181(N-81,87)	81	87		
Day 211(N-80,84)	80	84		
Day 361(N-82,87)	82	87		
Day 391(N-81,82)	81	82		
Day 541(N-80,84)	80	84		
Day 721 (N-77,79)	77	79		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti- PiIA antibody, as measured by ELISA, within each vaccination schedule

End point title	Number of seropositive subjects for anti- PilA antibody, as measured by ELISA, within each vaccination schedule
End point description:	
A Seropositive subject is defined as a subject whose antibody concentration is greater than or equal to the assay cut off (i.e. the ELISA lower limit of quantification = 8 EU/mL).Antibody concentrations as determined by Enzyme-linked Immunosorbent Assay (ELISA), and expressed in EU/mL. Analysis was performed on the Per Protocol Set which included all eligible subjects enrolled in this study, who provided informed consent, who complied with the vaccination schedule and who provided immunogenicity data according to blood sample timings specified in the protocol.	
End point type	Secondary
End point timeframe:	
At Day 1, Day 91, Day 181, Day 211, Day 361, Day 391, Day 541 and Day 721	

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	87		
Units: Participants				
Day 1(N-82,87)	40	36		
Day 91(N-79,82)	79	82		
Day 181(N-81,87)	81	87		
Day 211(N-81,84)	81	83		
Day 361(N-82,87)	82	84		
Day 391(N-81,82)	81	82		
Day 541(N-80,84)	80	84		
Day 721 (N-77,79)	75	79		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti- UspA2 antibody, as measured by ELISA, within each vaccination schedule

End point title	Number of seropositive subjects for anti- UspA2 antibody, as measured by ELISA, within each vaccination schedule
End point description:	
A Seropositive subject is defined as a subject whose antibody concentration is greater than or equal to the assay cut off (i.e. the ELISA lower limit of quantification = 28 EU/mL).Antibody concentrations as determined by Enzyme-linked Immunosorbent Assay (ELISA), and expressed in EU/mL. Analysis was performed on the Per Protocol Set which included all eligible subjects enrolled in this study, who provided informed consent, who complied with the vaccination schedule and who provided immunogenicity data according to blood sample timings specified in the protocol.	
End point type	Secondary
End point timeframe:	
At Day 1, Day 91, Day 181, Day 211, Day 361, Day 391, Day 541 and Day 721	

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	87		
Units: Participants				
Day 1(N-82,87)	82	87		
Day 91(N-79,82)	79	82		
Day 181(N-81,87)	81	87		
Day 211(N-81,84)	81	84		
Day 361(N-82,87)	82	87		
Day 391(N-81,82)	81	82		
Day 541(N-80,84)	80	84		
Day 721 (N-77,79)	77	79		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of Specific Cluster of Differentiation 4 (CD4+) T-cells producing 2 or more markers upon in vitro stimulation with the antigen, by NTHi Antigen

End point title	Frequency of Specific Cluster of Differentiation 4 (CD4+) T-cells producing 2 or more markers upon in vitro stimulation with the antigen, by NTHi Antigen
-----------------	---

End point description:

Frequency of specific CD4+ T-cells were measured by flow cytometry intracellular cytokine staining (ICS) expressing two or more markers [such as Interleukin-2 (IL-2), IL-13, IL-17, Interferon- γ (IFN- γ), Tumor Necrosis Factor- α (TNF- α) and Cluster of Differentiation 40 Ligand (CD40L)]. The frequency of specific CD4+ T-cells are summarized with following descriptive statistics: Mean and standard deviation (SD) against each antigen (PD, PE, PiIA and UspA2), by group and at each time point for which blood samples were collected for Cell-Mediated Immunity (CMI). The CMI sub-cohort subjects were selected from sites able to process the blood samples according to GSK procedures for peripheral blood mononuclear cell (PBMC) preparation. Analysis was performed on a subset of subjects (CMI sub cohort), which included approximately 20 subjects in each group, for which additional blood sample was taken at each pre-defined timepoint.

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

End point timeframe:

At Day 1, Day 91, Day 181, Day 211, Day 361 and Day 391

End point values	Schedule 0-2-6 Group	Schedule 0-2-12 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	19		
Units: CD4+ T-cells/million cells				
arithmetic mean (standard deviation)				
NTHi.PD, Day 1(N-21,19)	76.995 ($\pm$ 142.760)	55.173 ($\pm$ 109.539)		
NTHi.PD, Day 91(N-19,19)	865.933 ($\pm$ 919.585)	1076.136 ($\pm$ 970.670)		
NTHi.PD, Day 181(N-17,19)	381.265 ($\pm$ 356.496)	463.939 ($\pm$ 558.441)		

NTHi.PD, Day 211(N-17,19)	664.044 (± 610.930)	518.104 (± 513.462)		
NTHi.PD, Day 361(N-17,17)	444.129 (± 520.204)	378.78 (± 456.970)		
NTHi.PD, Day 391(N-17,17)	321.28 (± 316.073)	761.605 (± 974.791)		
NTHi.PE, Day 1(N-21,19)	28.869 (± 44.944)	21.223 (± 38.682)		
NTHi.PE, Day 91(N-19,19)	1406.663 (± 1900.558)	926.809 (± 785.046)		
NTHi.PE, Day 181(N-17,19)	551.444 (± 635.058)	352.471 (± 403.081)		
NTHi.PE, Day 211(N-17,19)	986.138 (± 1570.491)	463.076 (± 395.158)		
NTHi.PE, Day 361(N-17,17)	636.539 (± 995.486)	305.772 (± 337.400)		
NTHi.PE, Day 391(N-17,17)	590.426 (± 714.051)	481.133 (± 533.658)		
NTHi.PiIA, Day 1(N-21,19)	81.03 (± 178.861)	79.205 (± 210.642)		
NTHi.PiIA, Day 91(N-19,19)	615.698 (± 686.114)	523.195 (± 493.956)		
NTHi.PiIA, Day 181(N-17,19)	356.275 (± 350.909)	265.097 (± 267.351)		
NTHi.PiIA, Day 211(N-17,19)	524.754 (± 654.443)	257.806 (± 252.382)		
NTHi.PiIA, Day 361(N-17,17)	341.58 (± 433.970)	205.388 (± 220.979)		
NTHi.PiIA, Day 391(N-17,17)	334.088 (± 300.114)	368.693 (± 354.449)		
M catarrhalis.UspA2,Day 1(N-21,19)	85.785 (± 99.051)	53.391 (± 80.742)		
M catarrhalis.UspA2, Day 91(N-19,19)	964.521 (± 709.134)	730.725 (± 575.778)		
M catarrhalis.UspA2, Day 181(N-17,19)	559.062 (± 524.096)	355.992 (± 346.277)		
M catarrhalis.UspA2, Day 211(N-17,19)	846.177 (± 750.349)	424.981 (± 329.334)		
M catarrhalis.UspA2, Day 361(N-17,17)	635.022 (± 617.485)	347.65 (± 363.499)		
M catarrhalis.UspA2, Day 391(N-17,17)	545.436 (± 464.272)	474.238 (± 446.236)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs were collected during the 7-day follow-up period after any vaccination, Unsolicited AEs during the 30-day follow-up period after any vaccination, and SAEs from Day 1 to Day 721.

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

Dictionary used

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

Dictionary version	23.1
--------------------	------

Reporting groups

Reporting group title	Schedule 0-2-6 Group
-----------------------	----------------------

Reporting group description:

Subjects between, and including, 40 and 80 years of age at the time of the first vaccination, receiving three doses of the GSK3277511A investigational vaccine at Day 1 (Month 0), Day 61 (Month 2) and Day 181 (Month 6) and one dose of placebo at Day 361 (Month 12).

Reporting group title	Schedule 0-2-12 Group
-----------------------	-----------------------

Reporting group description:

Subjects between, and including, 40 and 80 years of age at the time of the first vaccination, receiving three doses of the GSK3277511A investigational vaccine at Day 1 (Month 0), Day 61 (Month 2) and Day 361 (Month 12) and one dose of placebo at Day 181 (Month 6).

Serious adverse events	Schedule 0-2-6 Group	Schedule 0-2-12 Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 100 (12.00%)	9 / 100 (9.00%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Lung neoplasm malignant subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (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 / 100 (2.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Chest injury			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth injury			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Right ventricular failure			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral artery occlusion			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (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	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
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			

Death			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
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			
Pulmonary embolism			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Pain of skin			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Conversion disorder			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (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 / 100 (0.00%)	1 / 100 (1.00%)	
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	Schedule 0-2-6 Group	Schedule 0-2-12 Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	93 / 100 (93.00%)	97 / 100 (97.00%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Hypertension			
subjects affected / exposed	0 / 100 (0.00%)	4 / 100 (4.00%)	
occurrences (all)	0	4	
General disorders and administration site conditions			

Administration site pruritus subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	1 / 100 (1.00%) 1
Chest pain subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	1 / 100 (1.00%) 1
Fatigue subjects affected / exposed occurrences (all)	44 / 100 (44.00%) 79	50 / 100 (50.00%) 97
Chills subjects affected / exposed occurrences (all)	24 / 100 (24.00%) 33	25 / 100 (25.00%) 34
Feeling hot subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	0 / 100 (0.00%) 0
Injection site erythema subjects affected / exposed occurrences (all)	21 / 100 (21.00%) 35	28 / 100 (28.00%) 41
Influenza like illness subjects affected / exposed occurrences (all)	2 / 100 (2.00%) 2	2 / 100 (2.00%) 2
Injection site pain subjects affected / exposed occurrences (all)	89 / 100 (89.00%) 213	92 / 100 (92.00%) 210
Injection site pruritus subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	1 / 100 (1.00%) 1
Injection site swelling subjects affected / exposed occurrences (all)	16 / 100 (16.00%) 25	20 / 100 (20.00%) 27
Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	0 / 100 (0.00%) 0
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	2 / 100 (2.00%) 2

Pyrexia			
subjects affected / exposed	11 / 100 (11.00%)	13 / 100 (13.00%)	
occurrences (all)	13	16	
Illness			
subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 100 (2.00%)	1 / 100 (1.00%)	
occurrences (all)	2	1	
Nasal congestion			
subjects affected / exposed	1 / 100 (1.00%)	3 / 100 (3.00%)	
occurrences (all)	1	3	
Oropharyngeal pain			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Rhinorrhoea			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Rhinitis allergic			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Hallucination			

subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	1 / 100 (1.00%) 1	
Anxiety subjects affected / exposed occurrences (all)	2 / 100 (2.00%) 2	0 / 100 (0.00%) 0	
Insomnia subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	0 / 100 (0.00%) 0	
Stress subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	0 / 100 (0.00%) 0	
Investigations Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	1 / 100 (1.00%) 1	
Weight increased subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	1 / 100 (1.00%) 1	
Injury, poisoning and procedural complications Concussion subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	1 / 100 (1.00%) 1	
Contusion subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	1 / 100 (1.00%) 1	
Muscle strain subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	0 / 100 (0.00%) 0	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	2 / 100 (2.00%) 2	2 / 100 (2.00%) 2	
Headache subjects affected / exposed occurrences (all)	39 / 100 (39.00%) 69	41 / 100 (41.00%) 71	
Hypoaesthesia			

subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Nerve compression			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Lymphadenopathy			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Ear pain			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Vertigo			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Eye disorders			

Cataract			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	1 / 100 (1.00%)	3 / 100 (3.00%)	
occurrences (all)	1	3	
Dyspepsia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	0 / 100 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Food poisoning			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Gastrointestinal disorder			

subjects affected / exposed	25 / 100 (25.00%)	28 / 100 (28.00%)	
occurrences (all)	34	40	
Haemorrhoids			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Large intestine polyp			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Rectal haemorrhage			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Night sweats			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	

Psoriasis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	2	
Back pain			
subjects affected / exposed	2 / 100 (2.00%)	4 / 100 (4.00%)	
occurrences (all)	2	4	
Joint swelling			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Limb discomfort			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	38 / 100 (38.00%)	41 / 100 (41.00%)	
occurrences (all)	63	73	
Pain in extremity			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Synovial cyst			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Arthralgia			

subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	2 / 100 (2.00%) 2	
Infections and infestations			
Eye infection			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Alveolar osteitis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Infected bite			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Gingival abscess			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	6 / 100 (6.00%)	6 / 100 (6.00%)	
occurrences (all)	6	6	
Localised infection			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Ophthalmic herpes simplex			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Tooth infection			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	1 / 100 (1.00%)	2 / 100 (2.00%)	
occurrences (all)	1	2	

Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 100 (3.00%) 3	0 / 100 (0.00%) 0	
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	0 / 100 (0.00%) 0	
Vaginal infection subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	1 / 100 (1.00%) 1	
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	0 / 100 (0.00%) 0	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	0 / 100 (0.00%) 0	
Gout subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	0 / 100 (0.00%) 0	
Diabetes mellitus inadequate control subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	1 / 100 (1.00%) 1	
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	0 / 100 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2018	MedDRA list for pIMDs updated with addition of gout as musculoskeletal disorder of interest
24 July 2019	ELISA cut off levels for humoral antibody response updated. CMI testing for CD8+ T cells measurement moved from secondary endpoints to tertiary endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported