Clinical trial results:
An observer-blind study to evaluate the safety, reactogenicity and immunogenicity of GSK Biologicals' investigational vaccine GSK2838504A when administered to COPD patients

Summary

EudraCT number	2013-003062-13
Trial protocol	GB SE
Global end of trial date	19 April 2017

Results information

Result version number	v1 (current)
This version publication date	06 April 2018
First version publication date	06 April 2018

Trial information

Trial identification

Sponsor protocol code	200157

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02075541
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 February 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 April 2017
Global end of trial reached?	Yes
Global end of trial date	19 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to describe the safety and reactogenicity of the investigational vaccine.

Protection of trial subjects:

All subjects were observed closely for at least 60 minutes following the administration of the vaccine, with appropriate medical treatment readily available in case of anaphylaxis. Vaccines were administered by qualified and trained personnel. Vaccine was given only to eligible subjects that had no contraindications to any components of the vaccines. Subjects will be followed up till 13 months after last vaccine administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 July 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 112
Country: Number of subjects enrolled	Sweden: 33
Worldwide total number of subjects	145
EEA total number of subjects	145

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)	45
From 65 to 84 years	100
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

145 subjects, aged 40 to 80 years were recruited from 4 sites in Sweden and 11 sites in the United Kingdom.

Pre-assignment

Screening details:

All enrolled subjects were included in the 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, Assessor

Blinding implementation details:

Vaccine preparation & administration will be done by authorised medical personnel who will not participate in any of the study clinical evaluation assays.Laboratory in charge of testing will be blinded to treatment & codes will be used to link the subject & study to each sample.An analysis of immunogenicity & safety data up to Day 90 will be done on as cleaned as possible data.At this point,statistician of the project will be unblinded.Other study personnel will remain blinded until study end.

Arms

Are arms mutually exclusive?	Yes
Arm title	10-AS01E Group

Arm description:

Approximately 70 subjects who received 2 doses of the investigational NTHi vaccine.

Arm type	Experimental
Investigational medicinal product name	NTHi-10-AS01E
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL adminsitered in 2 doses.

Arm title	Control Group

Arm description:

Approximately 70 subjects who received 2 doses of placebo.

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

Dosage and administration details:

0.5 mL adminsitered in 2 doses.

Number of subjects in period 1	10-AS01E Group	Control Group
Started	73	72
Completed	69	64
Not completed	4	8
Consent withdrawn by subject	1	3
Sponsor study termination	-	1
Other- unable to perform study procedure	1	-
Serious Adverse Event	1	4
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	10-AS01E Group
Reporting group description:	
Approximately 70 subjects who received 2 doses of the investigational NTHi vaccine.	
Reporting group title	Control Group
Reporting group description:	
Approximately 70 subjects who received 2 doses of placebo.	

Reporting group values	10-AS01E Group	Control Group	Total
Number of subjects	73	72	145
Age categorical Units: Subjects			
40-59 years old	12	11	23
60-80 years-old	61	60	121
>80 years old	0	1	1
Age continuous Units: years			
arithmetic mean	67	66.8	
standard deviation	± 8.41	± 7.21	-
Gender categorical Units: Subjects			
Female	34	36	70
Male	39	36	75
Race/Ethnicity, Customized Units: Subjects			
White- Caucasian/ European Heritage	73	72	145

End points

End points reporting groups

Reporting group title	10-AS01E Group
Reporting group description:	
Approximately 70 subjects who received 2 doses of the investigational NTHi vaccine.	
Reporting group title	Control Group
Reporting group description:	
Approximately 70 subjects who received 2 doses of placebo.	

Primary: Number of subjects with any solicited local adverse events (AEs).

End point title	Number of subjects with any solicited local adverse events (AEs).[1]
End point description:	
Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade.	
End point type	Primary
End point timeframe:	
During a 7-day follow-up period (from Day 0 to Day 6) after first dose.	

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	72		
Units: Participants				
Any Pain	49	5		
Any Redness (mm)	9	0		
Any Swelling (mm)	4	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any solicited local AEs.

End point title	Number of subjects with any solicited local AEs.[2]
End point description:	
Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade.	
End point type	Primary
End point timeframe:	
During a 7-day follow-up period (from Day 60 to Day 66) after second dose.	

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: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	68		
Units: Participants				
Any Pain	49	5		
Any Redness (mm)	15	2		
Any Swelling (mm)	8	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any solicited general AEs.

End point title	Number of subjects with any solicited general AEs.[3]

End point description:

Assessed solicited general symptoms are fatigue, gastrointestinal symptoms (included nausea, vomiting, diarrhoea and/or abdominal pain), headache, fever [defined as oral temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade.

End point type	Primary

End point timeframe:

During a 7-day follow-up period (from Day 0 to Day 6) following the first dose.

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	72		
Units: Participants				
Any Fatigue	21	19		
Any Gastrointestinal symptoms	12	10		
Any Headache	19	13		
Any Temperature/(Oral) (°C)	2	6		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any solicited general AEs

End point title	Number of subjects with any solicited general AEs[4]

End point description:

Assessed solicited general symptoms are fatigue, gastrointestinal symptoms (included nausea, vomiting, diarrhoea and/or abdominal pain), headache, fever (defined as oral temperature equal to or above 37.5 °C). Any = occurrence of the symptom regardless of intensity grade.

End point type	Primary

End point timeframe:

During a 7-day follow-up period (from Day 60 to Day 66) following the second dose.

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	68		
Units: Participants				
Any Fatigue	28	13		
Any Gastrointestinal symptoms	15	6		
Any Headache	20	13		
Any Temperature/(Oral) (°C)	10	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any unsolicited AEs.

End point title	Number of subjects with any unsolicited AEs.[5]

End point description:

Assessed unsolicited AEs covered any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. Any = occurrence of the symptom regardless of intensity grade or relation to vaccination.

End point type	Primary

End point timeframe:

During the 30-day follow-up period (from Day 0 to Day 29) following the first dose.

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: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	72		
Units: Participants				
Participants	27	26		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any unsolicited AEs

End point title	Number of subjects with any unsolicited AEs[6]

End point description:

Assessed unsolicited AEs covered any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. Any = occurrence of the symptom regardless of intensity grade or relation to vaccination.

End point type	Primary

End point timeframe:

During the 30-day follow-up period (from Day 60 to Day 89) following the second dose.

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	72		
Units: Participants				
Participants	25	22		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with each haematological/ biochemical laboratory abnormality.

End point title	Number of subjects with each haematological/ biochemical laboratory abnormality.[7]

End point description:

Assessed haematological parameters are complete blood cell count: Leukocytes [white blood cells (WBC)], differential count (basophils, eosinophils, lymphocytes, monocytes, neutrophils), platelets count, and hemoglobin level below or above the normal laboratory ranges tabulated by time point. Assessed biochemical parameters are alanine aminotransferase (ALT), aspartate aminotransferase (AST) or creatinine below or above the normal laboratory ranges tabulated by time point.

End point type	Primary

End point timeframe:

At Day 0.

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	70		
Units: Participants				
WBC below (N=72,70)	1	1		
WBC above N=72,70)	5	1		
Basophils below (N=71,70)	0	0		
Basophils above N=71,70)	0	0		
Eosinophils below (N=71,70)	0	0		
Eosinophils above (N=71,70)	3	4		
Lymphocytes below (N=71,70)	15	9		
Lymphocytes above (N=71,70)	7	3		
Monocytes below (N=71,70)	0	1		
Monocytes above (N=71,70)	6	6		
Neutrophils below (N=71,70)	1	1		
Neutrophils above (N=71,70)	6	3		
Platelets below (N=72,70)	2	4		
Platelets above (N=72,70)	12	9		
Haemoglobin below (N=72,70)	5	6		
Haemoglobin above (N=72,70)	12	5		
ALT below (N=72,70)	0	0		
ALT above (N=72,70)	4	1		
AST below (N=72,70)	0	0		
AST above (N=72,70)	2	1		
Creatinine below (N=73,70)	0	0		
Creatinine above (N=73,70)	10	8		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with each haematological/ biochemical laboratory abnormality.

End point title	Number of subjects with each haematological/ biochemical laboratory abnormality.[8]

End point description:

Assessed haematological parameters are complete blood cell count: Leukocytes [white blood cells (WBC)], differential count (basophils, eosinophils, lymphocytes, monocytes, neutrophils), platelets count, and hemoglobin level below or above the normal laboratory ranges tabulated by time point. Assessed biochemical parameters are alanine aminotransferase (ALT), aspartate aminotransferase (AST) or creatinine below or above the normal laboratory ranges tabulated by time point.

End point type	Primary

End point timeframe:

At Day 7.

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	67		
Units: Participants				
WBC below (N=69,67)	0	2		
WBC above (N=69,67)	4	0		
Basophils below (N=69,67)	0	0		
Basophils above (N=69,67)	0	0		
Eosinophils below (N=69,67)	0	0		
Eosinophils above (N=69,67)	4	2		
Lymphocytes below (N=69,67)	9	7		
Lymphocytes above (N=69,67)	4	2		
Monocytes below (N=69,67)	1	0		
Monocytes above (N=69,67)	4	5		
Neutrophils below (N=69,67)	1	1		
Neutrophils above (N=69,67)	8	1		
Platelets below (N=69,67)	2	3		
Platelets above (N=69,67)	15	12		
Haemoglobin below (N=69,67)	5	5		
Haemoglobin above (N=69,67)	12	4		
ALT below (N=69,67)	0	0		
ALT above (N=69,67)	5	1		
AST below (N=69,67)	0	0		
AST above (N=69,67)	1	2		
Creatinine below (N=69,67)	0	0		
Creatinine above (N=69,67)	7	10		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with each haematological/ biochemical laboratory abnormality.

End point title	Number of subjects with each haematological/ biochemical laboratory abnormality.[9]

End point description:

Assessed haematological parameters are complete blood cell count: Leukocytes [white blood cells (WBC)], differential count (basophils, eosinophils, lymphocytes, monocytes, neutrophils), platelets count, and hemoglobin level below or above the normal laboratory ranges tabulated by time point. Assessed biochemical parameters are alanine aminotransferase (ALT), aspartate aminotransferase (AST) or creatinine below or above the normal laboratory ranges tabulated by time point.

End point type	Primary

End point timeframe:

At Day 30.

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	68		
Units: Participants				
WBC below (N=68,68)	1	1		
WBC above (N=68,68)	8	2		
Basophils below (N=68,68)	0	0		
Basophils above (N=68,68)	0	0		
Eosinophils below (N=68,68)	0	0		
Eosinophils above (N=68,68)	3	2		
Lymphocytes below (N=68,68)	14	6		
Lymphocytes above (N=68,68)	7	6		
Monocytes below (N=68,68)	0	0		
Monocytes above (N=68,68)	8	10		
Neutrophils below (N=68,68)	1	2		
Neutrophils above (N=68,68)	9	1		
Platelets below (N=68,68)	3	2		
Platelets above (N=68,68)	14	11		
Haemoglobin below (N=68,68)	3	8		
Haemoglobin above (N=68,68)	10	6		
ALT below (N=68,68)	0	0		
ALT above (N=68,68)	5	4		
AST below (N=68,68)	0	0		
AST above (N=68,68)	1	4		
Creatinine below (N=68,68)	0	0		
Creatinine above (N=68,68)	6	12		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with each haematological/ biochemical laboratory abnormality.

End point title	Number of subjects with each haematological/ biochemical laboratory abnormality.[10]

End point description:

Assessed haematological parameters are complete blood cell count: Leukocytes [white blood cells (WBC)], differential count (basophils, eosinophils, lymphocytes, monocytes, neutrophils), platelets count, and hemoglobin level below or above the normal laboratory ranges tabulated by time point. Assessed biochemical parameters are alanine aminotransferase (ALT), aspartate aminotransferase (AST) or creatinine below or above the normal laboratory ranges tabulated by time point.

End point type	Primary

End point timeframe:

At Day 60.

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	69		
Units: Participants				
WBC below (N=70,69)	1	0		
WBC above (N=70,69)	3	8		
Basophils below (N=70,69)	0	0		
Basophils above (N=70,69)	0	0		
Eosinophils below (N=70,69)	0	0		
Eosinophils above (N=70,69)	5	2		
Lymphocytes below (N=70,69)	12	11		
Lymphocytes above (N=70,69)	4	5		
Monocytes below (N=70,69)	0	2		
Monocytes above (N=70,69)	7	12		
Neutrophils below (N=70,69)	1	2		
Neutrophils above (N=70,69)	8	7		
Platelets below (N=70,69)	1	3		
Platelets above (N=70,69)	13	9		
Haemoglobin below (N=70,69)	4	8		
Haemoglobin above (N=70,69)	7	5		
ALT below (N=70,68)	0	0		
ALT above (N=70,68)	4	1		
AST below (N=70,69)	0	0		
AST above (N=70,69)	3	2		
Creatinine below (N=70,69)	0	0		
Creatinine above (N=70,69)	5	8		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with each haematological/ biochemical laboratory abnormality.

End point title	Number of subjects with each haematological/ biochemical laboratory abnormality.[11]

End point description:

Assessed haematological parameters are complete blood cell count: Leukocytes [white blood cells (WBC)], differential count (basophils, eosinophils, lymphocytes, monocytes, neutrophils), platelets count, and hemoglobin level below or above the normal laboratory ranges tabulated by time point. Assessed biochemical parameters are alanine aminotransferase (ALT), aspartate aminotransferase (AST) or creatinine below or above the normal laboratory ranges tabulated by time point.

End point type	Primary

End point timeframe:

At Day 67.

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	64		
Units: Participants				
WBC below (N=65,64)	0	0		
WBC above (N=65,64)	4	2		
Basophils below (N=65,64)	0	0		
Basophils above (N=65,64)	0	0		
Eosinophils below (N=65,64)	0	0		
Eosinophils above (N=65,64)	5	2		
Lymphocytes below (N=65,64)	11	8		
Lymphocytes above (N=65,64)	6	3		
Monocytes below (N=65,64)	0	0		
Monocytes above (N=65,64)	4	12		
Neutrophils below (N=65,64)	2	1		
Neutrophils above (N=65,64)	5	4		
Platelets below (N=65,64)	0	4		
Platelets above (N=65,64)	16	11		
Haemoglobin below (N=65,64)	6	11		
Haemoglobin above (N=65,64)	8	3		
ALT below (N=64,64)	0	0		
ALT above (N=64,64)	5	2		
AST below (N=64,64)	0	0		
AST above (N=64,64)	3	3		
Creatinine below (N=64,64)	0	0		
Creatinine above (N=64,64)	5	9		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with each haematological/ biochemical laboratory abnormality.

End point title	Number of subjects with each haematological/ biochemical laboratory abnormality.[12]

End point description:

Assessed haematological parameters are complete blood cell count: Leukocytes [white blood cells (WBC)], differential count (basophils, eosinophils, lymphocytes, monocytes, neutrophils), platelets count, and hemoglobin level below or above the normal laboratory ranges tabulated by time point. Assessed biochemical parameters are alanine aminotransferase (ALT), aspartate aminotransferase (AST) or creatinine below or above the normal laboratory ranges tabulated by time point.

End point type	Primary

End point timeframe:

At Day 90.

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	69		
Units: Participants				
WBC below (N=72,69)	0	1		
WBC above (N=72,69)	3	2		
Basophils below (N=72,69)	0	0		
Basophils above (N=72,69)	0	0		
Eosinophils below (N=72,69)	0	0		
Eosinophils above (N=72,69)	7	5		
Lymphocytes below (N=72,69)	11	10		
Lymphocytes above (N=72,69)	6	4		
Monocytes below (N=72,69)	0	0		
Monocytes above (N=72,69)	10	6		
Neutrophils below (N=72,69)	1	0		
Neutrophils above (N=72,69)	5	5		
Platelets below (N=72,69)	1	3		
Platelets above (N=72,69)	13	13		
Haemoglobin below (N=72,69)	4	10		
Haemoglobin above (N=72,69)	10	6		
ALT below (N=72,69)	0	0		
ALT above (N=72,69)	3	4		
AST below (N=72,69)	0	0		
AST above (N=72,69)	2	2		
Creatinine below (N=72,69)	0	0		
Creatinine above (N=72,69)	5	8		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with each haematological/ biochemical laboratory abnormality.

End point title	Number of subjects with each haematological/ biochemical laboratory abnormality.[13]

End point description:

Assessed haematological parameters are complete blood cell count: Leukocytes [white blood cells (WBC)], differential count (basophils, eosinophils, lymphocytes, monocytes, neutrophils), platelets count, and hemoglobin level below or above the normal laboratory ranges tabulated by time point. Assessed biochemical parameters are alanine aminotransferase (ALT), aspartate aminotransferase (AST) or creatinine below or above the normal laboratory ranges tabulated by time point.

End point type	Primary

End point timeframe:

At Day 270.

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	65		
Units: Participants				
WBC below (N=67,65)	1	0		
WBC above (N=67,65)	7	5		
Basophils below (N=67,65)	0	0		
Basophils above (N=67,65)	0	0		
Eosinophils below (N=67,65)	0	0		
Eosinophils above (N=67,65)	4	3		
Lymphocytes below (N=67,65)	11	5		
Lymphocytes above (N=67,65)	7	3		
Monocytes below (N=67,65)	0	0		
Monocytes above (N=67,65)	10	9		
Neutrophils below (N=67,65)	1	1		
Neutrophils above (N=67,65)	10	6		
Platelets below (N=67,65)	1	3		
Platelets above (N=67,65)	9	11		
Haemoglobin below (N=67,65)	5	10		
Haemoglobin above (N=67,65)	13	3		
ALT below (N=67,65)	0	0		
ALT above (N=67,65)	5	2		
AST below (N=67,65)	0	0		
AST above (N=67,65)	5	2		
Creatinine below (N=67,65)	0	0		
Creatinine above (N=67,65)	9	9		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with each haematological/ biochemical laboratory abnormality.

End point title	Number of subjects with each haematological/ biochemical laboratory abnormality.[14]

End point description:

Assessed haematological parameters are complete blood cell count: Leukocytes [white blood cells (WBC)], differential count (basophils, eosinophils, lymphocytes, monocytes, neutrophils), platelets count, and hemoglobin level below or above the normal laboratory ranges tabulated by time point. Assessed biochemical parameters are alanine aminotransferase (ALT), aspartate aminotransferase (AST) or creatinine below or above the normal laboratory ranges tabulated by time point.

End point type	Primary

End point timeframe:

At Day 450.

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	61		
Units: Participants				
WBC below (N=68,61)	1	0		
WBC above (N=68,61)	3	1		
Basophils below (N=68,60)	0	0		
Basophils above (N=68,60)	0	0		
Eosinophils below (N=68,60)	0	0		
Eosinophils above (N=68,60)	6	3		
Lymphocytes below (N=68,60)	17	9		
Lymphocytes above (N=68,60)	8	3		
Monocytes below (N=68,60)	0	1		
Monocytes above (N=68,60)	6	5		
Neutrophils below (N=68,60)	1	1		
Neutrophils above (N=68,60)	7	4		
Platelets below (N=68,61)	3	3		
Platelets above (N=68,61)	14	13		
Haemoglobin below (N=68,61)	6	10		
Haemoglobin above (N=68,61)	10	6		
ALT below (N=69,61)	0	0		
ALT above (N=69,61)	3	3		
AST below (N=69,61)	0	0		
AST above (N=69,61)	1	3		
Creatinine below (N=69,61)	0	0		
Creatinine above (N=69,61)	7	9		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reporting any potential immune-mediated diseases (pIMDs).[15]

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	Primary

End point timeframe:

From first vaccination (Day 0) up to study conclusion (Day 450).

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	72		
Units: Participants				
Participants	2	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any serious adverse events (SAEs).

End point title	Number of subjects with any serious adverse events (SAEs).[16]

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 or are a congenital anomaly/ birth defect in the offspring of a study subject.

End point type	Primary

End point timeframe:

From first vaccination (Day 0) up to study conclusion (Day 450).

Notes:

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

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	72		
Units: Participants				
Participants	15	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of anti Protein D (anti-PD) total Immunoglobulin G (IgG) antibodies against the NTHi vaccine antigens.

End point title	Concentration of anti Protein D (anti-PD) total Immunoglobulin G (IgG) antibodies against the NTHi vaccine antigens.

End point description:

Antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA) and expressed as geometric mean concentrations (GMCs) in ELISA units per millilitre (EL.U/mL). The cut-off of the assay was 153 EL.U/mL for anti-PD.

End point type	Secondary

End point timeframe:

At Day 0, Day 30, Day 60, Day 90, Day 270 and at Day 450.

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	45		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD antibody, Day 0 (N=44,45)	107.3 (87.9 to 130.9)	100.3 (85.3 to 118)		
Anti-PD antibody, Day 30 (N=43,44)	840.1 (535.9 to 1317)	102.6 (86.2 to 122.1)		
Anti-PD antibody, Day 60 (N=46,45)	538 (358.6 to 807.1)	104.1 (87.6 to 123.6)		
Anti-PD antibody, Day 90 (N=46,45)	1692.1 (1242.6 to 2304)	103 (87.3 to 121.7)		
Anti-PD antibody, Day 270 (N=44,42)	598.3 (437 to 819.2)	109.3 (90.9 to 131.4)		
Anti-PD antibody, Day 450 (N=46,41)	463 (340.4 to 629.8)	108.4 (90.1 to 130.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of anti Protein E (anti-PE) total IgG antibodies against the NTHi vaccine antigens.

End point title	Concentration of anti Protein E (anti-PE) total IgG antibodies against the NTHi vaccine antigens.

End point description:

Antibody concentrations were measured by ELISA and expressed as GMCs in EL.U/mL. The cut-off of the assay was 8 EL.U/mL for anti-PE.

End point type	Secondary

End point timeframe:

At Day 0, Day 30, Day 60, Day 90, Day 270 and at Day 450

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	44		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				

Anti-PE antibody, Day 0 (N=43,44)	14.1 (9.5 to 21)	14.8 (10.2 to 21.5)		
Anti-PE antibody, Day 30 (N=43,43)	1007 (588.9 to 1722)	13.6 (9.4 to 19.5)		
Anti-PE antibody, Day 60 (N=46,44)	823.7 (503.3 to 1348.1)	13.9 (9.7 to 19.9)		
Anti-PE antibody, Day 90 (N=44,44)	10953.4 (8414.9 to 14257.9)	15 (10.3 to 21.9)		
Anti-PE antibody, Day 270 (N=44,41)	1743.3 (1226.9 to 2477)	12.6 (8.7 to 18.1)		
Anti-PE antibody, Day 450 (N=46,40)	1247.5 (866 to 1797)	13.6 (9.3 to 20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of anti-PilA total IgG antibodies against the NTHi vaccine antigens.

End point title	Concentration of anti-PilA total IgG antibodies against the NTHi vaccine antigens.

End point description:

Antibody concentrations were measured by ELISA and expressed as GMCs in EL.U/mL. The cut-off of the assay was 7 EL.U/mL for anti-PilA.

End point type	Secondary

End point timeframe:

At Day 0, Day 30, Day 60, Day 90, Day 270 and at Day 450.

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	43		
Units: El.U/mL				
geometric mean (confidence interval 95%)				
Anti-PilA antibody, Day 0 (N=39,43)	12.3 (8.6 to 17.6)	14.5 (10.2 to 20.5)		
Anti-PilA antibody, Day 30 (N=41,40)	234.3 (133.5 to 411.5)	15.6 (10.7 to 22.8)		
Anti-PilA antibody, Day 60 (N=43,43)	207.5 (122.4 to 351.6)	15.1 (10.7 to 21.3)		
Anti-PilA antibody, Day 90 (N=46,41)	1353.7 (989.7 to 1851.7)	16.5 (11.4 to 23.9)		
Anti-PilA antibody, Day 270 (N=43,39)	333.5 (240.2 to 463.2)	16.8 (11.6 to 24.3)		
Anti-PilA antibody, Day 450 (N=45,38)	206.8 (147.7 to 289.5)	16.2 (11.1 to 23.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of specific Cluster of Differentiation 4 (CD4+) T-cells against NTHi antigens collected for evaluation of cell-mediated immune response.

End point title	Frequency of specific Cluster of Differentiation 4 (CD4+) T-cells against NTHi antigens collected for evaluation of cell-mediated immune response.

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 summarised [descriptive statistics: Mean and standard deviation (SD)] against each antigen (PD, PE and PilA), by group at each time point during which blood samples are collected for CMI.

End point type	Secondary

End point timeframe:

At Day 0, Day 90, Day 270 and at Day 450.

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	9		
Units: CD4+ T-cells/ million cells				
arithmetic mean (standard deviation)				
CD4+ T-cells, PD, Day 0 (N=15,7)	33.1 (± 49.97)	79.7 (± 91.48)		
CD4+ T-cells, PD, Day 90 (N=15,8)	521.6 (± 287.39)	38.4 (± 51.61)		
CD4+ T-cells, PD, Day 270 (N=14,9)	189.6 (± 146.87)	51.8 (± 59.4)		
CD4+ T-cells, PD, Day 450 (N=14,5)	148.6 (± 141.11)	97.8 (± 98.4)		
CD4+ T-cells, PE, Day 0 (N=15,8)	51.3 (± 68.72)	69.1 (± 82.87)		
CD4+ T-cells, PE, Day 90 (N=15,8)	857.9 (± 642.76)	65 (± 92.86)		
CD4+ T-cells, PE, Day 270 (N=14,9)	304.4 (± 292.46)	71.6 (± 90.51)		
CD4+ T-cells, PE, Day 450 (N=14,5)	337.2 (± 302.42)	117.8 (± 53.24)		
CD4+ T-cells, PilA, Day 0 (N=15,7)	29.7 (± 53.21)	98.3 (± 74.27)		
CD4+ T-cells, PilA, Day 90 (N=15,8)	474.4 (± 321.58)	37.4 (± 46.53)		
CD4+ T-cells, PilA, Day 270 (N=14,9)	145 (± 164.58)	80.3 (± 95.6)		
CD4+ T-cells, PilA, Day 450 (N=14,5)	157.7 (± 117.76)	102.8 (± 116.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of specific CD8+ T-cells against NTHi antigens collected for

evaluation of cell-mediated immune response.

End point title	Frequency of specific CD8+ T-cells against NTHi antigens collected for evaluation of cell-mediated immune response.

End point description:

Frequency of specific CD8+ T-cells were measured by flow cytometry ICS expressing two or more markers (such as IL-2, IL-13, IL-17, IFN-γ, TNF-α and CD40L).The frequency of specific CD8+ T-cells are summarised [descriptive statistics: Mean and standard deviation (SD)] against each antigen (PD, PE and PilA), by group at each time point during which blood samples are collected for CMI.

End point type	Secondary

End point timeframe:

At Day 0, Day 90, Day 270 and at Day 450.

End point values	10-AS01E Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	9		
Units: CD8+ T-cells/ million cells				
arithmetic mean (standard deviation)				
CD8+ T-cells, PD, Day 0 (N=13,8)	97.1 (± 186.24)	47.9 (± 72.9)		
CD8+ T-cells, PD, Day 90 (N=12,8)	39.6 (± 73.78)	45.8 (± 77.53)		
CD8+ T-cells, PD, Day 270 (N=12,9)	55.3 (± 59.18)	48.7 (± 56.33)		
CD8+ T-cells, PD, Day 450 (N=13,5)	51.5 (± 60.19)	16.2 (± 24.04)		
CD8+ T-cells, PE, Day 0 (N=14,8)	97.7 (± 204.06)	73.9 (± 131.71)		
CD8+ T-cells, PE, Day 90 (N=14,8)	44.9 (± 47.72)	30.6 (± 59.01)		
CD8+ T-cells, PE, Day 270 (N=12,9)	29.9 (± 57.16)	60.3 (± 83.47)		
CD8+ T-cells, PE, Day 450 (N=13,5)	41 (± 74.41)	31.6 (± 43.34)		
CD8+ T-cells, PilA, Day 0 (N=13,8)	63.1 (± 122.12)	23.1 (± 45.92)		
CD8+ T-cells, PilA, Day 90 (N=13,8)	39.7 (± 73.42)	80.3 (± 125.84)		
CD8+ T-cells, PilA, Day 270 (N=12,9)	27.4 (± 34.15)	13 (± 15.12)		
CD8+ T-cells, PilA, Day 450 (N=13,5)	63.7 (± 98.87)	31 (± 36.17)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicted AEs: during the 7-day interval post each vaccine dose, Unsolicited AEs: during the 30-day interval post each vaccine dose, SAEs: throughout the entire study, from Day 0 up to Day 450.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Control Group

Reporting group description:

Approximately 70 subjects who received 2 doses of placebo.

Reporting group title	10-AS01E Group

Reporting group description:

Approximately 70 subjects who received 2 doses of the investigational NTHi vaccine.

Serious adverse events	Control Group	10-AS01E Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 72 (23.61%)	15 / 73 (20.55%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	1 / 72 (1.39%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic bronchial carcinoma			
subjects affected / exposed	1 / 72 (1.39%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal squamous cell carcinoma			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
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			

Radius fracture			
subjects affected / exposed	1 / 72 (1.39%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 73 (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	1 / 72 (1.39%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dressler's syndrome			
subjects affected / exposed	1 / 72 (1.39%)	0 / 73 (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	2 / 72 (2.78%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	

Nervous system disorders			
Dementia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
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			
Non-cardiac chest pain			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 72 (1.39%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Barrett's oesophagus			
subjects affected / exposed	1 / 72 (1.39%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
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	1 / 72 (1.39%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	10 / 72 (13.89%)	4 / 73 (5.48%)	
occurrences causally related to treatment / all	0 / 14	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung disorder			
subjects affected / exposed	1 / 72 (1.39%)	0 / 73 (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	0 / 72 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
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			
Neck pain			
subjects affected / exposed	1 / 72 (1.39%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis viral			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 72 (1.39%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	2 / 72 (2.78%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 72 (1.39%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 72 (2.78%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyelonephritis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 72 (0.00%)	1 / 73 (1.37%)	
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: 5 %

Non-serious adverse events	Control Group	10-AS01E Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 72 (58.33%)	65 / 73 (89.04%)	
Nervous system disorders			
Headache			
subjects affected / exposed	22 / 72 (30.56%)	30 / 73 (41.10%)	
occurrences (all)	34	42	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	23 / 72 (31.94%)	37 / 73 (50.68%)	
occurrences (all)	32	51	
Injection site erythema			
subjects affected / exposed	2 / 72 (2.78%)	19 / 73 (26.03%)	
occurrences (all)	2	26	
Injection site pain			
subjects affected / exposed	9 / 72 (12.50%)	59 / 73 (80.82%)	
occurrences (all)	10	98	
Injection site swelling			
subjects affected / exposed	0 / 72 (0.00%)	9 / 73 (12.33%)	
occurrences (all)	0	12	
Pyrexia			
subjects affected / exposed	7 / 72 (9.72%)	10 / 73 (13.70%)	
occurrences (all)	7	12	
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	15 / 72 (20.83%)	22 / 73 (30.14%)	
occurrences (all)	16	27	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 72 (1.39%)	5 / 73 (6.85%)	
occurrences (all)	1	5	
Oropharyngeal pain			
subjects affected / exposed	5 / 72 (6.94%)	5 / 73 (6.85%)	
occurrences (all)	6	5	
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 72 (5.56%) 4	7 / 73 (9.59%) 7	
Urinary tract infection subjects affected / exposed occurrences (all)	4 / 72 (5.56%) 4	1 / 73 (1.37%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 March 2014	• Because the volumes of the individual blood samples that will be collected were re-distributed after discussion with the central laboratory. The total volume of blood collected per subject across scheduled visits and at AECOPD visits remains similar. • Because information on processing and storage temperature until shipment was updated for some of the samples after discussion with the central laboratory. • To clarify that the plasma obtained during PBMC processing will be kept for potential future additional testing. • To clarify that white blood cell differential count will be done on blood samples for safety assessment. • In addition, some other, minor clarifications have been made and the list of contributing authors has been updated
15 December 2014	• To add clarification in the tertiary objectives: because acute exacerbations of COPD are complex events, triggered by multiple (interacting) pathogens, assessing the natural immunity to other pathogens might be important for interpretation of the data. • To add an additional blood sample for haematology assessment at each AECOPD visit. This blood sample will be collected to describe the systemic inflammation at time of exacerbation in terms of white blood cells and differential cell counts. • To clarify the list of concomitant medication that may lead to elimination of a subject from ATP analysis of immunogenicity (Section 7.6.2): because oral corticosteroids are commonly used in treatment of exacerbations, the administration of oral corticosteroids given for this indication will not fall under the definition of "chronic administration of immunosuppressants or other immune modifying drugs at any time during the study period", used to determine elimination from the ATP analysis of immunogenicity. • To add a benefit: risk assessment section (Section 1.3). • In addition, a typo in the footnote of the table of intervals between visits (Table 9) has been corrected and the list of contributing authors has been updated.

15 April 2016	• In compliance with ICH requirements, the protocol mentions that all results will be presented in an integrated report at the end of the study. • Following re-development and re-validation of the anti-PD ELISA, a new cut-off was defined. • Reference to the GSK Biologicals' Laval laboratory was removed, as this laboratory will not be used in the study. In addition, this laboratory is no longer part of GSK Biologicals' laboratories. • Internal assay qualification procedures were revised and it was decided that the level of characterisation of the ELISA assays can be minimal (set-up level) for this study as immunogenicity data are descriptive. In consequence, the assays will be standardized but not qualified as stated in the original version. This change will not impact the validity of the results. • A tertiary endpoint was added as the presence of viral pathogens in sputum will be examined as part of microbiome analysis. • In order to see early effects of the vaccine on the microbiome, analysis on fresh sputum samples (culture results) will be done on all available data up to the data lock point of the interim analysis. • In order to have a first look whether or not the inves-tigational vaccine has an impact on AECOPD, AECOPD analyses will be done up to the data lock point of the interim analysis. • Wording was added to clarify process for collection of sputum H. influenzae sweeps. • Wording was updated in order to be aligned with the Statistical Ananlysis Plan. • In addition, minor edits in other sections were made for clarification purposes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported