Clinical trial results:
A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability, and Efficacy of GEN-004, a Pneumococcal Protein Subunit Vaccine, on Colonization Following Intranasal Challenge with S. pneumoniae

Summary

EudraCT number	2014-000944-13
Trial protocol	GB
Global end of trial date	19 July 2016

Results information

Result version number	v1 (current)
This version publication date	07 July 2017
First version publication date	07 July 2017

Trial information

Trial identification

Sponsor protocol code	GEN-004-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02116998
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genocea Biosciences, Inc.
Sponsor organisation address	100 Acorn Park Drive, 5th Floor, Cambridge, United States, MA 02140
Public contact	Director of Regulatory Sciences, TMC Pharma Services, 44 01252842255, Allison.Gillespie@TMCPharma.com
Scientific contact	Director of Regulatory Sciences, TMC Pharma Services, 44 01252842255, Allison.Gillespie@TMCPharma.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	19 July 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to evaluate the efficacy of intramuscular GEN-004 (a recombinant S. pneumoniae protein subunit vaccine) with aluminum hydroxide as adjuvant compared with a placebo control. Efficacy was assessed in healthy adult subjects by evaluating the reduction in nasopharyngeal colonisation following intranasal inoculation with S. pneumoniae serotype 6B, as measured by the proportion of colonised subjects at 2, 7, and 14 days post-inoculation.

Protection of trial subjects:

Two weeks after the third dose of study treatment, subjects were inoculated intranasally with S. pneumoniae serotype 6B (c. 80,000 CFU/100 µl per nostril). If a suspected pneumococcal infection occurred during the 14 days after inoculation, subjects were to be treated with antibiotics.

Background therapy:

Not applicable

Evidence for comparator:

This was a placebo-controlled trial. The challenge model (intranasal inoculation with S.pneumoniae after 3 doses of study treatment, with a placebo control) permits demonstration of biologic activity of the test article, GEN-004, measured by prevention of acquisition or colonisation.

Actual start date of recruitment	21 August 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 96
Worldwide total number of subjects	96
EEA total number of subjects	96

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)	96
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All subjects were recruited at a single centre in the United Kingdom between 18 Aug 2014 and 16 Apr 2016.

Pre-assignment

Screening details:

Screening took place from -28 to -1 days before randomisation, when safety checks were undertaken: safety laboratory parameters (haematology, biochemistry, urinalysis, serology), physical examination, pregnancy test, and a review of medical history and concomitant medications. All screened subjects participated in the trial.

Period 1

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

Blinding implementation details:

An unblinded pharmacist (or other appropriately trained individual) at each site prepared each dose. This individual had no contact with the subjects and minimised contact with other study site personnel.

Arms

Are arms mutually exclusive?	Yes
Arm title	GEN-004

Arm description:

Each subject was to receive 3 doses at 4 week (28 ±3 days) intervals of 100 µg GEN-004 with 350 µg of aluminium hydroxide (Days 1, 29, and 57). On Day 71, each subject was challenged with an intranasal inoculation of S. pneumoniae. Nasal washes were performed on Days 73, 78, and 85 to evaluate colonisation.

Arm type	Experimental
Investigational medicinal product name	GEN-004
Investigational medicinal product code	GEN-004
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of 100 µg GEN-004 with 350 µg of aluminum hydroxide administered as an intramuscular injection at 4-week intervals.

Arm title	Placebo

Arm description:

Each subject was to receive 3 doses at 4 week (28 ±3 days) intervals of placebo (0.9% saline) (Days 1, 29, and 57). On Day 71, each subject was challenged with an intranasal inoculation of S.pneumoniae. Nasal washes were performed on Days 73, 78, and 85 to evaluate colonisation.

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

Dosage and administration details:

Three doses of placebo (0.9% saline) administered as an intramuscular injection at 4-week intervals.

Number of subjects in period 1	GEN-004	Placebo
Started	46	50
Completed	45	49
Not completed	1	1
Adverse event, non-fatal	1	-
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	GEN-004
Reporting group description:	
Each subject was to receive 3 doses at 4 week (28 ±3 days) intervals of 100 µg GEN-004 with 350 µg of aluminium hydroxide (Days 1, 29, and 57). On Day 71, each subject was challenged with an intranasal inoculation of S. pneumoniae. Nasal washes were performed on Days 73, 78, and 85 to evaluate colonisation.	
Reporting group title	Placebo
Reporting group description:	
Each subject was to receive 3 doses at 4 week (28 ±3 days) intervals of placebo (0.9% saline) (Days 1, 29, and 57). On Day 71, each subject was challenged with an intranasal inoculation of S.pneumoniae. Nasal washes were performed on Days 73, 78, and 85 to evaluate colonisation.	

Reporting group values	GEN-004	Placebo	Total
Number of subjects	46	50	96
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	46	50	96
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	22.3	23.1	
standard deviation	± 5.71	± 5.47	-
Gender categorical Units: Subjects			
Female	27	29	56
Male	19	21	40
Actual inoculation dose of S.pneumoniae after vaccination			
Actual challenge dose of S.pneumoniae on Day 71, 2 weeks after the last dose of trial treatment.			
Units: CFU/100 microlitres			
arithmetic mean	77396.9	77449.1	
standard deviation	± 4774.65	± 5250.73	-

End points

End points reporting groups

Reporting group title	GEN-004

Reporting group description:

Each subject was to receive 3 doses at 4 week (28 ±3 days) intervals of 100 µg GEN-004 with 350 µg of aluminium hydroxide (Days 1, 29, and 57). On Day 71, each subject was challenged with an intranasal inoculation of S. pneumoniae. Nasal washes were performed on Days 73, 78, and 85 to evaluate colonisation.

Reporting group title	Placebo

Reporting group description:

Each subject was to receive 3 doses at 4 week (28 ±3 days) intervals of placebo (0.9% saline) (Days 1, 29, and 57). On Day 71, each subject was challenged with an intranasal inoculation of S.pneumoniae. Nasal washes were performed on Days 73, 78, and 85 to evaluate colonisation.

Primary: S.pneumoniae colonisation 2 days post-inoculation measured by culture

End point title	S.pneumoniae colonisation 2 days post-inoculation measured by culture

End point description:

Subjects with intranasal colonisation as measured by culture

End point type	Primary

End point timeframe:

2 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[1]	50[2]		
Units: Subjects	18	26		

Notes:

[1] - ITT population

[2] - ITT population

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo

Statistical analysis description:

Fisher's exact test comparing proportions

Comparison groups	GEN-004 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.5109
Method	Fisher exact

Notes:

[3] - Fisher's exact test comparing proportions of subjects with colonisation

Primary: S.pneumoniae colonisation 7 days post-inoculation measured by culture

End point title	S.pneumoniae colonisation 7 days post-inoculation measured by culture

End point description:

Subjects with intranasal colonisation as measured by culture

End point type	Primary

End point timeframe:

7 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[4]	50[5]		
Units: Subjects	20	28		

Notes:

[4] - ITT population

[5] - ITT population

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo

Statistical analysis description:

Fisher's exact test comparing proportions of subjects with colonisation

Comparison groups	GEN-004 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3644
Method	Fisher exact

Primary: S.pneumoniae colonisation 14 days post-inoculation measured by culture

End point title	S.pneumoniae colonisation 14 days post-inoculation measured by culture

End point description:

Subjects with intranasal colonisation as measured by culture

End point type	Primary

End point timeframe:

14 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[6]	50[7]		
Units: Subjects	17	24		

Notes:
[6] - ITT population
[7] - ITT population

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo
Comparison groups	GEN-004 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.5111
Method	Fisher exact

Notes:
[8] - Fisher's exact test comparing proportions of subjects with colonisation

Primary: S.pneumoniae colonisation at any time post-inoculation measured by culture

End point title	S.pneumoniae colonisation at any time post-inoculation measured by culture

End point description:

End point type	Primary

End point timeframe:
At any time post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[9]	50[10]		
Units: Subjects	21	30		

Notes:
[9] - ITT population
[10] - ITT population

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo
Comparison groups	Placebo v GEN-004
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.378
Method	Fisher exact

Notes:
[11] - Fisher's Exact Test comparing proportions

Secondary: S.pneumoniae colonisation 2 days post-inoculation measured by PCR	
End point title	S.pneumoniae colonisation 2 days post-inoculation measured by PCR

End point description:

Subjects with intranasal colonisation as measured by culture

End point type	Secondary

End point timeframe:

2 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[12]	50[13]		
Units: Subjects	19	30		

Notes:

[12] - ITT population

[13] - ITT population

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo
Comparison groups	GEN-004 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.1866
Method	Fisher exact

Notes:

[14] - Fisher's Exact Test comparing proportions

Secondary: S.pneumoniae colonisation 7 days post-inoculation measured by PCR	
End point title	S.pneumoniae colonisation 7 days post-inoculation measured by PCR

End point description:

Subjects with intranasal colonisation as measured by PCR

End point type	Secondary

End point timeframe:

7 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[15]	50[16]		
Units: Subjects	21	28		

Notes:

[15] - ITT population

[16] - ITT population

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo
Comparison groups	GEN-004 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.4952
Method	Fisher exact

Notes:

[17] - Fisher's Exact Test comparing proportions

Secondary: S.pneumoniae colonisation 14 days post-inoculation measured by PCR

End point title	S.pneumoniae colonisation 14 days post-inoculation measured by PCR

End point description:

Subjects with intranasal colonisation as measured by PCR

End point type	Secondary

End point timeframe:

14 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[18]	50[19]		
Units: Subjects	16	27		

Notes:

[18] - ITT population

[19] - ITT population

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo

Statistical analysis description:

Fisher's Exact Test comparing proportions

Comparison groups	GEN-004 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1258
Method	Fisher exact

Secondary: S.pneumoniae colonisation any time post-inoculation measured by PCR

End point title	S.pneumoniae colonisation any time post-inoculation measured by PCR

End point description:

Subjects with intranasal colonisation as measured by PCR

End point type	Secondary

End point timeframe:

Any time post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[20]	50[21]		
Units: Subjects	24	31		

Notes:

[20] - ITT population

[21] - ITT population

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo

Statistical analysis description:

Fisher's Exact Test comparing proportions

Comparison groups	GEN-004 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8181
Method	Fisher exact

Secondary: Time of maximum colonisation density based on culture - 2 days

End point title	Time of maximum colonisation density based on culture - 2 days

End point description:

Microbiologic culture density was measured as the number of CFUs/mL of nasal wash.

End point type	Secondary

End point timeframe:

2 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[22]	50[23]		
Units: Subjects	3	12		

Notes:

[22] - ITT population

[23] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Time of maximum colonisation density based on culture - 7 days

End point title	Time of maximum colonisation density based on culture - 7 days

End point description:

Microbiologic culture density was measured as the number of CFUs/mL of nasal wash.

End point type	Secondary

End point timeframe:

7 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[24]	50[25]		
Units: Subjects	8	10		

Notes:

[24] - ITT population

[25] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Time of maximum colonisation density based on culture - 14 days

End point title	Time of maximum colonisation density based on culture - 14 days

End point description:

Microbiologic culture density was measured as the number of CFUs/mL of nasal wash.

End point type	Secondary

End point timeframe:

14 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[26]	50[27]		
Units: Subjects	5	4		

Notes:

[26] - ITT population

[27] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Time of maximum colonisation density based on PCR - 2 days

End point title	Time of maximum colonisation density based on PCR - 2 days

End point description:

qPCR density was measured as copies/mL of nasal wash.

End point type	Secondary

End point timeframe:

2 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[28]	50[29]		
Units: Subjects	5	12		

Notes:

[28] - ITT population

[29] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Time of maximum colonisation density based on PCR - 7 days

End point title	Time of maximum colonisation density based on PCR - 7 days

End point description:

qPCR density was measured as copies/mL of nasal wash.

End point type	Secondary

End point timeframe:

7 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[30]	50[31]		
Units: Subjects	6	9		

Notes:

[30] - ITT population

[31] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Time of maximum colonisation density based on PCR - 14 days

End point title	Time of maximum colonisation density based on PCR - 14 days

End point description:

qPCR density was measured as copies/mL of nasal wash.

End point type	Secondary

End point timeframe:

14 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[32]	50[33]		
Units: Subjects	7	4		

Notes:

[32] - ITT population

[33] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for colonisation density based on culture

End point title	AUC for colonisation density based on culture

End point description:

Area under the curve (AUC) for density of colonisation vs time post-inoculation was calculated for each subject, using the trapezoidal rule. AUC for colonisation density (based on culture) vs. post-inoculation time is presented by vaccine group for the ITT Population - all colonization (raw) data

End point type	Secondary

End point timeframe:

All post-inoculation colonisation data

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[34]	43[35]		
Units: CFUs/mL				
arithmetic mean (standard deviation)	101400.49 (± 361625.781)	31433.68 (± 163789.142)		

Notes:

[34] - Includes only subjects with all post-inoculation nasal wash samples

[35] - Includes only subjects with all post-inoculation nasal wash samples

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo

Statistical analysis description:

Only subjects who had all post-inoculation nasal wash samples collected were included in the analysis. Comparability of vaccine groups was assessed using Wilcoxon’s rank sum test based on untransformed colonisation density data.

Comparison groups	GEN-004 v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6474
Method	Wilcoxon’s rank sum test

Secondary: AUC for colonisation density based on PCR

End point title	AUC for colonisation density based on PCR

End point description:

Microbiologic culture density was measured as PCR copy number/mL of nasal wash.

End point type	Secondary

End point timeframe:

Anytime post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[36]	50[37]		
Units: copy number/mL				
arithmetic mean (standard deviation)	168622.55 (± 513395.953)	37952.22 (± 148218.136)		

Notes:

[36] - ITT population

[37] - ITT population

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo

Statistical analysis description:

Only subjects who had all post-inoculation nasal wash samples collected were included in the analysis. Comparability of vaccine groups was assessed using Wilcoxon’s rank sum test based on untransformed

colonisation density data.

Comparison groups	Placebo v GEN-004
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8827
Method	Wilcoxon’s rank sum test

Secondary: Duration of colonisation based on culture

End point title	Duration of colonisation based on culture

End point description:

Only subjects who had all 3 nasal washes collected were included in this analysis.

End point type	Secondary

End point timeframe:

Up to 14 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[38]	50[39]		
Units: Days				
arithmetic mean (standard deviation)	5.76 (± 6.058)	7.27 (± 6.155)		

Notes:

[38] - ITT population

[39] - ITT population

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo
Comparison groups	GEN-004 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2682
Method	Wilcoxon’s rank sum test

Secondary: Duration of colonisation based on PCR

End point title	Duration of colonisation based on PCR

End point description:

Only subjects who had all 3 nasal washes collected were included in this analysis.

End point type	Secondary

End point timeframe:

Up to 14 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46[40]	50[41]		
Units: Days				
arithmetic mean (standard deviation)	6.14 (± 5.778)	7.71 (± 6.258)		

Notes:

[40] - ITT population

[41] - ITT population

Statistical analyses

Statistical analysis title	Comparison of GEN-004 vs placebo
Comparison groups	GEN-004 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1824
Method	Wilcoxon’s rank sum test

Secondary: Positive IgG responders to SP0148 antigen

End point title	Positive IgG responders to SP0148 antigen

End point description:

IgG titers (measured by enzyme-linked immunosorbent assay [ELISA]) against each GEN-004 antigen (SP0148, SP2108, and SP1912) were transformed using a log base 10, and summarised by vaccine group for each time of sampling. The fold rise in titre defined as the post-baseline result divided by the baseline result was calculated for the 3 antibody titers. A positive responder was defined as a ≥4-fold rise in IgG titre from baseline.

End point type	Secondary

End point timeframe:

Up to 14 days post-baseline

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43[42]	50[43]		
Units: Subjects	43	0		

Notes:

[42] - Subjects with available data are included in the denominator for this analysis

[43] - Subjects with available data are included in the denominator for this analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Positive IgG responders to SP1912 antigen

End point title	Positive IgG responders to SP1912 antigen

End point description:

IgG titers (measured by enzyme-linked immunosorbent assay [ELISA]) against each GEN-004 antigen (SP0148, SP2108, and SP1912) were transformed using a log base 10, and summarised by vaccine group for each time of sampling. The fold rise in titre defined as the post-baseline result divided by the baseline result was calculated for the 3 antibody titers. A positive responder was defined as a ≥4-fold rise in IgG titre from baseline.

End point type	Secondary

End point timeframe:

Up to 14 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43[44]	50[45]		
Units: Subjects	36	0		

Notes:

[44] - Subjects with available data are included in the denominator for this analysis

[45] - Subjects with available data are included in the denominator for this analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Positive IgG responders to SP2108 antigen

End point title	Positive IgG responders to SP2108 antigen

End point description:

IgG titers (measured by enzyme-linked immunosorbent assay [ELISA]) against each GEN-004 antigen (SP0148, SP2108, and SP1912) were transformed using a log base 10, and summarised by vaccine group for each time of sampling. The fold rise in titre defined as the post-baseline result divided by the baseline result was calculated for the 3 antibody titers. A positive responder was defined as a ≥4-fold rise in IgG titre from baseline.

End point type	Secondary

End point timeframe:

Up to 14 days post-inoculation

End point values	GEN-004	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43[46]	50[47]		
Units: Subjects	43	0		

Notes:

[46] - Subjects with available data are included in the denominator for this analysis

[47] - Subjects with available data are included in the denominator for this analysis

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of trial medication (Day 1) to 14 days post-inoculation with S.pneumoniae (Day 85) for all adverse events. From Day 1 to Day 383 for SAEs.

Adverse event reporting additional description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. The Investigator evaluated the intensity of each AE in accordance with the FDA Vaccine Toxicity Scale 7.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	GEN-004

Reporting group description:

Subjects treated with up to 3 intramuscular doses of GEN-004 vaccine with aluminium adjuvant, at 4-week intervals.

Reporting group title	Placebo

Reporting group description:

Subjects treated with up to 3 intramuscular doses of placebo, at 4-week intervals.

Serious adverse events	GEN-004	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 46 (6.52%)	1 / 50 (2.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 46 (2.17%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 46 (2.17%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Swelling face			

subjects affected / exposed	1 / 46 (2.17%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 1	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	GEN-004	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 46 (76.09%)	38 / 50 (76.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 46 (23.91%)	9 / 50 (18.00%)	
occurrences (all)	11	9	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 46 (2.17%)	3 / 50 (6.00%)	
occurrences (all)	1	3	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	9 / 46 (19.57%)	3 / 50 (6.00%)	
occurrences (all)	9	3	
Cough			
subjects affected / exposed	3 / 46 (6.52%)	3 / 50 (6.00%)	
occurrences (all)	3	3	
Infections and infestations			
Rhinitis			
subjects affected / exposed	8 / 46 (17.39%)	10 / 50 (20.00%)	
occurrences (all)	8	10	
Upper respiratory tract infection			
subjects affected / exposed	2 / 46 (4.35%)	3 / 50 (6.00%)	
occurrences (all)	2	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported