Clinical trial results:
IMMUNOGENICITY AND SAFETY STUDY OF VLA15, A MULTIVALENT RECOMBINANT OSPA BASED VACCINE CANDIDATE AGAINST LYME BORRELIOSIS, IN HEALTHY ADULTS AGED 18 TO 65 YEARS - A RANDOMIZED, CONTROLLED, OBSERVER-BLIND PHASE 2 STUDY.

Summary

EudraCT number	2018-003379-37
Trial protocol	DE BE AT
Global end of trial date	02 October 2020

Results information

Result version number	v1 (current)
This version publication date	24 June 2022
First version publication date	24 June 2022

Trial information

Trial identification

Sponsor protocol code	VLA15-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03769194
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Valneva Austria GmbH
Sponsor organisation address	Campus Vienna Biocenter 3, Vienna, Austria, 1030
Public contact	Valneva Clinical Operations, Valneva Austria GmbH, 43 120620, info@valneva.com
Scientific contact	Valneva Clinical Operations, Valneva Austria GmbH, 43 120620, info@valneva.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	08 July 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the optimal dose of VLA15 in healthy adults aged 18 - 65 years up to Day 85.

Protection of trial subjects:

Number of study visits and interventions was limited to the minimum required to generate the required safety and immunogenicity data. Participants were closely monitored for safety during the entire study period. Solicited adverse events were monitored by way of e-diaries for 7 consecutive days after each vaccination. An independent Data Safety Monitoring Board was established that continuously reviewed accruing safety information or ad-hoc safety data, as needed, to ensure participants' wellbeing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 December 2018
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 States: 355
Country: Number of subjects enrolled	Belgium: 44
Country: Number of subjects enrolled	Germany: 173
Worldwide total number of subjects	572
EEA total number of subjects	217

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)	568
From 65 to 84 years	4

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited between 21-Dec-2018 and 26-Sep-2019 at one study site in Belgium, two study sites in Germany and six study sites in the USA.

Pre-assignment

Screening details:

In total, 658 subjects were screened, 85 were screening failures. The most frequent reason for screening failure was subjects not meeting the inclusion or exclusion criteria (42 [49.4%] subjects); followed by other reasons (26 [30.6%] subjects) and withdrawal of consent (20 [23.5%] subjects).

Period 1

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

Blinding implementation details:

The study sponsor and trial statisticians were unblinded at the time of the Interim Analysis, after the respective database snapshot has been performed

Arms

Are arms mutually exclusive?	Yes
Arm title	VLA15 90µg

Arm description:

At each vaccination day (Day 1, 29 and 57) treatment with VLA15 90 µg w/ alum

Arm type	Experimental
Investigational medicinal product name	VLA15 w/Alum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

VLA15 Drug Product w/ Alum consists of the three proteins Lip-D1B2B, Lip-D4Bva3B and Lip-D5B6B that are formulated in 1:1:1 ratio in buffer (10 mM L-Methionine, 10 mM NaH2PO4 dihydrate, 150 mM NaCl, 5% (w/v) Sucrose, 0.05% (v/v) Tween®20 at pH 6.7) to a concentration of 180 µg/mL total protein (i.e. 60 µg/mL for each protein). Depending on the assigned treatment group either 500 µl (treatment group VLA15 90 w/ Alum), 750µl (VLA15 135 w/ Alum) or 1ml (VLA15 180 w/ Alum) are administered per vaccination day

Arm title	VLA15 135 µg

Arm description:

At each vaccination day (Day 1, 29 and 57) treatment with VLA15 135 µg w/ alum

Arm type	Experimental
Investigational medicinal product name	VLA15 w/Alum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

VLA15 Drug Product w/ Alum consists of the three proteins Lip-D1B2B, Lip-D4Bva3B and Lip-D5B6B that are formulated in 1:1:1 ratio in buffer (10 mM L-Methionine, 10 mM NaH2PO4 dihydrate, 150 mM NaCl, 5% (w/v) Sucrose, 0.05% (v/v) Tween®20 at pH 6.7) to a concentration of 180 µg/mL total protein (i.e. 60 µg/mL for each protein). Depending on the assigned treatment group either 500 µl (treatment

group VLA15 90 w/ Alum), 750µl (VLA15 135 w/ Alum) or 1ml (VLA15 180 w/ Alum) are administered per vaccination day

Arm title	VLA15 180 µg
Arm description:	
At each vaccination day (Day 1, 29 and 57) treatment with VLA15 180 µg w/ alum	
Arm type	Experimental
Investigational medicinal product name	VLA15 w/Alum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

VLA15 Drug Product w/ Alum consists of the three proteins Lip-D1B2B, Lip-D4Bva3B and Lip-D5B6B that are formulated in 1:1:1 ratio in buffer (10 mM L-Methionine, 10 mM NaH2PO4 dihydrate, 150 mM NaCl, 5% (w/v) Sucrose, 0.05% (v/v) Tween®20 at pH 6.7) to a concentration of 180 µg/mL total protein (i.e. 60 µg/mL for each protein). Depending on the assigned treatment group either 500 µl (treatment group VLA15 90 w/ Alum), 750µl (VLA15 135 w/ Alum) or 1ml (VLA15 180 w/ Alum) are administered per vaccination day

Arm title	Placebo
Arm description:	
At each vaccination day (Day 1, 29 and 57) treatment with Placebo	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The VLA Placebo is a PBS buffer based on Dulbecco’s PBS media formulation without Calcium and Magnesium. Placebo was administered at 1 mL injection of PBS

Number of subjects in period 1	VLA15 90µg	VLA15 135 µg	VLA15 180 µg
Started	29	214	205
D85	28	204	201
Completed	25	196	197
Not completed	4	18	8
Consent withdrawn by subject	-	4	2
Physician decision	-	1	-
Adverse event, non-fatal	-	2	2
other	1	5	1
Lost to follow-up	3	6	3

Number of subjects in period 1	Placebo

Started	124
D85	121
Completed	115
Not completed	9
Consent withdrawn by subject	1
Physician decision	-
Adverse event, non-fatal	-
other	2
Lost to follow-up	6

Baseline characteristics

Reporting groups

Reporting group title	overall study period

Reporting group description: -

Reporting group values	overall study period	Total	
Number of subjects	572	572	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	568	568	
From 65-84 years	4	4	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	40.8		
standard deviation	± 12.9	-	
Gender categorical Units: Subjects			
Female	312	312	
Male	260	260	

Subject analysis sets

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Population includes all subjects who entered into the study and received at least one vaccination. The Safety Population will be used for all safety analyses as well as demographic data. All analyses based on the Safety Population will be carried out using the actual treatment received.

Subject analysis set title	mITT Population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mITT population is defined to include all subjects enrolled who received at least one vaccination. Subjects will be analyzed according to the treatment group they had been allocated to, rather than by the actual treatment, they received.

Subject analysis set title	PP population
Subject analysis set type	Per protocol

Subject analysis set description:

The PP Population was the primary analysis population and will exclude all subjects from the mITT that fulfilled at least one of the major protocol deviation criteria

Reporting group values	Safety Population	mITT Population	PP population
Number of subjects	572	572	536
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	568	568	532
From 65-84 years	4	4	4
85 years and over			
Age continuous			
Units: years			
arithmetic mean	40.8	40.8	41.1
standard deviation	± 12.9	± 12.9	± 12.7
Gender categorical			
Units: Subjects			
Female	312	312	298
Male	260	260	238

End points

End points reporting groups

Reporting group title	VLA15 90µg
Reporting group description:	
At each vaccination day (Day 1, 29 and 57) treatment with VLA15 90 µg w/ alum	
Reporting group title	VLA15 135 µg
Reporting group description:	
At each vaccination day (Day 1, 29 and 57) treatment with VLA15 135 µg w/ alum	
Reporting group title	VLA15 180 µg
Reporting group description:	
At each vaccination day (Day 1, 29 and 57) treatment with VLA15 180 µg w/ alum	
Reporting group title	Placebo
Reporting group description:	
At each vaccination day (Day 1, 29 and 57) treatment with Placebo	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Population includes all subjects who entered into the study and received at least one vaccination. The Safety Population will be used for all safety analyses as well as demographic data. All analyses based on the Safety Population will be carried out using the actual treatment received.	
Subject analysis set title	mITT Population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The mITT population is defined to include all subjects enrolled who received at least one vaccination. Subjects will be analyzed according to the treatment group they had been allocated to, rather than by the actual treatment, they received.	
Subject analysis set title	PP population
Subject analysis set type	Per protocol
Subject analysis set description:	
The PP Population was the primary analysis population and will exclude all subjects from the mITT that fulfilled at least one of the major protocol deviation criteria	

Primary: GMTs (Geometric Mean Titers) for IgG against each OspA serotype ST1 to ST6

End point title	GMTs (Geometric Mean Titers) for IgG against each OspA serotype ST1 to ST6
End point description:	
Geometric Mean Titers (GMTs) for Immunoglobulin G (IgG) against each Outer surface protein A (OspA) serotype ST1 to ST6, determined by Enzyme-Linked Immunosorbent Assay (ELISA) at Day 85	
End point type	Primary
End point timeframe:	
Day 85	

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	192	194	121
Units: U/mL				
geometric mean (confidence interval 95%)				
ST1	74.3 (46.4 to 119.0)	101.9 (87.1 to 119.4)	115.8 (98.8 to 135.7)	21.7 (20.0 to 23.6)
ST2	180.9 (124.8 to 262.3)	279.3 (247.1 to 315.8)	303.7 (266.5 to 346.1)	21.1 (20.0 to 22.3)
ST3	267.4 (194.8 to 367.1)	283.2 (248.2 to 323.1)	308.6 (266.8 to 356.8)	20.8 (19.8 to 21.8)
ST4	117.0 (76.6 to 178.7)	170.9 (150.5 to 194.2)	190.7 (165.9 to 219.2)	21.8 (20.4 to 23.4)
ST5	118.3 (78.3 to 178.9)	176.0 (154.2 to 201.0)	199.6 (172.5 to 230.9)	21.4 (20.2 to 22.6)
ST6	115.6 (76.5 to 174.7)	183.6 (161.7 to 208.4)	208.7 (181.8 to 239.6)	21.8 (20.3 to 23.4)

Statistical analyses

Statistical analysis title	Overall comparison between treatment groups

Statistical analysis description:

GMTs were compared by applying an analysis of covariance (ANCOVA) including the factors treatment group and country. This was done using log10 transformed data and taking the anti-log of the resulting point estimates for the least squares means, least squares means differences and the corresponding 95% CIs.

Comparison groups	VLA15 135 µg v VLA15 90µg v VLA15 180 µg v Placebo
Number of subjects included in analysis	536
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Secondary: GMTs (Geometric Mean Titers) for IgG against each OspA serotype ST1 to ST6

End point title	GMTs (Geometric Mean Titers) for IgG against each OspA serotype ST1 to ST6

End point description:

GMTs for IgG against each OspA serotype (ST1 to ST6), determined by ELISA, at Day 1, 29, 57, 180, 236, and Month 12

End point type	Secondary

End point timeframe:

Day 1, 29, 57, 180, 236, and Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	192	194	121
Units: U/ml				
geometric mean (confidence interval 95%)				
ST1 Day 1	20.8 (19.2 to 22.5)	20.5 (19.8 to 21.3)	20.2 (19.8 to 20.6)	21.6 (19.9 to 23.5)
ST1 Day 29	21.1 (18.9 to 23.5)	21.8 (20.0 to 23.8)	21.2 (20.1 to 22.4)	21.7 (20.0 to 23.7)
ST1 Day 57	32.7 (25.1 to 42.6)	37.5 (32.4 to 43.3)	41.2 (35.7 to 47.5)	21.9 (20.1 to 23.8)
ST1 Day 180	26.2 (19.9 to 34.5)	32.8 (28.8 to 37.3)	33.9 (30.0 to 38.3)	21.0 (19.8 to 22.3)
ST1 Day 236	22.2 (18.8 to 26.1)	25.7 (22.8 to 28.8)	26.2 (23.1 to 29.7)	21.5 (19.6 to 23.6)
ST1 Day 365	20.9 (19.1 to 22.9)	23.4 (21.4 to 25.6)	23.0 (21.3 to 24.9)	21.4 (19.9 to 22.9)
ST2 Day 1	21.3 (18.7 to 24.2)	20.0 (20.0 to 20.0)	20.1 (19.9 to 20.2)	20.7 (19.7 to 21.8)
ST2 Day 29	21.1 (18.9 to 23.7)	21.1 (20.0 to 22.2)	21.4 (20.5 to 22.4)	21.0 (19.9 to 22.1)
ST2 Day 57	69.0 (47.7 to 99.8)	89.2 (75.9 to 104.9)	107.8 (92.7 to 125.2)	21.3 (20.0 to 22.6)
ST2 Day 180	41.2 (29.3 to 57.9)	62.5 (54.5 to 71.7)	67.1 (58.3 to 77.1)	20.6 (19.7 to 21.5)
ST2 Day 236	26.6 (21.2 to 33.4)	36.8 (32.1 to 42.2)	35.7 (30.9 to 41.2)	20.5 (19.5 to 21.5)
ST2 Day 365	21.8 (19.2 to 24.7)	24.6 (22.8 to 26.6)	24.8 (23.1 to 26.6)	20.6 (19.7 to 21.5)
ST3 Day 1	21.9 (19.1 to 25.1)	20.4 (20.0 to 20.8)	20.1 (19.9 to 20.4)	20.4 (19.6 to 21.2)
ST3 Day 29	23.7 (20.0 to 28.0)	21.7 (20.2 to 23.2)	21.2 (20.3 to 22.1)	20.8 (19.8 to 21.9)
ST3 Day 57	110.2 (71.1 to 171.0)	123.8 (104.4 to 146.9)	145.8 (122.8 to 173.0)	21.2 (20.0 to 22.6)
ST3 Day 180	53.1 (35.6 to 79.1)	63.1 (55.2 to 72.2)	68.7 (59.5 to 79.2)	20.5 (19.8 to 21.3)
ST3 Day 236	35.3 (25.7 to 48.6)	35.8 (31.2 to 41.1)	39.0 (33.3 to 45.8)	20.6 (19.7 to 21.7)
ST3 Day 365	25.2 (19.9 to 31.8)	25.6 (23.5 to 27.9)	27.0 (24.5 to 29.8)	20.5 (19.8 to 21.3)
ST4 Day 1	21.4 (18.7 to 24.4)	21.0 (20.3 to 21.7)	20.2 (19.9 to 20.6)	21.7 (20.3 to 23.2)
ST4 Day 29	22.1 (19.1 to 25.6)	21.9 (20.4 to 23.6)	21.4 (20.4 to 22.4)	22.0 (20.4 to 23.6)
ST4 Day 57	45.9 (32.8 to 64.2)	57.4 (49.5 to 66.6)	64.7 (55.5 to 75.5)	22.0 (20.4 to 23.8)
ST4 Day 180	32.8 (24.1 to 44.6)	48.1 (42.5 to 54.5)	49.3 (43.1 to 56.3)	21.5 (20.2 to 22.9)
ST4 Day 236	25.5 (20.6 to 31.5)	32.8 (29.0 to 37.2)	31.9 (27.7 to 36.6)	21.7 (20.0 to 23.5)
ST4 Day 365	21.8 (19.2 to 24.7)	26.5 (24.2 to 28.9)	25.5 (23.2 to 27.9)	21.7 (20.3 to 23.2)
ST5 Day 1	20.6 (19.4 to 21.8)	20.7 (20.1 to 21.3)	20.2 (19.8 to 20.5)	21.4 (20.2 to 22.7)
ST5 Day 29	20.7 (19.2 to 22.4)	21.2 (20.0 to 22.5)	21.0 (20.2 to 21.9)	21.4 (20.1 to 22.7)
ST5 Day 57	42.7 (29.8 to 61.3)	57.9 (44.9 to 67.2)	72.2 (61.6 to 84.7)	21.5 (20.2 to 22.9)

ST5 Day 180	26.7 (20.7 to 34.3)	44.0 (38.8 to 49.8)	50.0 (43.5 to 57.4)	21.1 (20.0 to 22.3)
ST5 Day 236	23.0 (19.6 to 27.0)	31.0 (27.5 to 35.0)	32.4 (28.0 to 37.4)	21.5 (20.0 to 23.1)
ST5 Day 365	21.7 (19.3 to 24.3)	24.0 (22.3 to 25.8)	24.9 (22.7 to 27.2)	21.1 (20.0 to 22.2)
ST6 Day 1	21.1 (18.9 to 23.5)	21.3 (20.4 to 22.2)	20.8 (20.1 to 21.6)	21.6 (20.2 to 23.2)
ST6 Day 29	21.1 (18.9 to 23.6)	22.7 (21.2 to 24.3)	22.0 (20.9 to 23.2)	22.0 (20.4 to 23.7)
ST6 Day 57	42.3 (29.8 to 60.1)	55.5 (48.1 to 64.1)	65.3 (55.6 to 76.7)	22.1 (20.4 to 23.9)
ST6 Day 180	30.1 (22.6 to 40.2)	48.4 (42.8 to 54.8)	51.4 (44.7 to 59.0)	21.4 (20.1 to 22.8)
ST6 Day 236	25.6 (20.7 to 31.8)	33.4 (29.5 to 37.8)	33.2 (28.6 to 38.6)	22.1 (20.2 to 24.3)
ST6 Day 365	22.1 (19.2 to 25.5)	25.7 (23.8 to 27.9)	26.0 (23.6 to 28.7)	21.8 (20.3 to 23.3)

Statistical analyses

No statistical analyses for this end point

Secondary: SCRs (Seroconversion Rate) for each OspA (Outer Surface Protein A) Serotype Specific IgG (ST1 to ST6)

End point title	SCRs (Seroconversion Rate) for each OspA (Outer Surface Protein A) Serotype Specific IgG (ST1 to ST6)

End point description:

Seroconversion for ELISA is defined as:
• for subjects that are seronegative at Visit 1 (baseline): a change from seronegative at Visit 1 to seropositive (i.e. antibody titer of ≥40 U/mL) at a certain time point.
• for subjects that are seropositive at Visit 1 (baseline): a ≥ 4-fold rise in IgG antibody titer from Visit 1.
SCRs for each OspA serotype specific IgG (ST1 to ST6), determined by ELISA, at Day 29, 57, 85, 180, 236, and Month 12

End point type	Secondary

End point timeframe:

Day 29, 57, 85, 180, 236 and Months 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	192	194	121
Units: percentage of participants (%)				
number (confidence interval 95%)				
ST1 Day 29	0.0 (0.0 to 11.7)	3.7 (1.8 to 7.4)	3.1 (1.4 to 6.6)	0.8 (0.1 to 4.6)
ST1 Day 57	39.3 (23.6 to 57.6)	37.2 (30.6 to 44.2)	40.7 (34.1 to 47.8)	1.7 (0.5 to 5.8)
ST1 Day 85	65.4 (46.2 to 80.6)	81.3 (75.1 to 86.2)	81.5 (75.3 to 86.4)	0.8 (0.1 to 4.6)
ST1 Day 180	11.5 (4.0 to 29.0)	32.8 (26.4 to 39.9)	35.4 (29.0 to 42.5)	0.9 (0.2 to 4.8)

ST1 Day 236	7.7 (2.1 to 24.1)	17.2 (11.5 to 24.9)	18.5 (12.5 to 26.4)	2.6 (0.7 to 9.1)
ST1 Day 365	4.0 (0.7 to 19.5)	10.9 (7.2 to 16.3)	8.9 (5.6 to 13.8)	1.8 (0.5 to 6.2)
ST2 Day 29	0.0 (0.0 to 11.7)	2.6 (1.1 to 6.0)	5.7 (3.2 to 9.9)	0.8 (0.1 to 4.6)
ST2 Day 57	67.9 (49.3 to 82.1)	72.3 (65.5 to 78.1)	79.9 (73.7 to 84.9)	1.7 (0.5 to 6.0)
ST2 Day 85	88.5 (71.0 to 96.0)	98.4 (95.4 to 99.5)	95.2 (91.2 to 97.5)	1.7 (0.5 to 6.0)
ST2 Day 180	42.3 (25.5 to 61.1)	66.1 (59.0 to 72.6)	66.7 (59.7 to 73.0)	0.9 (0.2 to 4.8)
ST2 Day 236	19.2 (8.5 to 37.9)	42.6 (34.2 to 51.5)	38.7 (30.4 to 47.6)	0.0 (0.0 to 4.8)
ST2 Day 365	8.0 (2.2 to 25.0)	15.3 (10.8 to 21.2)	17.8 (13.0 to 23.8)	0.9 (0.2 to 4.8)
ST3 Day 29	6.9 (1.9 to 22.0)	4.2 (2.1 to 8.0)	3.6 (1.8 to 7.3)	1.7 (0.5 to 5.9)
ST3 Day 57	75.0 (56.6 to 87.3)	80.1 (73.9 to 85.1)	84.0 (78.2 to 88.5)	2.5 (0.8 to 7.0)
ST3 Day 85	96.2 (81.1 to 99.3)	97.3 (93.9 to 98.9)	95.8 (91.9 to 97.8)	1.7 (0.5 to 6.0)
ST3 Day 180	50.0 (32.1 to 67.9)	68.9 (61.8 to 75.1)	69.3 (62.4 to 75.4)	1.8 (0.5 to 6.2)
ST3 Day 236	34.6 (19.4 to 53.8)	39.3 (31.1 to 48.2)	42.0 (33.5 to 51.0)	2.6 (0.7 to 9.1)
ST3 Day 365	12.0 (4.2 to 30.0)	17.5 (12.7 to 23.6)	19.9 (14.9 to 26.1)	1.8 (0.5 to 6.2)
ST4 Day 29	3.4 (0.6 to 17.2)	2.6 (1.1 to 6.0)	3.6 (1.8 to 7.3)	0.8 (0.1 to 4.5)
ST4 Day 57	50.0 (32.6 to 67.4)	58.6 (51.6 to 65.4)	67.0 (60.1 to 73.2)	0.8 (0.1 to 4.5)
ST4 Day 85	80.8 (62.1 to 91.5)	94.1 (89.8 to 96.7)	93.7 (89.2 to 96.3)	0.8 (0.1 to 4.6)
ST4 Day 180	30.8 (16.5 to 50.0)	57.4 (50.1 to 64.3)	58.2 (51.1 to 65.0)	0.9 (0.2 to 4.8)
ST4 Day 236	15.4 (6.2 to 33.5)	36.1 (28.1 to 44.9)	31.9 (24.2 to 40.8)	1.3 (0.2 to 7.1)
ST4 Day 365	8.0 (2.2 to 25.0)	19.7 (14.6 to 26.0)	16.8 (12.1 to 22.7)	2.7 (0.9 to 7.5)
ST5 Day 29	0.0 (0.0 to 11.7)	1.6 (0.5 to 4.5)	2.6 (1.1 to 5.9)	0.0 (0.0 to 3.1)
ST5 Day 57	42.9 (26.5 to 60.9)	58.1 (51.0 to 64.9)	67.5 (60.7 to 73.7)	0.0 (0.0 to 3.1)
ST5 Day 85	80.8 (62.1 to 91.5)	91.4 (86.6 to 94.7)	90.5 (85.4 to 93.9)	0.0 (0.0 to 3.2)
ST5 Day 180	19.2 (8.5 to 37.9)	49.7 (42.6 to 56.9)	55.0 (47.9 to 61.9)	0.9 (0.2 to 4.8)
ST5 Day 236	11.5 (4.0 to 29.0)	32.0 (24.4 to 40.7)	31.9 (24.2 to 40.8)	1.3 (0.2 to 7.1)
ST5 Day 365	8.0 (2.2 to 25.0)	13.1 (9.0 to 18.8)	13.1 (9.0 to 18.6)	0.9 (0.2 to 4.8)
ST6 Day 29	0.0 (0.0 to 11.7)	6.3 (3.6 to 10.7)	4.6 (2.5 to 8.6)	1.7 (0.5 to 5.9)
ST6 Day 57	42.9 (26.5 to 60.9)	54.4 (47.4 to 61.4)	60.3 (53.3 to 66.9)	1.7 (0.5 to 5.8)
ST6 Day 85	80.8 (62.1 to 91.5)	93.0 (88.5 to 95.9)	91.5 (86.7 to 94.7)	0.8 (0.1 to 4.6)
ST6 Day 180	23.1 (11.0 to 42.1)	54.1 (46.9 to 61.2)	53.4 (46.3 to 60.4)	2.6 (0.9 to 7.5)
ST6 Day 236	15.4 (6.2 to 33.5)	35.2 (27.3 to 44.1)	31.1 (23.5 to 39.9)	3.9 (1.4 to 11.0)

ST6 Day 365	8.0 (2.2 to 25.0)	16.9 (12.2 to 23.0)	13.6 (9.5 to 19.2)	3.5 (1.4 to 8.7)

Statistical analyses

No statistical analyses for this end point

Secondary: GMFR (Geometric Mean of the fold rise as compared to baseline) for IgG against each OspA serotype (ST1 to ST6),

End point title	GMFR (Geometric Mean of the fold rise as compared to baseline) for IgG against each OspA serotype (ST1 to ST6),

End point description:

GMFR (Geometric Mean of the fold rise as compared to Day 1) for IgG against each OspA serotype (ST1 to ST6), determined by ELISA, at Day 29, 57, 85, 180, 236 and Month 12

End point type	Secondary

End point timeframe:

Day 29,57,85,180,236 and Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	192	194	121
Units: Geometric Mean of the Fold Rise				
number (confidence interval 95%)				
ST1 Day 29	1.0 (1.0 to 1.0)	1.1 (1.0 to 1.1)	1.1 (1.0 to 1.1)	1.0 (1.0 to 1.0)
ST1 Day 57	1.6 (1.2 to 2.1)	1.8 (1.6 to 2.1)	2.0 (1.8 to 2.4)	1.0 (1.0 to 1.0)
ST1 Day 85	3.6 (2.2 to 5.6)	5.0 (4.3 to 5.8)	5.7 (4.9 to 6.7)	1.0 (1.0 to 1.0)
ST1 Day 180	1.3 (1.0 to 1.6)	1.6 (1.4 to 1.8)	1.7 (1.5 to 1.9)	1.0 (1.0 to 1.0)
ST1 Day 236	1.1 (0.9 to 1.3)	1.3 (1.1 to 1.4)	1.3 (1.2 to 1.5)	1.0 (1.0 to 1.1)
ST1 Day 365	1.0 (0.9 to 1.1)	1.1 (1.1 to 1.2)	1.1 (1.1 to 1.2)	1.0 (1.0 to 1.1)
ST2 Day 29	1.0 (1.0 to 1.0)	1.1 (1.0 to 1.1)	1.1 (1.0 to 1.1)	1.0 (1.0 to 1.0)
ST2 Day 57	3.2 (2.2 to 4.7)	4.5 (3.8 to 5.2)	5.4 (4.6 to 6.2)	1.0 (1.0 to 1.1)
ST2 Day 85	8.4 (5.7 to 12.4)	14.0 (12.4 to 15.8)	15.1 (13.3 to 17.3)	1.0 (1.0 to 1.0)
ST2 Day 180	1.9 (1.4 to 2.7)	3.1 (2.7 to 3.6)	3.3 (2.9 to 3.8)	1.0 (1.0 to 1.0)
ST2 Day 236	1.2 (1.0 to 1.6)	1.8 (1.6 to 2.1)	1.8 (1.5 to 2.1)	1.0 (1.0 to 1.0)
ST2 Day 365	1.1 (1.0 to 1.2)	1.2 (1.1 to 1.3)	1.2 (1.1 to 1.3)	1.0 (1.0 to 1.0)
ST3 Day 29	1.1 (1.0 to 1.2)	1.1 (1.0 to 1.1)	1.1 (1.0 to 1.1)	1.0 (1.0 to 1.1)
ST3 Day 57	5.0 (3.2 to 7.8)	6.1 (5.1 to 7.2)	7.2 (6.1 to 8.6)	1.0 (1.0 to 1.1)
ST3 Day 85	12.1 (8.6 to 17.0)	13.9 (12.3 to 15.9)	15.3 (13.3 to 17.7)	1.0 (1.0 to 1.1)
ST3 Day 180	2.4 (1.6 to 3.6)	3.1 (2.7 to 3.5)	3.4 (3.0 to 3.9)	1.0 (1.0 to 1.1)
ST3 Day 236	1.6 (1.2 to 2.2)	1.8 (1.5 to 2.0)	1.9 (1.6 to 2.3)	1.0 (1.0 to 1.1)
ST3 Day 365	1.2 (1.0 to 1.4)	1.3 (1.2 to 1.4)	1.3 (1.2 to 1.5)	1.0 (1.0 to 1.1)
ST4 Day 29	1.0 (1.0 to 1.1)	1.0 (1.0 to 1.1)	1.1 (1.0 to 1.1)	1.0 (1.0 to 1.0)
ST4 Day 57	2.1 (1.5 to 3.0)	2.7 (2.4 to 3.2)	3.2 (2.7 to 3.7)	1.0 (1.0 to 1.0)
ST4 Day 85	5.4 (3.5 to 8.5)	8.2 (7.2 to 9.3)	9.4 (8.2 to 10.8)	1.0 (1.0 to 1.0)

ST4 Day 180	1.5 (1.1 to 2.1)	2.3 (2.0 to 2.6)	2.4 (2.1 to 2.8)	1.0 (1.0 to 1.1)
ST4 Day 236	1.2 (0.9 to 1.5)	1.6 (1.4 to 1.8)	1.6 (1.4 to 1.8)	1.0 (1.0 to 1.1)
ST4 Day 365	1.1 (1.0 to 1.2)	1.3 (1.2 to 1.4)	1.3 (1.1 to 1.4)	1.0 (1.0 to 1.1)
ST5 Day 29	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.1)	1.0 (1.0 to 1.1)	1.0 (1.0 to 1.0)
ST5 Day 57	2.1 (1.5 to 3.0)	2.8 (2.4 to 3.2)	3.6 (3.1 to 4.2)	1.0 (1.0 to 1.0)
ST5 Day 85	5.7 (3.8 to 8.7)	8.6 (7.5 to 9.8)	9.9 (8.5 to 11.4)	1.0 (1.0 to 1.0)
ST5 Day 180	1.3 (1.0 to 1.7)	2.1 (1.9 to 2.4)	2.5 (2.2 to 2.8)	1.0 (1.0 to 1.0)
ST5 Day 236	1.1 (0.9 to 1.3)	1.5 (1.4 to 1.7)	1.6 (1.4 to 1.8)	1.0 (1.0 to 1.0)
ST5 Day 365	1.1 (1.0 to 1.2)	1.2 (1.1 to 1.2)	1.2 (1.1 to 1.3)	1.0 (1.0 to 1.0)
ST6 Day 29	1.0 (1.0 to 1.0)	1.1 (1.0 to 1.1)	1.1 (1.0 to 1.1)	1.0 (1.0 to 1.0)
ST6 Day 57	2.0 (1.4 to 2.8)	2.6 (2.3 to 3.0)	3.1 (2.7 to 3.7)	1.0 (1.0 to 1.0)
ST6 Day 85	5.4 (3.6 to 8.3)	8.7 (7.7 to 9.8)	10.0 (8.7 to 11.5)	1.0 (1.0 to 1.0)
ST6 Day 180	1.4 (1.1 to 1.9)	2.3 (2.0 to 2.6)	2.5 (2.1 to 2.8)	1.0 (1.0 to 1.1)
ST6 Day 236	1.2 (1.0 to 1.5)	1.6 (1.4 to 1.8)	1.6 (1.4 to 1.9)	1.0 (1.0 to 1.1)
ST6 Day 365	1.1 (1.0 to 1.3)	1.2 (1.1 to 1.3)	1.2 (1.1 to 1.4)	1.0 (1.0 to 1.1)

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs for IgG against each OspA serotype (ST1 to ST6) - group 18 to 49 years

End point title	GMTs for IgG against each OspA serotype (ST1 to ST6) - group 18 to 49 years

End point description:

GMTs IgG against each OspA serotype (ST1 to ST6), determined by ELISA, at Day 1, 29, 57, 85, 180, 236, and Month 12, stratified by age group (18- 49 years)

End point type	Secondary

End point timeframe:

Day 1, 29, 57, 85, 180, 236 and Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	133	136	88
Units: U/ml				
geometric mean (confidence interval 95%)				
ST1 Day 1	20.8 (19.2 to 22.5)	20.3 (19.7 to 21.0)	20.3 (19.7 to 20.8)	22.0 (19.6 to 24.6)
ST1 Day 29	21.1 (18.9 to 23.5)	20.9 (19.7 to 22.1)	21.4 (19.9 to 23.0)	22.0 (19.6 to 24.6)
ST1 Day 57	32.7 (25.1 to 42.6)	34.8 (30.0 to 40.3)	43.6 (36.5 to 52.0)	22.4 (19.9 to 25.2)
ST1 Day 85	74.3 (46.4 to 119.0)	105.2 (88.8 to 124.5)	129.6 (107.6 to 156.2)	21.9 (19.6 to 24.5)
ST1 Day 180	26.2 (19.9 to 34.5)	31.7 (27.5 to 36.4)	34.7 (29.7 to 40.5)	21.0 (19.5 to 22.7)

ST1 Day 236	22.2 (18.8 to 26.1)	26.1 (22.5 to 30.3)	26.4 (22.4 to 31.2)	21.7 (19.3 to 24.4)
ST1 Day 365	20.9 (19.1 to 22.9)	23.0 (21.1 to 25.1)	23.8 (21.4 to 26.5)	21.7 (19.7 to 23.9)
ST2 Day 1	21.3 (18.7 to 24.2)	20.0 (20.0 to 20.0)	20.1 (19.9 to 20.3)	21.0 (19.6 to 22.5)
ST2 Day 29	21.1 (18.9 to 23.7)	20.7 (19.9 to 21.5)	21.4 (20.5 to 22.3)	21.0 (19.6 to 22.4)
ST2 Day 57	69.0 (47.7 to 99.8)	89.5 (74.2 to 107.9)	121.4 (102.4 to 143.9)	21.4 (19.8 to 23.2)
ST2 Day 85	180.9 (124.8 to 262.3)	296.5 (258.6 to 339.9)	322.1 (277.1 to 374.4)	21.2 (19.8 to 22.7)
ST2 Day 180	41.2 (29.3 to 57.9)	64.5 (54.7 to 76.0)	71.8 (60.8 to 84.7)	20.5 (19.5 to 21.6)
ST2 Day 236	26.6 (21.2 to 33.4)	39.6 (33.5 to 46.8)	37.0 (31.2 to 43.9)	20.6 (19.4 to 22.0)
ST2 Day 365	21.8 (19.2 to 24.7)	24.5 (22.4 to 26.8)	25.1 (23.0 to 27.4)	20.5 (19.5 to 21.6)
ST3 Day 1	21.9 (19.1 to 25.1)	20.3 (19.9 to 20.7)	20.2 (19.8 to 20.5)	20.6 (19.5 to 21.7)
ST3 Day 29	23.7 (20.0 to 28.0)	21.0 (20.1 to 21.9)	21.7 (20.5 to 23.0)	20.7 (19.6 to 21.9)
ST3 Day 57	110.2 (71.1 to 171.0)	122.6 (101.3 to 148.3)	159.4 (130.1 to 195.2)	21.3 (19.7 to 22.9)
ST3 Day 85	267.4 (194.8 to 367.1)	295.1 (255.6 to 340.8)	334.2 (282.1 to 395.9)	20.7 (19.6 to 21.8)
ST3 Day 180	53.1 (35.6 to 79.1)	60.7 (51.7 to 71.2)	73.0 (61.3 to 86.9)	20.0 (20.0 to 20.0)
ST3 Day 236	35.3 (25.7 to 48.6)	35.8 (30.4 to 42.2)	39.9 (33.0 to 48.3)	20.2 (19.8 to 20.7)
ST3 Day 365	25.2 (19.9 to 31.8)	25.4 (23.2 to 27.8)	28.0 (24.7 to 31.8)	20.2 (19.8 to 20.7)
ST4 Day 1	21.4 (18.7 to 24.4)	20.8 (20.0 to 21.6)	20.3 (19.9 to 20.8)	22.0 (20.2 to 24.0)
ST4 Day 29	22.1 (19.1 to 25.6)	21.5 (20.4 to 22.8)	21.5 (20.3 to 22.8)	22.3 (20.4 to 24.4)
ST4 Day 57	45.9 (32.8 to 64.2)	56.9 (48.3 to 67.1)	71.4 (59.1 to 86.3)	22.4 (20.4 to 24.6)
ST4 Day 85	117.0 (76.6 to 178.7)	177.1 (154.5 to 203.1)	206.8 (175.0 to 244.3)	22.1 (20.3 to 24.1)
ST4 Day 180	32.8 (24.1 to 44.6)	48.2 (41.8 to 55.6)	53.2 (44.9 to 63.0)	21.7 (20.0 to 23.5)
ST4 Day 236	25.5 (20.6 to 31.5)	34.9 (29.9 to 40.8)	33.6 (28.1 to 40.1)	21.2 (19.5 to 23.2)
ST4 Day 365	21.8 (19.2 to 24.7)	26.7 (24.2 to 29.5)	26.7 (23.5 to 30.3)	21.4 (19.9 to 23.0)
ST5 Day 1	20.6 (19.4 to 21.8)	20.4 (19.9 to 20.9)	20.2 (19.8 to 20.8)	21.5 (20.0 to 23.1)
ST5 Day 29	20.7 (19.2 to 22.4)	20.6 (19.9 to 21.3)	21.1 (20.1 to 22.1)	21.4 (20.0 to 22.9)
ST5 Day 57	42.7 (29.8 to 61.3)	56.6 (47.8 to 67.0)	80.7 (66.3 to 98.1)	21.6 (20.0 to 23.3)
ST5 Day 85	118.3 (78.3 to 178.9)	180.7 (156.8 to 208.2)	218.3 (183.6 to 259.7)	21.4 (20.0 to 22.9)
ST5 Day 180	26.7 (20.7 to 34.3)	42.5 (36.7 to 49.1)	54.6 (45.9 to 64.8)	20.8 (19.7 to 21.9)
ST5 Day 236	23.0 (19.6 to 27.0)	31.9 (27.5 to 37.1)	33.4 (27.7 to 40.2)	21.0 (19.6 to 22.6)
ST5 Day 365	21.7 (19.3 to 24.3)	24.0 (22.2 to 26.0)	26.0 (23.0 to 29.5)	20.8 (19.7 to 21.9)
ST6 Day 1	21.1 (18.9 to 23.5)	20.8 (20.0 to 21.5)	21.2 (20.1 to 22.4)	21.7 (20.0 to 23.6)

ST6 Day 29	21.1 (18.9 to 23.6)	22.3 (21.0 to 23.7)	22.2 (20.8 to 23.7)	22.1 (20.3 to 24.0)
ST6 Day 57	42.3 (29.8 to 60.1)	54.5 (46.2 to 64.3)	72.3 (59.2 to 88.3)	22.3 (20.3 to 24.4)
ST6 Day 85	115.6 (76.5 to 174.7)	185.8 (162.2 to 213.0)	225.6 (191.9 to 265.3)	21.8 (20.1 to 23.7)
ST6 Day 180	30.1 (22.6 to 40.2)	46.7 (40.4 to 53.9)	54.2 (45.5 to 64.4)	20.6 (19.7 to 21.4)
ST6 Day 236	25.6 (20.7 to 31.8)	34.6 (29.8 to 40.2)	34.6 (28.7 to 41.9)	21.4 (19.7 to 23.2)
ST6 Day 365	22.1 (19.2 to 25.5)	25.5 (23.3 to 27.9)	27.7 (24.3 to 31.6)	21.4 (20.1 to 22.7)

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs for IgG against each OspA serotype (ST1 to ST6) - group 50 to 65 years

End point title	GMTs for IgG against each OspA serotype (ST1 to ST6) - group 50 to 65 years[1]

End point description:

GMTs for IgG against each OspA serotype (ST1 to ST6), determined by ELISA, at Day 1, 29, 57, 85, 180, 236, and Month 12, stratified by age group. (50-65 years)

End point type	Secondary

End point timeframe:

Day 1, 29, 57, 85, 180, 236 and Month 12

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The 90µg arm was only applicable in the run in phase for subjects aged 18-40 years

End point values	VLA15 135 µg	VLA15 180 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	58	33	
Units: U/ml				
geometric mean (confidence interval 95%)				
ST1 Day 1	21.0 (19.0 to 23.3)	20.0 (20.0 to 20.0)	20.6 (19.4 to 22.0)	
ST1 Day 29	24.2 (18.7 to 31.4)	20.9 (19.5 to 22.5)	21.0 (19.6 to 22.6)	
ST1 Day 57	44.5 (31.7 to 62.3)	36.2 (28.6 to 45.8)	20.5 (19.5 to 21.6)	
ST1 Day 85	95.3 (67.2 to 135.1)	89.2 (66.0 to 120.4)	21.2 (19.5 to 23.1)	
ST1 Day 180	35.4 (26.8 to 46.9)	32.1 (26.4 to 39.0)	21.0 (19.6 to 22.5)	
ST1 Day 236	24.5 (20.4 to 29.4)	25.6 (21.4 to 30.5)	20.9 (19.1 to 22.9)	
ST1 Day 365	24.3 (19.6 to 30.1)	21.4 (19.6 to 23.2)	20.5 (19.4 to 21.7)	
ST2 Day 1	20.0 (20.0 to 20.0)	20.0 (20.0 to 20.0)	20.0 (20.0 to 20.0)	

ST2 Day 29	22.0 (18.9 to 25.7)	21.6 (19.4 to 24.0)	20.9 (19.1 to 22.8)	
ST2 Day 57	88.7 (64.1 to 122.5)	81.5 (60.4 to 110.2)	20.9 (19.1 to 22.8)	
ST2 Day 85	245.5 (190.3 to 316.6)	265.0 (204.2 to 344.0)	20.8 (19.2 to 22.4)	
ST2 Day 180	58.5 (45.4 to 75.3)	57.4 (44.1 to 74.5)	20.8 (19.2 to 22.4)	
ST2 Day 236	30.5 (24.1 to 38.7)	32.7 (24.8 to 43.1)	20.0 (20.0 to 20.0)	
ST2 Day 365	24.9 (21.3 to 29.2)	24.1 (21.3 to 27.3)	20.9 (19.1 to 22.7)	
ST3 Day 1	20.7 (19.7 to 21.7)	20.0 (20.0 to 20.0)	20.0 (20.0 to 20.0)	
ST3 Day 29	23.3 (18.9 to 28.7)	20.0 (20.0 to 20.0)	21.2 (18.8 to 23.8)	
ST3 Day 57	126.7 (88.0 to 182.4)	118.3 (85.7 to 163.1)	21.1 (18.9 to 23.6)	
ST3 Day 85	258.9 (194.9 to 343.8)	256.5 (193.5 to 340.0)	21.1 (19.0 to 23.4)	
ST3 Day 180	68.8 (53.5 to 88.4)	59.7 (46.4 to 76.7)	21.9 (19.1 to 25.0)	
ST3 Day 236	35.7 (27.3 to 46.8)	36.9 (27.2 to 50.1)	22.0 (18.0 to 26.9)	
ST3 Day 365	26.0 (21.5 to 31.5)	24.8 (21.6 to 28.4)	21.3 (18.7 to 24.2)	
ST4 Day 1	21.3 (19.8 to 23.0)	20.0 (20.0 to 20.0)	20.9 (19.1 to 22.9)	
ST4 Day 29	22.9 (18.7 to 28.0)	21.0 (19.4 to 22.8)	21.2 (18.8 to 23.8)	
ST4 Day 57	58.6 (42.6 to 80.6)	51.4 (39.8 to 66.4)	21.2 (18.8 to 23.9)	
ST4 Day 85	158.2 (119.5 to 209.4)	158.1 (122.5 to 203.9)	21.1 (18.9 to 23.4)	
ST4 Day 180	48.0 (37.5 to 61.5)	41.3 (33.6 to 50.9)	21.1 (18.9 to 23.6)	
ST4 Day 236	28.0 (23.1 to 33.8)	28.0 (22.7 to 34.7)	23.1 (18.7 to 28.5)	
ST4 Day 365	26.0 (21.7 to 31.1)	22.9 (20.9 to 25.1)	22.5 (19.4 to 26.1)	
ST5 Day 1	21.4 (19.8 to 23.0)	20.0 (20.0 to 20.0)	21.0 (19.0 to 23.4)	
ST5 Day 29	22.7 (19.0 to 27.1)	20.8 (19.2 to 22.6)	21.3 (18.7 to 24.3)	
ST5 Day 57	61.0 (44.9 to 82.9)	55.7 (42.5 to 72.8)	21.3 (18.7 to 24.2)	
ST5 Day 85	166.4 (124.1 to 223.0)	162.1 (124.0 to 211.9)	21.2 (18.8 to 23.9)	
ST5 Day 180	47.4 (37.2 to 60.5)	40.8 (32.6 to 51.1)	21.9 (19.1 to 25.2)	
ST5 Day 236	28.8 (23.4 to 35.6)	30.2 (24.1 to 37.7)	23.1 (18.6 to 28.7)	
ST5 Day 365	23.9 (20.5 to 27.8)	22.4 (20.2 to 24.7)	21.9 (19.1 to 25.2)	
ST6 Day 1	22.6 (20.3 to 25.1)	20.0 (20.0 to 20.0)	21.4 (18.7 to 24.4)	
ST6 Day 29	23.6 (19.9 to 28.1)	21.6 (19.6 to 23.9)	21.7 (18.3 to 25.8)	
ST6 Day 57	58.0 (43.2 to 77.7)	51.4 (39.3 to 67.1)	21.7 (18.4 to 25.6)	
ST6 Day 85	178.7 (135.2 to 236.3)	174.3 (133.9 to 226.9)	21.6 (18.5 to 25.3)	

ST6 Day 180	52.3 (41.1 to 66.5)	45.5 (36.1 to 57.3)	23.6 (19.2 to 28.8)	
ST6 Day 236	30.3 (24.1 to 38.1)	30.1 (23.6 to 38.3)	24.6 (18.0 to 33.6)	
ST6 Day 385	26.2 (22.2 to 30.9)	22.5 (20.2 to 25.0)	22.8 (18.7 to 27.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: SCRs (Seroconversion Rate) for each OspA (Outer Surface Protein A) Serotype Specific IgG (ST1 to ST6) group 18-49 years

End point title	SCRs (Seroconversion Rate) for each OspA (Outer Surface Protein A) Serotype Specific IgG (ST1 to ST6) group 18-49 years

End point description:

Seroconversion for ELISA is defined as:
• for subjects that are seronegative at Visit 1 (baseline): a change from seronegative at Visit 1 to seropositive (i.e. antibody titer of ≥40 U/mL) at a certain time point.
• for subjects that are seropositive at Visit 1 (baseline): a ≥ 4-fold rise in IgG antibody titer from Visit 1.
SCRs for each OspA serotype specific IgG (ST1 to ST6), determined by ELISA, at Day 1, 29, 57, 85, 180, 236, and Month 12, stratified by age group (18-49 years)

End point type	Secondary

End point timeframe:

Day 1, 29, 57, 85, 180, 236 and Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	133	136	88
Units: percentage of participants (%)				
number (confidence interval 95%)				
ST1 Day 29	0.0 (0.0 to 11.7)	2.3 (0.8 to 6.4)	2.9 (1.1 to 7.3)	0.0 (0.0 to 4.2)
ST1 Day 57	39.3 (23.6 to 57.6)	36.1 (28.4 to 44.5)	43.4 (35.3 to 51.8)	1.1 (0.2 to 6.2)
ST1 Day 85	65.4 (46.2 to 80.6)	85.9 (78.9 to 90.0)	85.6 (78.6 to 90.6)	0.0 (0.0 to 4.3)
ST1 Day 180	11.5 (4.0 to 29.0)	31.2 (23.7 to 39.8)	36.4 (28.7 to 44.8)	0.0 (0.0 to 4.5)
ST1 Day 236	7.7 (2.1 to 24.1)	18.2 (11.5 to 27.5)	17.9 (11.1 to 27.4)	1.7 (0.3 to 9.1)
ST1 Day 365	4.0 (0.7 to 19.5)	11.3 (6.8 to 18.1)	10.5 (6.4 to 16.9)	1.2 (0.2 to 6.6)
ST2 Day 29	0.0 (0.0 to 0.0)	2.3 (0.8 to 6.4)	6.6 (3.5 to 12.1)	0.0 (0.0 to 4.2)
ST2 Day 57	67.9 (49.3 to 82.1)	72.9 (64.8 to 79.8)	85.3 (78.4 to 90.3)	1.1 (0.2 to 6.4)
ST2 Day 85	88.5 (71.0 to 96.0)	100 (97.1 to 100)	96.2 (91.4 to 98.4)	1.2 (0.2 to 6.4)
ST2 Day 180	42.3 (25.5 to 61.1)	68.0 (59.4 to 75.5)	69.7 (61.4 to 76.9)	0.0 (0.0 to 4.5)

ST2 Day 236	19.2 (8.5 to 37.9)	47.7 (37.6 to 58.0)	41.7 (41.7 to 52.3)	0.0 (0.0 to 6.2)
ST2 Day 365	8.0 (2.2 to 25.0)	15.3 (10.0 to 22.7)	18.8 (13.1 to 26.3)	0.0 (0.0 to 4.5)
ST3 Day 29	6.9 (1.9 to 22.0)	3.0 (1.2 to 7.5)	5.1 (2.5 to 10.2)	1.1 (0.2 to 6.2)
ST3 Day 57	75.0 (56.6 to 87.3)	81.2 (73.7 to 86.9)	85.3 (78.4 to 90.3)	2.3 (0.2 to 6.4)
ST3 Day 85	96.2 (81.1 to 99.3)	98.4 (94.5 to 99.6)	97.0 (92.5 to 98.8)	1.2 (0.2 to 6.4)
ST3 Day 180	50.0 (32.1 to 67.9)	66.4 (57.7 to 74.1)	70.5 (66.2 to 77.6)	0.0 (0.0 to 4.5)
ST3 Day 236	34.6 (19.4 to 53.8)	39.8 (30.2 to 50.2)	44.0 (33.9 to 54.7)	1.7 (0.3 to 9.1)
ST3 Day 365	12.0 (4.2 to 30.0)	19.4 (13.4 to 27.2)	21.8 (15.6 to 29.6)	1.2 (0.2 to 6.6)
ST4 Day 29	3.4 (0.6 to 17.2)	2.3 (0.8 to 6.5)	3.7 (1.6 to 8.3)	1.1 (0.2 to 6.2)
ST4 Day 57	50.0 (32.6 to 67.4)	60.2 (51.7 to 68.1)	71.3 (63.2 to 78.3)	1.1 (0.2 to 6.2)
ST4 Day 85	80.8 (62.1 to 91.5)	96.1 (91.2 to 98.3)	94.7 (89.5 to 97.4)	1.2 (0.2 to 6.4)
ST4 Day 180	30.8 (16.5 to 50.0)	58.4 (49.6 to 66.7)	60.6 (52.1 to 68.5)	1.2 (0.2 to 6.6)
ST4 Day 236	15.4 (6.2 to 33.5)	38.6 (29.1 to 49.1)	34.5 (25.2 to 45.2)	0.0 (0.0 to 6.2)
ST4 Day 365	8.0 (2.2 to 25.0)	21.0 (14.7 to 29.0)	18.0 (12.4 to 25.4)	1.2 (0.2 to 6.6)
ST5 Day 29	0.0 (0.0 to 11.7)	0.8 (0.1 to 4.1)	2.9 (1.1 to 7.3)	0.0 (0.0 to 4.2)
ST5 Day 57	42.9 (26.5 to 60.9)	59.4 (50.9 to 67.4)	72.8 (64.8 to 79.6)	0.0 (0.0 to 4.2)
ST5 Day 85	80.8 (62.1 to 91.5)	94.5 (89.1 to 97.3)	91.7 (85.7 to 95.3)	0.0 (0.0 to 4.3)
ST5 Day 180	19.2 (8.5 to 37.9)	48.8 (40.2 to 57.5)	59.1 (50.6 to 67.1)	0.0 (0.0 to 4.3)
ST5 Day 236	11.5 (4.0 to 29.0)	33.0 (24.0 to 43.3)	32.1 (23.1 to 42.7)	0.0 (0.0 to 4.5)
ST5 Day 365	8.0 (2.2 to 25.0)	15.3 (10.0 to 22.7)	15.0 (10.0 to 22.1)	0.0 (0.0 to 4.5)
ST6 Day 29	0.0 (0.0 to 11.7)	6.8 (3.6 to 12.4)	4.4 (2.0 to 9.3)	2.3 (0.6 to 7.9)
ST6 Day 57	42.9 (26.5 to 60.9)	55.6 (47.2 to 63.8)	64.0 (55.6 to 71.6)	2.3 (0.6 to 7.9)
ST6 Day 85	80.8 (62.1 to 91.5)	95.3 (90.2 to 97.8)	92.4 (86.6 to 95.8)	1.2 (0.2 to 6.4)
ST6 Day 180	23.1 (11.0 to 42.1)	54.4 (45.7 to 62.9)	53.8 (45.3 to 62.1)	1.2 (0.2 to 6.6)
ST6 Day 236	15.4 (6.2 to 33.5)	38.6 (29.1 to 49.1)	32.1 (23.1 to 42.7)	3.4 (1.0 to 11.7)
ST6 Day 365	8.0 (2.2 to 25.0)	17.7 (12.0 to 25.4)	15.8 (10.6 to 22.9)	3.7 (1.3 to 10.2)

Statistical analyses

No statistical analyses for this end point

Secondary: SCRs (Seroconversion Rate) for each OspA (Outer Surface Protein A)

Serotype Specific IgG (ST1 to ST6) group 50-65 years

End point title	SCRs (Seroconversion Rate) for each OspA (Outer Surface Protein A) Serotype Specific IgG (ST1 to ST6) group 50-65 years[2]

End point description:

Seroconversion for ELISA is defined as:
• for subjects that are seronegative at Visit 1 (baseline): a change from seronegative at Visit 1 to seropositive (i.e. antibody titer of ≥40 U/mL) at a certain time point.
• for subjects that are seropositive at Visit 1 (baseline): a ≥ 4-fold rise in IgG antibody titer from Visit 1.
SCRs for each OspA serotype specific IgG (ST1 to ST6), determined by ELISA, at Day 1, 29, 57, 85, 180, 236, and Month 12, stratified by age group (50-65 years)

End point type	Secondary

End point timeframe:

Day 1, 29, 57, 85, 180 and Month 12

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 90µg arm was only applicable in the run in phase for subjects aged 18-40 years

End point values	VLA15 135 µg	VLA15 180 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	58	33	
Units: percentage of participants (%)				
number (confidence interval 95%)				
ST1 Day 29	6.9 (2.7 to 16.4)	3.4 (1.0 to 11.7)	3.1 (0.6 to 15.7)	
ST1 Day 57	39.7 (28.1 to 52.5)	34.5 (23.6 to 47.3)	3.0 (0.5 to 15.3)	
ST1 Day 85	71.2 (58.6 to 81.2)	71.9 (59.2 to 81.9)	3.0 (0.5 to 15.3)	
ST1 Day 180	36.2 (25.1 to 49.1)	33.3 (22.5 to 46.3)	3.1 (0.6 to 15.7)	
ST1 Day 236	14.7 (6.4 to 30.1)	20.0 (10.0 to 35.9)	5.6 (1.0 to 25.8)	
ST1 Day 365	10.2 (4.7 to 20.5)	5.2 (1.8 to 14.1)	3.2 (0.6 to 16.2)	
ST2 Day 29	3.4 (1.0 to 11.7)	3.4 (1.0 to 11.7)	3.1 (0.6 to 15.7)	
ST2 Day 57	70.7 (58.0 to 80.8)	67.2 (54.4 to 77.9)	3.0 (0.5 to 15.3)	
ST2 Day 85	94.9 (86.1 to 98.3)	93.0 (83.3 to 97.2)	3.0 (0.5 to 15.3)	
ST2 Day 180	62.1 (49.2 to 73.4)	59.6 (46.7 to 71.4)	3.1 (0.6 to 15.7)	
ST2 Day 236	29.4 (16.8 to 46.2)	31.4 (18.6 to 48.0)	0.0 (0.0 to 17.6)	
ST2 Day 365	15.3 (8.2 to 26.5)	15.5 (8.4 to 26.9)	3.2 (0.6 to 16.2)	
ST3 Day 29	6.9 (2.7 to 16.4)	0.0 (0.0 to 6.2)	3.1 (0.6 to 15.7)	
ST3 Day 57	77.6 (65.3 to 86.4)	81.0 (69.1 to 89.1)	3.0 (0.5 to 15.3)	
ST3 Day 85	94.9 (86.1 to 98.3)	93.0 (83.3 to 97.2)	3.0 (0.5 to 15.3)	
ST3 Day 180	74.1 (61.6 to 83.7)	66.7 (53.7 to 77.5)	6.3 (1.7 to 20.1)	
ST3 Day 236	38.2 (23.9 to 55.0)	37.1 (23.2 to 53.7)	5.6 (1.0 to 25.8)	

ST3 Day 365	13.6 (7.0 to 24)	15.5 (8.4 to 26.9)	3.2 (0.6 to 16.2)	
ST4 Day 29	3.4 (1.0 to 11.7)	3.4 (1.0 to 11.7)	0.0 (0.0 to 10.7)	
ST4 Day 57	55.2 (42.5 to 67.3)	56.9 (44.1 to 68.8)	0.0 (0.0 to 10.4)	
ST4 Day 85	89.8 (79.5 to 95.3)	91.2 (81.1 to 96.2)	0.0 (0.0 to 10.4)	
ST4 Day 180	55.2 (42.5 to 67.3)	52.6 (39.9 to 65.0)	0.0 (0.0 to 10.7)	
ST4 Day 236	29.4 (16.8 to 46.2)	25.7 (14.2 to 42.1)	5.6 (1.0 to 25.8)	
ST4 Day 365	16.9 (9.5 to 28.5)	13.8 (7.2 to 24.9)	6.5 (1.8 to 20.7)	
ST5 Day 29	3.4 (1.0 to 11.7)	1.7 (0.3 to 9.1)	0.0 (0.0 to 10.7)	
ST5 Day 57	55.2 (42.5 to 67.3)	55.2 (42.5 to 67.3)	0 (0.0 to 10.4)	
ST5 Day 85	84.7 (73.5 to 91.8)	87.7 (76.8 to 93.9)	0.0 (0.0 to 10.4)	
ST5 Day 180	51.7 (39.2 to 64.1)	45.6 (33.4 to 58.4)	3.1 (0.6 to 15.7)	
ST5 Day 236	29.4 (16.8 to 46.2)	31.4 (18.6 to 48.0)	5.6 (1.0 to 25.8)	
ST5 Day 365	8.5 (3.7 to 18.4)	8.6 (3.7 to 18.6)	3.2 (0.6 to 16.2)	
ST6 Day 29	5.2 (1.8 to 14.1)	5.2 (1.8 to 14.1)	0.0 (0.0 to 10.7)	
ST6 Day 57	51.7 (39.2 to 64.1)	51.7 (39.2 to 64.1)	0.0 (0.0 to 10.4)	
ST6 Day 85	88.1 (77.5 to 94.1)	89.5 (78.9 to 95.1)	0.0 (0.0 to 10.4)	
ST6 Day 180	53.4 (40.8 to 65.7)	52.6 (39.9 to 65.0)	6.3 (1.7 to 20.1)	
ST6 Day 236	26.5 (14.6 to 43.1)	28.6 (16.3 to 45.1)	5.6 (1.0 to 25.8)	
ST6 Day 365	15.3 (8.2 to 26.5)	8.6 (3.7 to 18.6)	3.2 (0.6 to 16.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: GMFR (Geometric Mean of the fold rise as compared to baseline) for IgG against each OspA serotype (ST1 to ST6) group 18-49 years

End point title	GMFR (Geometric Mean of the fold rise as compared to baseline) for IgG against each OspA serotype (ST1 to ST6) group 18-49 years

End point description:

GMFR (Geometric Mean of the fold rise as compared to Day 1) for IgG against each OspA serotype (ST1 to ST6), determined by ELISA, at Day 29, 57, 85, 180, 236 and Month 12; stratified by age (18-49 years)

End point type	Secondary

End point timeframe:

Day 29, 57, 85, 180, 236 and Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	133	136	88
Units: Geometric Mean of the Fold Rise				
number (confidence interval 95%)				
ST1 Day 29	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.1)	1.1 (1.0 to 1.1)	1.0 (1.0 to 1.0)
ST1 Day 57	1.6 (1.2 to 2.1)	1.7 (1.5 to 2.0)	2.2 (1.8 to 2.6)	1.0 (1.0 to 1.1)
ST1 Day 85	3.6 (2.2 to 5.6)	5.3 (4.4 to 6.2)	6.4 (5.3 to 7.7)	1.0 (1.0 to 1.0)
ST1 Day 180	1.3 (1.0 to 1.6)	1.6 (1.4 to 1.8)	1.7 (1.5 to 2.0)	1.0 (1.0 to 1.0)
ST1 Day 236	1.1 (0.9 to 1.3)	1.3 (1.1 to 1.4)	1.3 (1.1 to 1.6)	1.0 (1.0 to 1.1)
ST1 Day 365	1.0 (0.9 to 1.1)	1.1 (1.1 to 1.2)	1.2 (1.1 to 1.3)	1.0 (1.0 to 1.1)
ST2 Day 29	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.1)	1.1 (1.0 to 1.1)	1.0 (1.0 to 1.0)
ST2 Day 57	3.2 (2.2 to 4.7)	4.5 (3.7 to 5.4)	6.0 (5.1 to 7.2)	1.0 (1.0 to 1.1)
ST2 Day 85	8.4 (5.7 to 12.4)	14.8 (12.9 to 17.0)	16.0 (13.8 to 18.6)	1.0 (1.0 to 1.0)
ST2 Day 180	1.9 (1.4 to 2.7)	3.2 (2.7 to 3.8)	3.6 (3.0 to 4.2)	1.0 (1.0 to 1.0)
ST2 Day 236	1.2 (1.0 to 1.6)	2.0 (1.7 to 2.3)	1.8 (1.5 to 2.2)	1.0 (1.0 to 1.0)
ST2 Day 365	1.1 (1.0 to 1.2)	1.2 (1.1 to 1.3)	1.2 (1.1 to 1.4)	1.0 (1.0 to 1.0)
ST3 Day 29	1.1 (1.0 to 1.2)	1.0 (1.0 to 1.1)	1.1 (1.0 to 1.1)	1.0 (1.0 to 1.0)
ST3 Day 57	5.0 (3.2 to 7.8)	6.0 (5.0 to 7.3)	7.9 (6.4 to 9.7)	1.0 (1.0 to 1.1)
ST3 Day 85	12.1 (8.6 to 17.0)	14.7 (12.7 to 16.9)	16.6 (14.0 to 19.6)	1.0 (1.0 to 1.0)
ST3 Day 180	2.4 (1.6 to 3.6)	3.0 (2.6 to 3.5)	3.6 (3.0 to 4.3)	1.0 (1.0 to 1.0)
ST3 Day 236	1.6 (1.2 to 2.2)	1.8 (1.5 to 2.1)	2.0 (1.6 to 2.4)	1.0 (1.0 to 1.0)
ST3 Day 365	1.2 (1.0 to 1.4)	1.3 (1.2 to 1.4)	1.4 (1.2 to 1.4)	1.0 (1.0 to 1.0)
ST4 Day 29	1.0 (1.0 to 1.1)	1.0 (1.0 to 1.1)	1.1 (1.0 to 1.1)	1.0 (1.0 to 1.0)
ST4 Day 57	2.1 (1.5 to 3.0)	2.7 (2.3 to 3.2)	3.5 (2.9 to 4.2)	1.0 (1.0 to 1.0)
ST4 Day 85	5.4 (3.5 to 8.5)	8.6 (7.5 to 9.8)	10.2 (8.6 to 12.0)	1.0 (1.0 to 1.0)
ST4 Day 180	1.5 (1.1 to 2.1)	2.3 (2.0 to 2.7)	2.6 (2.2 to 3.1)	1.0 (1.0 to 1.1)
ST4 Day 236	1.2 (0.9 to 1.5)	1.7 (1.4 to 2.0)	1.7 (1.4 to 2.0)	1.0 (1.0 to 1.0)
ST4 Day 365	1.1 (1.0 to 1.2)	1.3 (1.2 to 1.4)	1.3 (1.2 to 1.5)	1.0 (1.0 to 1.0)
ST5 Day 29	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.0)	1.0 (1.0 to 1.1)	1.0 (1.0 to 1.0)
ST5 Day 57	2.1 (1.5 to 3.0)	2.8 (2.4 to 3.3)	4.0 (3.3 to 4.8)	1.0 (1.0 to 1.0)
ST5 Day 85	5.7 (3.8 to 8.7)	9.0 (7.8 to 10.3)	10.8 (9.1 to 12.8)	1.0 (1.0 to 1.0)
ST5 Day 180	1.3 (1.0 to 1.7)	2.1 (1.8 to 2.4)	2.7 (2.3 to 3.2)	1.0 (1.0 to 1.0)
ST5 Day 236	1.1 (0.9 to 1.3)	1.6 (1.4 to 1.8)	1.6 (1.4 to 2.0)	1.0 (1.0 to 1.0)
ST5 Day 365	1.1 (1.0 to 1.2)	1.2 (1.1 to 1.3)	1.3 (1.1 to 1.4)	1.0 (1.0 to 1.0)
ST6 Day 29	1.0 (1.0 to 1.0)	1.1 (1.0 to 1.1)	1.0 (1.0 to 1.1)	1.0 (1.0 to 1.0)
ST6 Day 57	2.0 (1.4 to 2.8)	2.6 (2.2 to 3.1)	3.4 (2.8 to 4.2)	1.0 (1.0 to 1.1)
ST6 Day 85	5.4 (3.6 to 8.3)	9.1 (7.9 to 10.4)	10.6 (9.0 to 12.5)	1.0 (1.0 to 1.0)
ST6 Day 180	1.4 (1.1 to 1.9)	2.3 (2.0 to 2.6)	2.5 (2.2 to 3.0)	1.0 (1.0 to 1.0)
ST6 Day 236	1.2 (1.0 to 1.5)	1.7 (1.5 to 2.0)	1.7 (1.4 to 2.0)	1.0 (1.0 to 1.1)
ST6 Day 365	1.1 (1.0 to 1.3)	1.2 (1.1 to 1.4)	1.3 (1.2 to 1.5)	1.0 (1.0 to 1.1)

Statistical analyses

No statistical analyses for this end point

Secondary: GMFR (Geometric Mean of the fold rise as compared to baseline) for IgG against each OspA serotype (ST1 to ST6) group 50-65 years

End point title	GMFR (Geometric Mean of the fold rise as compared to baseline) for IgG against each OspA serotype (ST1 to ST6) group 50-65 years[3]

End point description:

GMFR (Geometric Mean of the fold rise as compared to Day 1) for IgG against each OspA serotype (ST1 to ST6), determined by ELISA, at Day 29, 57, 85, 180, 236 and Month 12, stratified by age ,group 50-65 years

End point type	Secondary

End point timeframe:

Day 29, 57, 85, 180, 236 and Month 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 90µg arm was only applicable in the run in phase for subjects aged 18-40 years

End point values	VLA15 135 µg	VLA15 180 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	58	33	
Units: Geometric Mean of the Fold Rise				
number (confidence interval 95%)				
ST1 Day 29	1.2 (1.0 to 1.4)	1.0 (1.0 to 1.1)	1.0 (1.0 to 1.1)	
ST1 Day 57	2.1 (1.6 to 2.8)	1.8 (1.4 to 2.3)	1.0 (0.9 to 1.1)	
ST1 Day 85	4.5 (3.3 to 6.1)	4.5 (3.3 to 6.0)	1.0 (1.0 to 1.1)	
ST1 Day 180	1.7 (1.4 to 2.1)	1.6 (1.3 to 1.9)	1.0 (1.0 to 1.1)	
ST1 Day 236	1.2 (1.0 to 1.5)	1.3 (1.1 to 1.5)	1.0 (1.0 to 1.1)	
ST1 Day 365	1.2 (1.0 to 1.3)	1.1 (1.0 to 1.2)	1.0 (0.9 to 1.1)	
ST2 Day 29	1.1 (0.9 to 1.3)	1.1 (1.0 to 1.2)	1.0 (1.0 to 1.1)	
ST2 Day 57	4.4 (3.2 to 6.1)	4.1 (3.0 to 5.5)	1.0 (1.0 to 1.1)	
ST2 Day 85	12.3 (9.5 to 15.8)	13.3 (10.2 to 17.2)	1.0 (1.0 to 1.1)	
ST2 Day 180	2.9 (2.3 to 3.8)	2.9 (2.2 to 3.7)	1.0 (1.0 to 1.1)	
ST2 Day 236	1.5 (1.2 to 1.9)	1.6 (1.2 to 2.2)	1.0 (1.0 to 1.0)	
ST2 Day 365	1.2 (1.1 to 1.5)	1.2 (1.1 to 1.4)	1.0 (1.0 to 1.1)	
ST3 Day 29	1.1 (1.0 to 1.4)	1.0 (1.0 to 1.0)	1.1 (0.9 to 1.2)	
ST3 Day 57	6.1 (4.3 to 8.7)	5.9 (4.3 to 8.2)	1.1 (0.9 to 1.2)	
ST3 Day 85	12.5 (9.6 to 16.4)	12.8 (9.7 to 17.0)	1.1 (0.9 to 1.2)	
ST3 Day 180	3.3 (2.6 to 4.2)	3.0 (2.3 to 3.8)	1.1 (1.0 to 1.2)	
ST3 Day 236	1.7 (1.3 to 2.2)	1.8 (1.4 to 2.5)	1.1 (0.9 to 1.3)	
ST3 Day 365	1.3 (1.1 to 1.5)	1.2 (1.1 to 1.4)	1.1 (0.9 to 1.2)	
ST4 Day 29	1.1 (0.9 to 1.3)	1.1 (1.0 to 1.1)	1.0 (1.0 to 1.0)	
ST4 Day 57	2.7 (2.0 to 3.7)	2.6 (2.0 to 3.3)	1.0 (1.0 to 1.0)	
ST4 Day 85	7.4 (5.7 to 9.7)	7.9 (6.1 to 10.2)	1.0 (1.0 to 1.0)	
ST4 Day 180	2.2 (1.8 to 2.8)	2.1 (1.7 to 2.5)	1.0 (1.0 to 1.0)	
ST4 Day 236	1.4 (1.2 to 1.7)	1.4 (1.1 to 1.7)	1.1 (0.9 to 1.2)	
ST4 Day 365	1.2 (1.0 to 1.4)	1.1 (1.0 to 1.3)	1.1 (1.0 to 1.2)	
ST5 Day 29	1.1 (0.9 to 1.2)	1.0 (1.0 to 1.1)	1.0 (1.0 to 1.0)	

ST5 Day 57	2.9 (2.1 to 3.8)	2.8 (2.1 to 3.6)	1.0 (1.0 to 1.0)	
ST5 Day 85	7.8 (5.9 to 10.3)	8.1 (6.2 to 10.6)	1.0 (1.0 to 1.0)	
ST5 Day 180	2.2 (1.8 to 2.8)	2.0 (1.6 to 2.6)	1.0 (1.0 to 1.1)	
ST5 Day 236	1.4 (1.2 to 1.8)	1.5 (1.2 to 1.9)	1.1 (0.9 to 1.2)	
ST5 Day 365	1.1 (1.0 to 1.3)	1.1 (1.0 to 1.2)	1.0 (1.0 to 1.1)	
ST6 Day 29	1.1 (0.9 to 1.2)	1.1 (1.0 to 1.2)	1.0 (1.0 to 1.0)	
ST6 Day 57	2.6 (1.9 to 3.4)	2.6 (2.0 to 3.4)	1.0 (1.0 to 1.0)	
ST6 Day 85	7.9 (6.1 to 10.4)	8.7 (6.7 to 11.3)	1.0 (1.0 to 1.0)	
ST6 Day 180	2.3 (1.9 to 2.9)	2.3 (1.8 to 2.9)	1.1 (1.0 to 1.2)	
ST6 Day 236	1.4 (1.1 to 1.7)	1.5 (1.2 to 1.9)	1.1 (0.9 to 1.3)	
ST6 Day 365	1.2 (1.0 to 1.3)	1.1 (1.0 to 1.3)	1.1 (1.0 to 1.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of SAEs during the entire study

End point title	Frequency of SAEs during the entire study
End point description: Frequency of SAEs during the entire study	
End point type	Secondary
End point timeframe: up to Month 12	

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
SAEs	0.0 (0.0 to 11.7)	1.9 (0.7 to 4.7)	2.4 (1.0 to 5.6)	2.4 (0.8 to 6.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of related SAEs during the entire study

End point title	Frequency of related SAEs during the entire study
End point description: Frequency of related SAE during the entire study	
End point type	Secondary

End point timeframe:
up to Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Related SAEs	0.0 (0.0 to 11.7)	0.0 (0.0 to 1.8)	0.0 (0.0 to 1.8)	0.0 (0.0 to 3.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of AESIs during the entire study

End point title	Frequency of AESIs during the entire study

End point description:
Frequency of AESIs during the entire study

End point type	Secondary

End point timeframe:
up to Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
AESIs	0.0 (0.0 to 11.7)	1.9 (0.7 to 4.7)	0.5 (0.1 to 2.7)	0.0 (0.0 to 3.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of related AESIs during the entire study

End point title	Frequency of related AESIs during the entire study

End point description:
Frequency of related AESIs during the entire study

End point type	Secondary

End point timeframe:
up to Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Related AESIs	0.0 (0.0 to 11.7)	0.5 (0.1 to 2.6)	0.0 (0.0 to 1.8)	0.0 (0.0 to 3.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of unsolicited AEs during the entire study

End point title	Frequency of unsolicited AEs during the entire study

End point description:
Frequency of unsolicited AEs during the entire study (incl. clinically relevant laboratory parameters)

End point type	Secondary

End point timeframe:
up to Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Unsolicited AEs	27.6 (14.7 to 45.7)	51.9 (45.2 to 58.5)	56.6 (49.7 to 63.2)	51.6 (42.9 to 60.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of related unsolicited AEs during the entire study

End point title	Frequency of related unsolicited AEs during the entire study

End point description:
Frequency of related unsolicited AEs during the entire study (incl. clinically relevant laboratory parameters)

End point type	Secondary

End point timeframe:
up to Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Related unsolicited AEs	6.9 (1.9 to 22.0)	9.3 (6.1 to 14.0)	14.6 (10.4 to 20.1)	8.9 (5.0 to 15.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited local AEs within 7 days after 1st Vaccination

End point title	Frequency of solicited local AEs within 7 days after 1st Vaccination

End point description:
Frequency of solicited local AEs within 7 days after 1st Vaccination, percentages are based on N.

End point type	Secondary

End point timeframe:
7 days after first vaccination

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited local AEs	89.7 (73.6 to 96.4)	92.1 (87.6 to 95.0)	94.1 (90.0 to 96.6)	21.0 (14.7 to 29.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited local AE within 7 days after 2nd Vaccination

End point title	Frequency of solicited local AE within 7 days after 2nd Vaccination

End point description:
Frequency of solicited local AE within 7 days after 2nd Vaccination, percentages are based on N.

End point type	Secondary

End point timeframe:

within 7 days after 2nd Vaccination

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited local AE	72.4 (54.3 to 85.3)	78.5 (72.5 to 83.5)	85.9 (80.4 to 90.0)	13.7 (8.7 to 20.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited local AE within 7 days after 3rd Vaccination

End point title	Frequency of solicited local AE within 7 days after 3rd Vaccination

End point description:

Frequency of solicited local AE within 7 days after 3rd Vaccination, percentages are based on N.

End point type	Secondary

End point timeframe:

within 7 days after 3rd vaccination

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited local AE	62.1 (44.0 to 77.3)	74.8 (68.5 to 80.1)	76.1 (69.8 to 81.4)	11.3 (6.8 to 18.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited local AE within 7 days after any Vaccination

End point title	Frequency of solicited local AE within 7 days after any Vaccination

End point description:

Frequency of solicited local AE within 7 days after any Vaccination, percentages are based on N

End point type	Secondary

End point timeframe:

within 7 days after any vaccination

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited local AE	89.7 (73.6 to 96.4)	93.0 (88.8 to 95.7)	96.1 (92.5 to 98.0)	29.8 (22.5 to 38.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited systemic AE within 7 days after 1st Vaccination

End point title	Frequency of solicited systemic AE within 7 days after 1st Vaccination

End point description:

Frequency of solicited systemic AE within 7 days after 1st Vaccination, percentages are based on N.

End point type	Secondary

End point timeframe:

within 7 days after 1st Vaccination

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited systemic AE	55.2 (37.5 to 71.6)	52.8 (46.1 to 59.4)	59.0 (52.2 to 65.5)	29.8 (22.5 to 38.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited systemic AE within 7 days after 2nd Vaccination

End point title	Frequency of solicited systemic AE within 7 days after 2nd Vaccination

End point description:

Frequency of solicited systemic AE within 7 days after 2nd Vaccination, percentages are based on N

End point type	Secondary

End point timeframe:

within 7 days after 2nd Vaccination

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited systemic AE	31.0 (17.3 to 49.2)	37.9 (31.6 to 44.5)	41.0 (34.5 to 47.8)	17.7 (12.0 to 25.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited systemic AE within 7 days after 3rd Vaccination

End point title	Frequency of solicited systemic AE within 7 days after 3rd Vaccination

End point description:

Frequency of solicited systemic AE within 7 days after 3rd Vaccination, percentages are based on N.

End point type	Secondary

End point timeframe:

within 7 days after 3rd Vaccination

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited systemic AE	27.6 (14.7 to 45.7)	30.4 (24.6 to 36.8)	30.2 (24.4 to 36.8)	17.7 (12.0 to 25.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited systemic AE within 7 days after any Vaccination

End point title	Frequency of solicited systemic AE within 7 days after any Vaccination

End point description:

Frequency of solicited systemic AE within 7 days after any Vaccination, percentages are based on N

End point type	Secondary

End point timeframe:

within 7 days after any Vaccination

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	214	205	124
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited systemic AE	62.1 (44.0 to 77.3)	67.8 (61.2 to 73.7)	71.7 (65.2 to 77.4)	42.7 (34.4 to 51.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of SAEs during the entire study group 18-49 years

End point title	Frequency of SAEs during the entire study group 18-49 years

End point description:

Frequency of SAEs during the entire study group 18-49 years

End point type	Secondary

End point timeframe:

Up to Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	147	145	91
Units: percentage of participants (%)				
number (confidence interval 95%)				
SAEs	0.0 (0.0 to 11.7)	2.0 (0.7 to 5.8)	2.1 (0.7 to 5.9)	1.1 (0.2 to 6.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of SAEs during the entire study group 50-65 years

End point title	Frequency of SAEs during the entire study group 50-65 years[4]

End point description:

Frequency of SAEs during the entire study group 50-65 years

End point type	Secondary

End point timeframe:

Up to Month 12

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 90µg arm was only applicable in the run in phase for subjects aged 18-40 years

End point values	VLA15 135 µg	VLA15 180 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	33	
Units: percentage of participants (%)				
number (confidence interval 95%)				
SAEs	1.5 (0.3 to 8.0)	3.3 (0.9 to 11.4)	6.1 (1.7 to 19.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of AESIs during the entire study group 18-49 years

End point title	Frequency of AESIs during the entire study group 18-49 years

End point description:

Frequency of AESIs during the entire study group 18-49 years

End point type	Secondary

End point timeframe:

Up to Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	147	145	91
Units: percentage of participants				
number (confidence interval 95%)				
AESIs	0.0 (0.0 to 11.7)	0.7 (0.1 to 3.8)	0.0 (0.0 to 2.6)	0.0 (0.0 to 4.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of AESIs during the entire study group 50-65 years

End point title	Frequency of AESIs during the entire study group 50-65

End point description:

Frequency of AESIs during the entire study group 50-65 years

End point type	Secondary

End point timeframe:

Up to Month 12

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 90µg arm was only applicable in the run in phase for subjects aged 18-40 years

End point values	VLA15 135 µg	VLA15 180 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	33	
Units: percentage of participants (%)				
number (confidence interval 95%)				
AESIs	4.5 (1.5 to 12.4)	1.7 (0.3 to 8.9)	0.0 (0.0 to 10.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of unsolicited AEs during the entire study group 18-49 years

End point title	Frequency of unsolicited AEs during the entire study group 18-49 years

End point description:

Frequency of unsolicited AEs during the entire study group 18-49 years

End point type	Secondary

End point timeframe:

Up to Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	147	145	91
Units: percentage of participants (%)				
number (confidence interval 95%)				
Unsolicited AEs	27.6 (14.7 to 45.7)	49.0 (41.0 to 57.0)	55.2 (47.0 to 63.0)	50.5 (40.5 to 60.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of unsolicited AEs during the entire study group 50-65 years

End point title	Frequency of unsolicited AEs during the entire study group 50-65 years[6]

End point description:

Frequency of unsolicited AEs during the entire study group 50-65 years

End point type	Secondary

End point timeframe:

Up to Month 12

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 90µg arm was only applicable in the run in phase for subjects aged 18-40 years

End point values	VLA15 135 µg	VLA15 180 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	33	
Units: percentage of participants (%)				
number (confidence interval 95%)				
Unsolicited AEs	58.2 (46.3 to 69.3)	60.0 (47.4 to 71.4)	54.5 (38.0 to 70.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of related unsolicited AEs during the entire study group 18-49 years

End point title	Frequency of related unsolicited AEs during the entire study group 18-49 years

End point description:

Frequency of related unsolicited AEs during the entire study group 18-49 years

End point type	Secondary

End point timeframe:

Up to Month 12

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	147	145	91
Units: percentage of participants (%)				
number (confidence interval 95%)				
Related unsolicited AEs	6.9 (1.9 to 22.0)	8.8 (5.2 to 14.5)	14.5 (9.7 to 21.1)	7.7 (3.8 to 15.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of related unsolicited AEs during the entire study group 50-65 years

End point title	Frequency of related unsolicited AEs during the entire study group 50-65 years[7]

End point description:

Frequency of related unsolicited AEs during the entire study group 50-65 years

End point type	Secondary

End point timeframe:

Up to Month 12

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The 90µg arm was only applicable in the run in phase for subjects aged 18-40 years

End point values	VLA15 135 µg	VLA15 180 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	33	
Units: percentage of participants (%)				
number (confidence interval 95%)				
Related unsolicited AEs	10.4 (5.2 to 20.0)	15.0 (8.1 to 26.1)	12.1 (4.8 to 27.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited local AE within 7 days after any Vaccination group 18-49 years

End point title	Frequency of solicited local AE within 7 days after any Vaccination group 18-49 years

End point description:

Frequency of solicited local AE within 7 days after any Vaccination group 18-49 years

End point type	Secondary

End point timeframe:

within 7 days after any Vaccination

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	147	145	91
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited local AE	89.7 (73.6 to 96.4)	93.2 (87.9 to 96.3)	96.6 (92.2 to 98.5)	29.7 (21.3 to 39.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited local AE within 7 days after any Vaccination group 50-65 years

End point title	Frequency of solicited local AE within 7 days after any Vaccination group 50-65 years[8]

End point description:

Frequency of solicited local AE within 7 days after any Vaccination group 50-65 years

End point type	Secondary

End point timeframe:

Within 7 days after any Vaccination

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 90µg arm was only applicable in the run in phase for subjects aged 18-40 years

End point values	VLA15 135 µg	VLA15 180 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	33	
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited local AE	92.5 (83.7 to 96.8)	95.0 (86.3 to 98.3)	30.3 (17.4 to 47.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited systemic AE within 7 days after any Vaccination group 18-49 years

End point title	Frequency of solicited systemic AE within 7 days after any Vaccination group 18-49 years

End point description:

Frequency of solicited systemic AE within 7 days after any Vaccination group 18-49 years

End point type	Secondary

End point timeframe:

Within 7 days after any Vaccination

End point values	VLA15 90µg	VLA15 135 µg	VLA15 180 µg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	147	145	91
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited systemic AE	62.1 (44.0 to 77.3)	70.1 (62.2 to 76.9)	71.7 (63.9 to 78.4)	42.9 (33.2 to 53.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of solicited systemic AE within 7 days after any Vaccination group 50-65 years

End point title	Frequency of solicited systemic AE within 7 days after any Vaccination group 50-65 years[9]

End point description:

Frequency of solicited systemic AE within 7 days after any Vaccination group 50-65 years

End point type	Secondary

End point timeframe:

Within 7 days after any Vaccination

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The 90µg arm was only applicable in the run in phase for subjects aged 18-40 years

End point values	VLA15 135 µg	VLA15 180 µg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	33	
Units: percentage of participants (%)				
number (confidence interval 95%)				
Solicited systemic AE	62.7 (50.7 to 73.3)	71.7 (59.2 to 81.5)	42.4 (27.2 to 59.2)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Event (AE) collection started at the time of first study vaccination. AEs were captured until the last study visit. Solicited local and systemic AEs were captured in a diary during 7 consecutive days after each vaccination

Adverse event reporting additional description:

In addition memory aids were used for documentation of AEs up to Visit 7/Month 12 (Day 365) during Main Study
Phase . Diary and memory aid were returned to and reviewed with site staff at the next visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	VLA15 90µg

Reporting group description:

At each vaccination day (Day 1, 29 and 57) treatment with VLA15 90 µg w/ alum

Reporting group title	VLA15 135 µg

Reporting group description:

At each vaccination day (Day 1, 29 and 57) treatment with VLA15 135 µg w/ alum

Reporting group title	VLA15 180 µg

Reporting group description:

At each vaccination day (Day 1, 29 and 57) treatment with VLA15 180 µg w/ alum

Reporting group title	Placebo

Reporting group description:

At each vaccination day (Day 1, 29 and 57) treatment with Placebo

Serious adverse events	VLA15 90µg	VLA15 135 µg	VLA15 180 µg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	4 / 214 (1.87%)	5 / 205 (2.44%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasmacytoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 214 (0.00%)	1 / 205 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Multiple injuries			
alternative assessment type: Non-			

systematic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 214 (0.00%)	1 / 205 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 214 (0.00%)	1 / 205 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 29 (0.00%)	0 / 214 (0.00%)	1 / 205 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 214 (0.00%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 214 (0.00%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 29 (0.00%)	1 / 214 (0.47%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 29 (0.00%)	1 / 214 (0.47%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 29 (0.00%)	1 / 214 (0.47%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 29 (0.00%)	1 / 214 (0.47%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 214 (0.00%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 214 (0.00%)	1 / 205 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurosyphilis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 214 (0.00%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 124 (2.42%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasmacytoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Multiple injuries			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary colic			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychotic disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary retention			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 124 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neurosyphilis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	VLA15 90µg	VLA15 135 µg	VLA15 180 µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 29 (89.66%)	203 / 214 (94.86%)	202 / 205 (98.54%)
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 29 (34.48%)	73 / 214 (34.11%)	84 / 205 (40.98%)
occurrences (all)	19	115	135
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	26 / 29 (89.66%)	198 / 214 (92.52%)	196 / 205 (95.61%)
occurrences (all)	111	924	941
Fatigue			
subjects affected / exposed	8 / 29 (27.59%)	66 / 214 (30.84%)	81 / 205 (39.51%)
occurrences (all)	14	111	130
Injection site erythema			
subjects affected / exposed	8 / 29 (27.59%)	68 / 214 (31.78%)	72 / 205 (35.12%)
occurrences (all)	10	116	123
Injection site induration			
subjects affected / exposed	3 / 29 (10.34%)	64 / 214 (29.91%)	65 / 205 (31.71%)
occurrences (all)	6	108	108
Injection site swelling			
subjects affected / exposed	4 / 29 (13.79%)	57 / 214 (26.64%)	68 / 205 (33.17%)
occurrences (all)	6	84	104
Influenza like illness			

subjects affected / exposed	3 / 29 (10.34%)	32 / 214 (14.95%)	42 / 205 (20.49%)
occurrences (all)	3	44	49
Pyrexia			
subjects affected / exposed	2 / 29 (6.90%)	9 / 214 (4.21%)	7 / 205 (3.41%)
occurrences (all)	2	10	7
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 29 (17.24%)	23 / 214 (10.75%)	32 / 205 (15.61%)
occurrences (all)	5	31	36
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	15 / 29 (51.72%)	106 / 214 (49.53%)	97 / 205 (47.32%)
occurrences (all)	22	173	156
Arthralgia			
subjects affected / exposed	2 / 29 (6.90%)	42 / 214 (19.63%)	37 / 205 (18.05%)
occurrences (all)	4	67	55
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 29 (3.45%)	14 / 214 (6.54%)	10 / 205 (4.88%)
occurrences (all)	1	16	12
Nasopharyngitis			
subjects affected / exposed	0 / 29 (0.00%)	9 / 214 (4.21%)	10 / 205 (4.88%)
occurrences (all)	0	10	11

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	86 / 124 (69.35%)		
Nervous system disorders			
Headache			
subjects affected / exposed	33 / 124 (26.61%)		
occurrences (all)	46		
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	30 / 124 (24.19%)		
occurrences (all)	57		
Fatigue			

subjects affected / exposed occurrences (all)	29 / 124 (23.39%) 40		
Injection site erythema subjects affected / exposed occurrences (all)	12 / 124 (9.68%) 18		
Injection site induration subjects affected / exposed occurrences (all)	2 / 124 (1.61%) 3		
Injection site swelling subjects affected / exposed occurrences (all)	4 / 124 (3.23%) 6		
Influenza like illness subjects affected / exposed occurrences (all)	20 / 124 (16.13%) 25		
Pyrexia subjects affected / exposed occurrences (all)	3 / 124 (2.42%) 3		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	11 / 124 (8.87%) 5		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	21 / 124 (16.94%) 29		
Arthralgia subjects affected / exposed occurrences (all)	12 / 124 (9.68%) 23		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	7 / 124 (5.65%) 8		
Nasopharyngitis subjects affected / exposed occurrences (all)	9 / 124 (7.26%) 10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2020	Global Amendment 1 to CSP v4.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported