Clinical trial results:
Safety and immunogenicity of a Klebsiella pneumoniae tetravalent bioconjugate vaccine (Kleb4V) administered to healthy adults: A FTIH phase I/II randomized and controlled study.

Summary

EudraCT number	2020-005090-26
Trial protocol	DE
Global end of trial date	26 September 2022

Results information

Result version number	v1 (current)
This version publication date	11 October 2023
First version publication date	11 October 2023

Trial information

Trial identification

Sponsor protocol code	Kleb4V01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	LimmaTech Biologics AG
Sponsor organisation address	Grabenstrasse 3, Schlieren, Switzerland, 8952
Public contact	Carmen Rinaldo, LimmaTech Biologics AG, +41 733 85 85,
Scientific contact	Carmen Rinaldo, LimmaTech Biologics AG, +41 733 85 85,

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	07 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 September 2022
Global end of trial reached?	Yes
Global end of trial date	26 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this Phase I/II study is to obtain first-in-human safety and immunogenicity data following administration of Kleb4V to 55-70 years old adults and identify the preferred formulation of Kleb4V.

Protection of trial subjects:

The subjects were observed closely for at least 1 hour following the administration of the vaccines, with appropriate medical treatment readily available in case of anaphylaxis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 June 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 166
Worldwide total number of subjects	166
EEA total number of subjects	166

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)	130
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

166 participants were enrolled in the study and 166 participants received at least the 1st dose of study treatment.

Period 1

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

Blinding implementation details:

oberserver-blind

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo (PBS buffer)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

intramuscular injection

Arm title	Kleb4V Target dose

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Kleb4V
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

intramuscular injection

Arm title	Kleb4V Low dose

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Kleb4V
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

intramuscular injection

Arm title	Kleb4V Target dose + adjuvant
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Kleb4V
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection , Intramuscular use
Dosage and administration details: intramuscular injection	
Investigational medicinal product name	Kleb4V
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection , Intramuscular use
Dosage and administration details: intramuscular injection	
Arm title	Kleb4V Low dose + adjuvant
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Kleb4V
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection , Intramuscular use
Dosage and administration details: intramuscular injection	

Number of subjects in period 1	Placebo	Kleb4V Target dose	Kleb4V Low dose
Started	34	36	30
Completed	33	33	30
Not completed	1	3	0
Adverse event, non-fatal	-	1	-
subject withdrawal from study due time/Covid-19	-	1	-
discontinued study after first placebo dose	1	-	-
subject withdrawal from study due to time problems	-	1	-
discontinued study after first vaccination	-	-	-

Number of subjects in period 1	Kleb4V Target dose + adjuvant	Kleb4V Low dose + adjuvant
Started	36	30
Completed	35	30
Not completed	1	0
Adverse event, non-fatal	-	-

subject withdrawal from study due time/Covid-19	-	-
discontinued study after first placebo dose	-	-
subject withdrawal from study due to time problems	-	-
discontinued study after first vaccination	1	-

Baseline characteristics

Reporting groups

Reporting group title	Overall Study (overall period)

Reporting group description: -

Reporting group values	Overall Study (overall period)	Total	
Number of subjects	166	166	
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)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
18-40 years	16	16	
55-70 years	150	150	
Age continuous Units: years			
median	57.7		
standard deviation	± 10.39	-	
Gender categorical Units: Subjects			
Female	68	68	
Male	98	98	

Subject analysis sets

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

Subject analysis set description:

All subjects who were randomized and treated were included in the safety set

Subject analysis set title	Immunogenicity analysis set - Target Population 55-70 years
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects in the target age population who did not receive the 2nd vaccination and/or had no immunogenicity evaluation available for the visit 1 month post 2nd vaccination (Visit 8) were excluded from the immunogenicity analysis set.

Subject analysis set title	Immunogenicity analysis set - Population 18-40 years
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects in the aged 18-40 years who did not receive the 2nd vaccination and/or had no immunogenicity evaluation available for the visit 1 month post 2nd vaccination (Visit 8) were excluded from the immunogenicity analysis set.

Reporting group values	Safety set	Immunogenicity analysis set - Target Population 55-70 years	Immunogenicity analysis set - Population 18-40 years
Number of subjects	166	146	14
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)			
From 65-84 years			
85 years and over			
18-40 years	16	0	14
55-70 years	150	146	0
Age continuous			
Units: years			
median			
standard deviation	±	±	±
Gender categorical			
Units: Subjects			
Female	68	60	8
Male	98	86	6

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Kleb4V Target dose
Reporting group description: -	
Reporting group title	Kleb4V Low dose
Reporting group description: -	
Reporting group title	Kleb4V Target dose + adjuvant
Reporting group description: -	
Reporting group title	Kleb4V Low dose + adjuvant
Reporting group description: -	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who were randomized and treated were included in the safety set	
Subject analysis set title	Immunogenicity analysis set - Target Population 55-70 years
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Subjects in the target age population who did not receive the 2nd vaccination and/or had no immunogenicity evaluation available for the visit 1 month post 2nd vaccination (Visit 8) were excluded from the immunogenicity analysis set.	
Subject analysis set title	Immunogenicity analysis set - Population 18-40 years
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Subjects in the aged 18-40 years who did not receive the 2nd vaccination and/or had no immunogenicity evaluation available for the visit 1 month post 2nd vaccination (Visit 8) were excluded from the immunogenicity analysis set.	

Primary: Number of Subjects with Solicited AEs by Severity - After First Injection

End point title	Number of Subjects with Solicited AEs by Severity - After First Injection[1]
End point description:	
End point type	Primary
End point timeframe:	
7 days after first vaccination	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Safety data were evaluated descriptively

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	30	36
Units: number of subjects				
Mild	10	17	6	31
Moderate	2	7	1	13
Severe	0	1	0	3

End point values	Kleb4V Low dose + adjuvant	Safety set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	166		
Units: number of subjects				
Mild	23	87		
Moderate	6	29		
Severe	1	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Solicited AEs by Severity - After Second Injection

End point title	Number of Subjects with Solicited AEs by Severity - After Second Injection[2]

End point description:

End point type	Primary

End point timeframe:

7 days after second vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Safety data were evaluated descriptively

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	30	36
Units: number of subjects				
Mild	5	21	15	26
Moderate	3	9	5	15
Severe	0	2	0	4

End point values	Kleb4V Low dose + adjuvant	Safety set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	166		
Units: number of subjects				
Mild	22	89		
Moderate	7	39		

Severe	4	10		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Solicited AEs by Relationship

End point title	Number of Subjects with Solicited AEs by Relationship[3]

End point description:

End point type	Primary

End point timeframe:

from first vaccination until 7 days post second vaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Safety data were evaluated descriptively

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	30	36
Units: number of subjects				
related	13	30	18	35
not related	1	1	0	1

End point values	Kleb4V Low dose + adjuvant	Safety set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	166		
Units: number of subjects				
related	27	123		
not related	0	3		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Unsolicited AEs by Severity

End point title	Number of Subjects with Unsolicited AEs by Severity[4]

End point description:

End point type	Primary

End point timeframe:

28 days after first vaccination

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Safety data were evaluated descriptively

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	30	36
Units: number of subjects				
Mild	11	19	8	19
Moderate	10	12	4	9
Severe	4	1	1	2
Potentially Life Threatening	0	0	0	1

End point values	Kleb4V Low dose + adjuvant	Safety set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	166		
Units: number of subjects				
Mild	6	62		
Moderate	7	42		
Severe	0	8		
Potentially Life Threatening	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Unsolicited AEs by Relationship

End point title	Number of Subjects with Unsolicited AEs by Relationship[5]

End point description:

End point type	Primary

End point timeframe:

from first vaccination until 28 post second vaccination

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Safety data were evaluated descriptively

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	30	36
Units: number of subjects				
related	7	13	5	16
not related	14	15	8	12

End point values	Kleb4V Low dose + adjuvant	Safety set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	166		
Units: number of subjects				
related	5	46		
not related	7	56		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with a SAEs

End point title	Number of Subjects with a SAEs[6]

End point description:

End point type	Primary

End point timeframe:

from first vaccination until study end

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Safety data were evaluated descriptively

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	30	36
Units: number of subjects				
related to study treatment	0	0	0	0
not related to study treatment	3	1	0	1

End point values	Kleb4V Low dose + adjuvant	Safety set		

Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	166		
Units: number of subjects				
related to study treatment	0	0		
not related to study treatment	0	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with AESIs

End point title	Number of Subjects with AESIs[7]

End point description:

End point type	Primary

End point timeframe:

from first vaccination until study end

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Safety data were evaluated descriptively

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	36	30	36
Units: number of subjects	0	0	0	0

End point values	Kleb4V Low dose + adjuvant	Safety set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	166		
Units: number of subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric mean titre of Serum IgG for all serotypes 28 days after the second injection - target population 55-70 years

End point title	Geometric mean titre of Serum IgG for all serotypes 28 days after the second injection - target population 55-70 years

End point description:

End point type	Primary

End point timeframe:

28 days post second vaccination

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	29	29	29
Units: titer				
geometric mean (confidence interval 95%)				
O1v1	92.3 (54.0 to 157.9)	4115.5 (2405.0 to 7042.6)	2709.3 (1582.2 to 4639.4)	4107.5 (2398.8 to 7033.4)
O2a	78.7 (44.7 to 138.2)	1161.6 (660.4 to 2043.2)	853.3 (483.2 to 1507.1)	1984.6 (1129.1 to 3488.4)
O2afg	40.1 (22.5 to 71.6)	757.1 (424.7 to 1349.6)	487.0 (273.2 to 868.0)	1692.6 (948.5 to 3020.5)
O3b	35.9 (23.0 to 56.2)	121.6 (78.1 to 189.5)	126.9 (81.5 to 197.7)	238.6 (153.1 to 371.9)

End point values	Kleb4V Low dose + adjuvant			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: titer				
geometric mean (confidence interval 95%)				
O1v1	2520.4 (1472.3 to 4314.7)			
O2a	1398.1 (794.9 to 2458.8)			
O2afg	690.4 (387.4 to 1230.7)			
O3b	168.8 (108.4 to 263.0)			

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

For treatment group comparison, the primary endpoint was evaluated in terms of ratio of GMTs, referred to as geometric mean ratio (GMR) between treatment groups (i.e., GMR of the post-vaccination immunogenicity values) evaluated via analysis of covariance (ANCOVA) including treatment as fixed factor and baseline titre as covariate. The ANCOVA was conducted for the cohort of 55-70y by serotype on the log-transformed values and considered the immunogenicity analysis set for evaluation.

Comparison groups	Placebo v Kleb4V Target dose v Kleb4V Low dose v Kleb4V Target dose + adjuvant v Kleb4V Low dose + adjuvant
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Geometric mean ratios
Confidence interval	
level	95 %
sides	2-sided

Notes:

[8] - The four statistical comparisons at V8 of each active treatment group versus the placebo group were carried in a formal way, using the Dunnett's procedure for dealing with multiplicity (study-wise alpha=0.05). Treatment ratios, adjusted p-values and two-sided confidence intervals with adjusted coverage were computed for these primary comparisons after back-transformation of the results to the original scale.

Primary: Geometric mean titre of Serum IgG for all serotypes at baseline - population 18-40 years

End point title	Geometric mean titre of Serum IgG for all serotypes at baseline - population 18-40 years[9][10]

End point description:

End point type	Primary

End point timeframe:

28 days after the second injection

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical evaluation performed in the target population 55-70 years

[10] - 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: Statistical evaluation performed in the target population 55-70 years

End point values	Placebo	Kleb4V Target dose	Kleb4V Target dose + adjuvant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	5	6	
Units: titer				
geometric mean (confidence interval 95%)				
O1v1	116.31 (1.07 to 12631.75)	121.49 (11.62 to 1270.23)	110.14 (67.43 to 179.91)	
O2a	20.83 (0.21 to 2101.48)	97.85 (23.45 to 408.27)	61.12 (16.37 to 228.24)	
O2afg	43.44 (4.17 to 452.70)	98.11 (70.47 to 136.61)	77.73 (24.49 to 246.73)	
O3b	43.68 (1.90 to 1002.81)	60.04 (10.58 to 340.82)	125.06 (51.81 to 301.83)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric mean titre of Serum IgG for all serotypes at baseline - target population 55-70 years

End point title	Geometric mean titre of Serum IgG for all serotypes at baseline - target population 55-70 years

End point description:

End point type	Primary

End point timeframe:

at baseline

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	29	29	29
Units: titer				
geometric mean (confidence interval 95%)				
O1v1	53.51 (27.65 to 103.56)	47.96 (22.42 to 102.59)	43.89 (26.30 to 73.25)	71.42 (37.17 to 137.24)
O2a	63.04 (35.40 to 112.28)	72.85 (39.67 to 133.76)	39.10 (22.61 to 67.63)	65.21 (37.12 to 114.57)
O2afg	23.10 (13.72 to 38.89)	27.46 (13.62 to 55.36)	32.06 (16.75 to 61.37)	38.23 (19.68 to 74.30)
O3b	25.94 (13.69 to 49.14)	48.09 (28.35 to 81.59)	35.22 (19.28 to 64.32)	50.28 (28.09 to 90.00)

End point values	Kleb4V Low dose + adjuvant			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: titer				
geometric mean (confidence interval 95%)				
O1v1	71.29 (38.04 to 133.58)			
O2a	76.50 (41.88 to 139.77)			
O2afg	34.74 (20.72 to 58.25)			
O3b	52.64 (30.38 to 91.19)			

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

For treatment group comparison, the primary endpoint was evaluated in terms of ratio of GMTs, referred to as geometric mean ratio (GMR) between treatment groups (i.e., GMR of the post-vaccination immunogenicity values) evaluated via analysis of covariance (ANCOVA) including treatment as fixed factor and baseline titre as covariate. The ANCOVA was conducted for the cohort of 55-70y by serotype on the log-transformed values and considered the Immunogenicity Analysis Set for evaluation

Comparison groups	Placebo v Kleb4V Target dose v Kleb4V Low dose v Kleb4V Target dose + adjuvant v Kleb4V Low dose + adjuvant
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Geometric mean ratios
Confidence interval	
level	95 %
sides	2-sided

Primary: Geometric mean titre of Serum IgG for all serotypes 28 days after the second injection - population 18-40 years

End point title	Geometric mean titre of Serum IgG for all serotypes 28 days after the second injection - population 18-40 years[11][12]

End point description:

End point type	Primary

End point timeframe:

28 days after the second injection

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical evaluation performed in the target population 55-70 years

[12] - 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: Statistical evaluation performed in the target population 55-70 years

End point values	Placebo	Kleb4V Target dose	Kleb4V Target dose + adjuvant	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	5	6	
Units: titer				
geometric mean (confidence interval 95%)				
O1v1	34.65 (0.12 to 9982.14)	9186.73 (1726.37 to 48886.50)	3553.19 (2379.79 to 5305.15)	
O2a	10.00 (0.45 to 223.70)	1040.84 (14.08 to 76953.88)	1271.22 (301.04 to 5368.15)	
O2afg	4.85 (0.28 to 83.52)	2396.04 (749.01 to 7664.86)	753.84 (163.39 to 3477.98)	

O3b	11.35 (4.59 to 28.06)	25.93 (8.08 to 83.26)	242.10 (137.91 to 425.01)	

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean titre of Serum IgG for all serotypes 28 days after the first injection - target population 55-70 years

End point title	Geometric mean titre of Serum IgG for all serotypes 28 days after the first injection - target population 55-70 years
End point description:	
End point type	Secondary
End point timeframe: V5, 28 days after first injection	

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	29	29	29
Units: titer				
geometric mean (confidence interval 95%)				
O1v1	49.22 (26.15 to 92.64)	3209.11 (1729.01 to 5956.22)	1930.72 (875.16 to 4259.44)	5791.70 (2770.82 to 12106.06)
O2a	58.15 (33.79 to 100.07)	1350.09 (598.66 to 3044.71)	528.42 (219.02 to 1274.89)	2674.16 (1257.11 to 5688.54)
O2afg	20.14 (11.84 to 34.25)	471.19 (188.72 to 1176.45)	431.10 (143.59 to 1294.29)	1940.48 (703.69 to 5351.01)
O3b	24.97 (13.14 to 47.44)	104.91 (57.04 to 192.93)	84.95 (45.26 to 159.43)	239.19 (131.24 to 435.94)

End point values	Kleb4V Low dose + adjuvant			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: titer				
geometric mean (confidence interval 95%)				

O1v1	3514.79 (1757.17 to 7030.47)			
O2a	1682.20 (775.48 to 3649.08)			
O2afg	399.22 (186.50 to 854.53)			
O3b	124.66 (68.01 to 228.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Functionality for O1v1 - target population 55-70 years

End point title	Antibody Functionality for O1v1 - target population 55-70 years

End point description:

End point type	Secondary

End point timeframe:

baseline (V2), 28 days after first vaccination (V5), 28 days after second vaccination (V8)

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	29	29	29
Units: titer				
geometric mean (confidence interval 95%)				
Baseline	2529.6 (1254.1 to 5102.2)	3394.7 (1445.5 to 7972.5)	1338.4 (489.9 to 3656.4)	4382.5 (2304.7 to 8333.5)
V5	2552.0 (1185.1 to 5495.4)	30124.9 (20582.3 to 44091.8)	19135.3 (12368.4 to 29604.3)	31342.4 (20545.8 to 47812.6)
V8	2858.6 (1467.2 to 5569.7)	30636.7 (23077.3 to 40672.4)	17459.6 (11910.5 to 25594.0)	28983.9 (21535.1 to 39009.3)

End point values	Kleb4V Low dose + adjuvant			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: titer				
geometric mean (confidence interval				

95%)				
Baseline	3310.1 (2172.7 to 5042.9)			
V5	23544.4 (16030.9 to 34579.5)			
V8	18892.7 (9496.9 to 37584.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Functionality for O2afg - target population 55-70 years

End point title	Antibody Functionality for O2afg - target population 55-70 years

End point description:

End point type	Secondary

End point timeframe:

baseline (V2), 28 days after first vaccination (V5), 28 days after second vaccination (V8)

End point values	Placebo	Kleb4V Target dose	Kleb4V Low dose	Kleb4V Target dose + adjuvant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	29	29	29
Units: titer				
geometric mean (confidence interval 95%)				
V2	857.4 (519.9 to 1413.9)	1341.0 (888.2 to 2024.6)	1256.3 (764.4 to 2064.7)	1826.5 (1133.4 to 2943.5)
V5	859.0 (504.2 to 1463.4)	4834.5 (3208.1 to 7285.4)	3872.4 (2511.4 to 5970.9)	10080.2 (6712.1 to 15138.4)
V8	1157.9 (704.5 to 1903.1)	9453.0 (6557.6 to 13626.7)	6896.2 (4474.1 to 10629.6)	16258.4 (11700.1 to 22592.5)

End point values	Kleb4V Low dose + adjuvant			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: titer				
geometric mean (confidence interval				

95%)				
V2	1080.4 (559.2 to 2087.2)			
V5	4038.3 (2595.3 to 6283.5)			
V8	12751.6 (8551.7 to 19014.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited adverse events were collected for 7 days after each injection.
Unsolicited adverse events were collected for 28 days after each injection.
Medically relevant AEs, AESIs and SAEs were collected for the entire study duration.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Kleb4V Low dose
Reporting group description: -	
Reporting group title	Kleb4V Low dose + adjuvant
Reporting group description: -	
Reporting group title	Kleb4V Target dose
Reporting group description: -	
Reporting group title	Kleb4V Target dose + adjuvant
Reporting group description: -	

Serious adverse events	Placebo	Kleb4V Low dose	Kleb4V Low dose + adjuvant
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 34 (8.82%)	0 / 30 (0.00%)	0 / 30 (0.00%)
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)			
Oesophageal carcinoma	Additional description: Oesophageal carcinoma		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (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
Injury, poisoning and procedural complications			
Tendon rupture	Additional description: Tendon rupture		
subjects affected / exposed	2 / 34 (5.88%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome	Additional description: Acute coronary syndrome		

subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (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
Respiratory, thoracic and mediastinal disorders			
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Kleb4V Target dose	Kleb4V Target dose + adjuvant	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oesophageal carcinoma	Additional description: Oesophageal carcinoma		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (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			
Tendon rupture	Additional description: Tendon rupture		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome	Additional description: Acute coronary syndrome		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Kleb4V Low dose	Kleb4V Low dose + adjuvant
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 34 (64.71%)	18 / 30 (60.00%)	27 / 30 (90.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma	Additional description: Lipoma		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Lesion excision	Additional description: Lesion excision		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Axillary pain	Additional description: Axillary pain		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Chills	Additional description: Chills		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Chest pain	Additional description: Chest pain		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	10 / 34 (29.41%)	7 / 30 (23.33%)	15 / 30 (50.00%)
occurrences (all)	17	15	22
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Injection site erythema	Additional description: Injection site erythema		
subjects affected / exposed	1 / 34 (2.94%)	4 / 30 (13.33%)	7 / 30 (23.33%)
occurrences (all)	1	5	16

Injection site haematoma	Additional description: Injection site haematoma		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Injection site induration	Additional description: Injection site induration		
subjects affected / exposed	0 / 34 (0.00%)	3 / 30 (10.00%)	5 / 30 (16.67%)
occurrences (all)	0	4	9
Injection site macule	Additional description: Injection site macule		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Injection site muscle weakness	Additional description: Injection site muscle weakness		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Injection site pain	Additional description: Injection site pain		
subjects affected / exposed	4 / 34 (11.76%)	11 / 30 (36.67%)	26 / 30 (86.67%)
occurrences (all)	4	17	48
Injection site pruritus	Additional description: Injection site pruritus		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences (all)	0	3	3
Injection site warmth	Additional description: Injection site warmth		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Injection site swelling	Additional description: Injection site swelling		
subjects affected / exposed	1 / 34 (2.94%)	4 / 30 (13.33%)	6 / 30 (20.00%)
occurrences (all)	1	5	11
Injection site reaction	Additional description: Injection site reaction		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Malaise	Additional description: Malaise		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Pain	Additional description: Pain		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2

Thirst	Additional description: Thirst		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy	Additional description: Seasonal allergy		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchospasm	Additional description: Bronchospasm		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	2
Cough	Additional description: Cough		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Dysphonia	Additional description: Dysphonia		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood potassium decreased	Additional description: Blood potassium decreased		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased	Additional description: C-reactive protein increased		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion	Additional description: Contusion		

subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Face injury	Additional description: Face injury		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Limb injury	Additional description: Limb injury		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Superficial injury of eye	Additional description: Superficial injury of eye		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Cardiovascular disorder	Additional description: Cardiovascular disorder		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Palpitations	Additional description: Palpitations		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	2
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Disturbance in attention	Additional description: Disturbance in attention		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Dizziness	Additional description: Dizziness		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Headache	Additional description: Headache		
subjects affected / exposed	5 / 34 (14.71%)	4 / 30 (13.33%)	10 / 30 (33.33%)
occurrences (all)	8	5	15
Hyperaesthesia	Additional description: Hyperaesthesia		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Migraine	Additional description: Migraine		

subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Presyncope	Additional description: Presyncope		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Somnolence	Additional description: Somnolence		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	2 / 34 (5.88%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Lymphadenopathy	Additional description: Lymphadenopathy		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Abdominal pain upper	Additional description: Abdominal pain upper		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer	Additional description: Aphthous ulcer		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Diarrhoea	Additional description: Diarrhoea		

subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Irritable bowel syndrome	Additional description: Irritable bowel syndrome		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Lip oedema	Additional description: Lip oedema		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Nausea	Additional description: Nausea		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Tongue dry	Additional description: Tongue dry		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Vomiting	Additional description: Vomiting		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Angiodermatitis	Additional description: Angiodermatitis		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Alopecia	Additional description: Alopecia		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Blister	Additional description: Blister		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Dermal cyst	Additional description: Dermal cyst		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0

Erythema	Additional description: Erythema		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Eczema	Additional description: Eczema		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	2
Pruritus	Additional description: Pruritus		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Urticaria	Additional description: Urticaria		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria	Additional description: Dysuria		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	3 / 30 (10.00%)
occurrences (all)	0	0	3
Back pain	Additional description: Back pain		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Muscle tightness	Additional description: Muscle tightness		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Myalgia	Additional description: Myalgia		
subjects affected / exposed	4 / 34 (11.76%)	2 / 30 (6.67%)	11 / 30 (36.67%)
occurrences (all)	4	2	16
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Periostosis	Additional description: Periostosis		

subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Asymptomatic COVID-19	Additional description: Asymptomatic COVID-19		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Campylobacter gastroenteritis	Additional description: Campylobacter gastroenteritis		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
COVID-19	Additional description: COVID-19		
subjects affected / exposed	3 / 34 (8.82%)	4 / 30 (13.33%)	1 / 30 (3.33%)
occurrences (all)	3	4	1
Cystitis	Additional description: Cystitis		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Ear infection	Additional description: Ear infection		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis	Additional description: Gastroenteritis		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	2 / 34 (5.88%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences (all)	2	1	2
Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Periodontitis	Additional description: Periodontitis		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Pulpitis dental	Additional description: Pulpitis dental		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1

Rhinitis	Additional description: Rhinitis		
subjects affected / exposed	0 / 34 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Sinusitis	Additional description: Sinusitis		
subjects affected / exposed	1 / 34 (2.94%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus	Additional description: Diabetes mellitus		
subjects affected / exposed	0 / 34 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1

Non-serious adverse events	Kleb4V Target dose	Kleb4V Target dose + adjuvant	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 36 (91.67%)	36 / 36 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma	Additional description: Lipoma		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Surgical and medical procedures			
Lesion excision	Additional description: Lesion excision		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Axillary pain	Additional description: Axillary pain		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Chills	Additional description: Chills		
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences (all)	1	2	
Chest pain	Additional description: Chest pain		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Fatigue	Additional description: Fatigue		

subjects affected / exposed	15 / 36 (41.67%)	10 / 36 (27.78%)	
occurrences (all)	28	27	
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	2	
Injection site erythema	Additional description: Injection site erythema		
subjects affected / exposed	9 / 36 (25.00%)	12 / 36 (33.33%)	
occurrences (all)	15	32	
Injection site haematoma	Additional description: Injection site haematoma		
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Injection site induration	Additional description: Injection site induration		
subjects affected / exposed	7 / 36 (19.44%)	12 / 36 (33.33%)	
occurrences (all)	13	32	
Injection site macule	Additional description: Injection site macule		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Injection site muscle weakness	Additional description: Injection site muscle weakness		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Injection site pain	Additional description: Injection site pain		
subjects affected / exposed	26 / 36 (72.22%)	35 / 36 (97.22%)	
occurrences (all)	47	83	
Injection site pruritus	Additional description: Injection site pruritus		
subjects affected / exposed	1 / 36 (2.78%)	5 / 36 (13.89%)	
occurrences (all)	1	8	
Injection site warmth	Additional description: Injection site warmth		
subjects affected / exposed	0 / 36 (0.00%)	3 / 36 (8.33%)	
occurrences (all)	0	5	
Injection site swelling	Additional description: Injection site swelling		
subjects affected / exposed	4 / 36 (11.11%)	15 / 36 (41.67%)	
occurrences (all)	7	32	
Injection site reaction	Additional description: Injection site reaction		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Malaise	Additional description: Malaise		

subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Pain	Additional description: Pain		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Thirst	Additional description: Thirst		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Immune system disorders			
Seasonal allergy	Additional description: Seasonal allergy		
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm	Additional description: Bronchospasm		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Cough	Additional description: Cough		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Dysphonia	Additional description: Dysphonia		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood potassium decreased	Additional description: Blood potassium decreased		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
C-reactive protein increased	Additional description: C-reactive protein increased		

subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Contusion	Additional description: Contusion		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Face injury	Additional description: Face injury		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Limb injury	Additional description: Limb injury		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Superficial injury of eye	Additional description: Superficial injury of eye		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Cardiovascular disorder	Additional description: Cardiovascular disorder		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Palpitations	Additional description: Palpitations		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Disturbance in attention	Additional description: Disturbance in attention		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Dizziness	Additional description: Dizziness		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Headache	Additional description: Headache		

subjects affected / exposed	11 / 36 (30.56%)	13 / 36 (36.11%)	
occurrences (all)	22	30	
Hyperaesthesia	Additional description: Hyperaesthesia		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Migraine	Additional description: Migraine		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	
occurrences (all)	0	2	
Presyncope	Additional description: Presyncope		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Somnolence	Additional description: Somnolence		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	1 / 36 (2.78%)	1 / 36 (2.78%)	
occurrences (all)	1	1	
Lymphadenopathy	Additional description: Lymphadenopathy		
subjects affected / exposed	2 / 36 (5.56%)	3 / 36 (8.33%)	
occurrences (all)	2	4	
Gastrointestinal disorders			
Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	0 / 36 (0.00%)	3 / 36 (8.33%)	
occurrences (all)	0	3	
Abdominal pain upper	Additional description: Abdominal pain upper		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Aphthous ulcer	Additional description: Aphthous ulcer		

subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	2 / 36 (5.56%)	1 / 36 (2.78%)	
occurrences (all)	3	1	
Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Irritable bowel syndrome	Additional description: Irritable bowel syndrome		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Lip oedema	Additional description: Lip oedema		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Nausea	Additional description: Nausea		
subjects affected / exposed	2 / 36 (5.56%)	2 / 36 (5.56%)	
occurrences (all)	3	2	
Tongue dry	Additional description: Tongue dry		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Vomiting	Additional description: Vomiting		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Angiodermatitis	Additional description: Angiodermatitis		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Alopecia	Additional description: Alopecia		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	

Blister	Additional description: Blister		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Dermal cyst	Additional description: Dermal cyst		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Erythema	Additional description: Erythema		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Eczema	Additional description: Eczema		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Pruritus	Additional description: Pruritus		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Urticaria	Additional description: Urticaria		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria	Additional description: Dysuria		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Back pain	Additional description: Back pain		
subjects affected / exposed	2 / 36 (5.56%)	3 / 36 (8.33%)	
occurrences (all)	2	4	
Muscle tightness	Additional description: Muscle tightness		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Myalgia	Additional description: Myalgia		

subjects affected / exposed	9 / 36 (25.00%)	14 / 36 (38.89%)	
occurrences (all)	16	24	
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	3	
Periostosis	Additional description: Periostosis		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Asymptomatic COVID-19	Additional description: Asymptomatic COVID-19		
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Campylobacter gastroenteritis	Additional description: Campylobacter gastroenteritis		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
COVID-19	Additional description: COVID-19		
subjects affected / exposed	5 / 36 (13.89%)	4 / 36 (11.11%)	
occurrences (all)	5	4	
Cystitis	Additional description: Cystitis		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Ear infection	Additional description: Ear infection		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis	Additional description: Gastroenteritis		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	7 / 36 (19.44%)	1 / 36 (2.78%)	
occurrences (all)	8	1	
Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	

Periodontitis	Additional description: Periodontitis		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Pulpitis dental	Additional description: Pulpitis dental		
subjects affected / exposed	1 / 36 (2.78%)	0 / 36 (0.00%)	
occurrences (all)	1	0	
Rhinitis	Additional description: Rhinitis		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Sinusitis	Additional description: Sinusitis		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	0 / 36 (0.00%)	1 / 36 (2.78%)	
occurrences (all)	0	1	
Diabetes mellitus	Additional description: Diabetes mellitus		
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 December 2021	Definition of the Immunogenicity Analysis set. Update in the protocol with regards to opening of step 2: The Data Safety Review Committee (DSRC) opened enrolment of step 2 after DSRC meeting 3 instead of DSRC meeting 2 to assess cumulative safety data collected for 7 days from the 2nd injection of step 1-subjects before opening step 2.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported