



Clinical trial results:

A Phase 3 Study to Assess the Persistence of hSBA Response up to 48 Months After Completion of a Primary Series of Bivalent rLP2086, and the Safety, Tolerability, and Immunogenicity of a Booster Dose of Bivalent rLP2086

Summary

EudraCT number	2011-005697-31
Trial protocol	CZ SE DE DK FI PL
Global end of trial date	05 January 2018

Results information

Result version number	v1
This version publication date	21 July 2018
First version publication date	21 July 2018

Trial information

Trial identification

Sponsor protocol code	B1971033
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01543087
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 1-800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 1-800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.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?	Yes

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	29 March 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	05 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Stage 1 • To describe the immunogenicity of bivalent recombinant lipoprotein 2086 vaccine (rLP2086) as determined by serum bactericidal assay using human complement (hSBA) titers to 4 primary test strains at approximately 6, 12, 18, 24, 36, and 48 months after the last dose (second or third dose) of bivalent rLP2086 or saline in the primary study. Booster Stage • To describe the immune response as measured by hSBA titers to 4 primary test strains 1 month following the last vaccination with bivalent rLP2086 in the primary study, before the booster vaccination, and 1 month, 12 months, and 26 months after a single booster dose of bivalent rLP2086. • To evaluate the safety profile of bivalent rLP2086 as measured by the incidence of local reactions, systemic events, adverse events (AEs), serious adverse events (SAEs), newly diagnosed chronic medical conditions (NDCMCs), medically attended events, and immediate AEs following a booster vaccination of bivalent rLP2086.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 September 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	26 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 153
Country: Number of subjects enrolled	Denmark: 216
Country: Number of subjects enrolled	Finland: 40
Country: Number of subjects enrolled	Germany: 54
Country: Number of subjects enrolled	Sweden: 42
Country: Number of subjects enrolled	United States: 193
Worldwide total number of subjects	698
EEA total number of subjects	505

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)	73
Adolescents (12-17 years)	468
Adults (18-64 years)	157
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total 698 subjects enrolled in study, who completed 1 of primary studies B1971010, B1971012 and B1971015. This study consisted of 2 stages: Stage 1 and Booster stage. Only subjects from primary studies B1971010 and B1971012 who received bivalent rLP2086 in primary study and completed Stage 1 were eligible to participate in booster stage.

Period 1

Period 1 title	Stage 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: MCV4+Tdap+Saline (0-, 2-, and 6-Month Schedule)

Arm description:

Subjects received Quadrivalent meningococcal polysaccharide conjugate (MCV4) and Tetanus, diphtheria, and acellular pertussis (Tdap) vaccine on 0- month, saline on a 0-, 2-, 6- month schedule in primary study B1971015.

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)

Arm description:

Subjects who received bivalent rLP2086 vaccine on 0-, 1-, and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	PF-05212366
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of bivalent rLP2086 injection into the deltoid muscle.

Arm title	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)
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Arm description:

Subjects who received bivalent rLP2086 vaccine on 0-, 2-, and 6-month schedule in primary study B1971010, B1971012 and B1971015, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	PF-05212366
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of bivalent rLP2086 injection into the deltoid muscle.

Arm title	Group 4: rLP2086 (0-and 6-Month Schedule)
Arm description: Subjects who received bivalent rLP2086 vaccine on 0- and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	PF-05212366
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of bivalent rLP2086 injection into the deltoid muscle.

Arm title	Group 5: rLP2086 (0- and 2-Month Schedule)
Arm description: Subjects who received bivalent rLP2086 vaccine on 0- and 2-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	PF-05212366
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of bivalent rLP2086 injection into the deltoid muscle.

Arm title	Group 6: rLP2086 (0- and 4-Month Schedule)
Arm description: Subjects who received bivalent rLP2086 vaccine on 0- and 4-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	PF-05212366
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of bivalent rLP2086 injection into the deltoid muscle.

Number of subjects in period 1	Group 1: MCV4+Tdap+Saline (0-, 2-, and 6-Month Schedule)	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)
Started	70	103	277
Safety Population	70	101	277
Completed	56	93	237
Not completed	14	10	40
No longer meets eligibility criteria	1	-	1

No longer willing to participate	5	3	18
Other than specified	5	-	9
Lost to follow-up	3	4	12
Protocol deviation	-	3	-

Number of subjects in period 1	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0- and 2-Month Schedule)	Group 6: rLP2086 (0- and 4-Month Schedule)
Started	116	86	46
Safety Population	116	86	46
Completed	108	83	46
Not completed	8	3	0
No longer meets eligibility criteria	2	-	-
No longer willing to participate	6	3	-
Other than specified	-	-	-
Lost to follow-up	-	-	-
Protocol deviation	-	-	-

Period 2

Period 2 title	Booster Stage
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)

Arm description:

Subjects who received bivalent rLP2086 vaccine on 0-, 1-, and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	PF-05212366
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of bivalent rLP2086 injection into the deltoid muscle.

Arm title	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)
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Arm description:

Subjects who received bivalent rLP2086 vaccine on 0-, 2-, and 6-month schedule in primary study B1971010, B1971012 and B1971015, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Arm type	Experimental
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Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	PF-05212366
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received 0.5 mL of bivalent rLP2086 injection into the deltoid muscle.	
Arm title	Group 4: rLP2086 (0-and 6-Month Schedule)

Arm description:

Subjects who received bivalent rLP2086 vaccine on 0- and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	PF-05212366
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received 0.5 mL of bivalent rLP2086 injection into the deltoid muscle.	
Arm title	Group 5: rLP2086 (0- and 2-Month Schedule)

Arm description:

Subjects who received bivalent rLP2086 vaccine on 0- and 2-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	PF-05212366
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received 0.5 mL of bivalent rLP2086 injection into the deltoid muscle.	
Arm title	Group 6: rLP2086 (0- and 4-Month Schedule)

Arm description:

Subjects who received bivalent rLP2086 vaccine on 0- and 4-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	PF-05212366
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received 0.5 mL of bivalent rLP2086 injection into the deltoid muscle.	

Number of subjects in period 2^[1]	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)
Started	60	92	64
Vaccinated	59	92	64
Completed	59	91	64
Not completed	1	1	0
Withdrawal before booster vaccination	1	-	-
Lost to follow-up	-	1	-

Number of subjects in period 2^[1]	Group 5: rLP2086 (0- and 2-Month Schedule)	Group 6: rLP2086 (0- and 4-Month Schedule)
Started	56	32
Vaccinated	54	32
Completed	54	32
Not completed	2	0
Withdrawal before booster vaccination	2	-
Lost to follow-up	-	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only those subjects from primary study who were eligible to participate in the Booster Stage have started this period.

Baseline characteristics

Reporting groups

Reporting group title	Group 1: MCV4+Tdap+Saline (0-, 2-, and 6-Month Schedule)
Reporting group description: Subjects received Quadrivalent meningococcal polysaccharide conjugate (MCV4) and Tetanus, diphtheria, and acellular pertussis (Tdap) vaccine on 0- month, saline on a 0-, 2-, 6- month schedule in primary study B1971015.	
Reporting group title	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0-, 1-, and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0-, 2-, and 6-month schedule in primary study B1971010, B1971012 and B1971015, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 4: rLP2086 (0- and 6-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0- and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 5: rLP2086 (0- and 2-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0- and 2-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 6: rLP2086 (0- and 4-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0- and 4-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	

Reporting group values	Group 1: MCV4+Tdap+Saline (0-, 2-, and 6-Month Schedule)	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)
Number of subjects	70	103	277
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	11.7 ± 0.7	15.9 ± 2.2	14.3 ± 2.8
Sex: Female, Male Units: Subjects			
Female	32	55	144
Male	38	48	133
Race/Ethnicity, Customized Units: Subjects			
White	59	103	256

Black	9	0	12
Other	2	0	8
Asian	0	0	1
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	16	0	25
Not Hispanic or Latino	54	103	252
Unknown or Not Reported	0	0	0

Reporting group values	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0- and 2-Month Schedule)	Group 6: rLP2086 (0- and 4-Month Schedule)
Number of subjects	116	86	46
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean	15.8	16.1	15.9
standard deviation	± 2.1	± 2.4	± 2.1
Sex: Female, Male			
Units: Subjects			
Female	67	38	26
Male	49	48	20
Race/Ethnicity, Customized			
Units: Subjects			
White	115	85	46
Black	1	0	0
Other	0	1	0
Asian	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	2	0
Not Hispanic or Latino	115	84	46
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	698		
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Subjects			
Female	362		
Male	336		

Race/Ethnicity, Customized Units: Subjects			
White	664		
Black	22		
Other	11		
Asian	1		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	44		
Not Hispanic or Latino	654		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Group 1: MCV4+Tdap+Saline (0-, 2-, and 6-Month Schedule)
Reporting group description: Subjects received Quadrivalent meningococcal polysaccharide conjugate (MCV4) and Tetanus, diphtheria, and acellular pertussis (Tdap) vaccine on 0- month, saline on a 0-, 2-, 6- month schedule in primary study B1971015.	
Reporting group title	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0-, 1-, and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0-, 2-, and 6-month schedule in primary study B1971010, B1971012 and B1971015, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 4: rLP2086 (0- and 6-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0- and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 5: rLP2086 (0- and 2-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0- and 2-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 6: rLP2086 (0- and 4-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0- and 4-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0-, 1-, and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0-, 2-, and 6-month schedule in primary study B1971010, B1971012 and B1971015, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 4: rLP2086 (0- and 6-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0- and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 5: rLP2086 (0- and 2-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0- and 2-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.	
Reporting group title	Group 6: rLP2086 (0- and 4-Month Schedule)
Reporting group description: Subjects who received bivalent rLP2086 vaccine on 0- and 4-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7	

Primary: Percentage of Subjects Reporting Local Reactions Within 7 Days After Booster Vaccination

End point title	Percentage of Subjects Reporting Local Reactions Within 7 Days After Booster Vaccination ^[1]
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End point description:

Local reactions included pain at injection site, redness and swelling collected by using an e-diary. Redness and swelling were graded as: mild (2.5-5.0 centimeter [cm]), moderate (greater than [$>$] 5.0-10.0 cm) and severe ($>$ 10.0 cm). Pain was graded as: mild (does not interfere with activity), moderate (Interferes with activity) and severe (prevents daily activity). Booster stage safety population included all subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety data was available.

End point type	Primary
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End point timeframe:

Within 7 days after booster 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0-and 2-Month Schedule)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	92	64	54
Units: percentage of subjects				
number (confidence interval 95%)				
Pain at injection site:Any	91.5 (81.3 to 97.2)	93.5 (86.3 to 97.6)	89.1 (78.8 to 95.5)	88.9 (77.4 to 95.8)
Pain at injection site:Mild	37.3 (25.0 to 50.9)	29.3 (20.3 to 39.8)	28.1 (17.6 to 40.8)	35.2 (22.7 to 49.4)
Pain at injection site:Moderate	40.7 (28.1 to 54.3)	54.3 (43.6 to 64.8)	51.6 (38.7 to 64.2)	44.4 (30.9 to 58.6)
Pain at injection site:Severe	13.6 (6.0 to 25.0)	9.8 (4.6 to 17.8)	9.4 (3.5 to 19.3)	9.3 (3.1 to 20.3)
Redness:Any	20.3 (11.0 to 32.8)	20.7 (12.9 to 30.4)	20.3 (11.3 to 32.2)	27.8 (16.5 to 41.6)
Redness:Mild	6.8 (1.9 to 16.5)	5.4 (1.8 to 12.2)	10.9 (4.5 to 21.2)	5.6 (1.2 to 15.4)
Redness:Moderate	11.9 (4.9 to 22.9)	10.9 (5.3 to 19.1)	7.8 (2.6 to 17.3)	16.7 (7.9 to 29.3)
Redness:Severe	1.7 (0.0 to 9.1)	4.3 (1.2 to 10.8)	1.6 (0.0 to 8.4)	5.6 (1.2 to 15.4)
Swelling:Any	18.6 (9.7 to 30.9)	20.7 (12.9 to 30.4)	17.2 (8.9 to 28.7)	14.8 (6.6 to 27.1)
Swelling:Mild	11.9 (4.9 to 22.9)	8.7 (3.8 to 16.4)	10.9 (4.5 to 21.2)	3.7 (0.5 to 12.7)
Swelling:Moderate	6.8 (1.9 to 16.5)	10.9 (5.3 to 19.1)	6.3 (1.7 to 15.2)	11.1 (4.2 to 22.6)
Swelling:Severe	0.0 (0.0 to 6.1)	1.1 (0.0 to 5.9)	0.0 (0.0 to 5.6)	0.0 (0.0 to 6.6)

End point values	Group 6: rLP2086 (0- and 4-Month Schedule)			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (confidence interval 95%)				
Pain at injection site:Any	84.4 (67.2 to 94.7)			
Pain at injection site:Mild	25.0 (11.5 to 43.4)			
Pain at injection site:Moderate	46.9 (29.1 to 65.3)			
Pain at injection site:Severe	12.5 (3.5 to 29.0)			
Redness:Any	6.3 (0.8 to 20.8)			
Redness:Mild	3.1 (0.1 to 16.2)			
Redness:Moderate	3.1 (0.1 to 16.2)			
Redness:Severe	0.0 (0.0 to 10.9)			
Swelling:Any	9.4 (2.0 to 25.0)			
Swelling:Mild	9.4 (2.0 to 25.0)			
Swelling:Moderate	0.0 (0.0 to 10.9)			
Swelling:Severe	0.0 (0.0 to 10.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Booster Vaccination

End point title	Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Booster Vaccination ^[2]
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End point description:

Systemic reactions included: fever, vomiting, diarrhea, headache, fatigue, chills, muscle pain and joint pain, were recorded by using an e-diary. Fever was graded as: greater than equal to (\geq) 38.0 degree celsius (C), 38.0 to less than ($<$) 38.5 degree C, 38.5 to $<$ 39.0 degree C, 39.0 to 40.0 degree C and greater than ($>$) 40.0°C. Vomiting was graded as: mild (1 to 2 times in 24 hours [hrs]), moderate ($>$ 2 times in 24 hrs) and severe (requires intravenous [IV] hydration); Diarrhea was graded as: mild (2 to 3 loose stools in 24 hrs), moderate (4 to 5 loose stools in 24 hrs) and severe (6 or more loose stools in 24 hrs); Headache, fatigue, chills, muscle pain and joint pain was graded as: mild (does not interfere with activity), moderate (some interference with activity) and severe (prevents daily routine activity). Booster stage safety population included all subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety data was available.

End point type	Primary
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End point timeframe:

Within 7 days after booster 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0-and 2-Month Schedule)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	92	64	54
Units: percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C	5.1 (1.1 to 14.1)	1.1 (0.0 to 5.9)	4.7 (1.0 to 13.1)	1.9 (0.0 to 9.9)
Fever 38.0 to <38.5 degrees C	5.1 (1.1 to 14.1)	1.1 (0.0 to 5.9)	3.1 (0.4 to 10.8)	0.0 (0.0 to 6.6)
Fever 38.5 to <39.0 degrees C	0.0 (0.0 to 6.1)	0.0 (0.0 to 3.9)	1.6 (0.0 to 8.4)	1.9 (0.0 to 9.9)
Fever 39.0 to 40.0 degrees C	0.0 (0.0 to 6.1)	0.0 (0.0 to 3.9)	0.0 (0.0 to 5.6)	0.0 (0.0 to 6.6)
Fever >40.0 degrees C	0.0 (0.0 to 6.1)	0.0 (0.0 to 3.9)	0.0 (0.0 to 5.6)	0.0 (0.0 to 6.6)
Vomiting:Any	1.7 (0.0 to 9.1)	3.3 (0.7 to 9.2)	3.1 (0.4 to 10.8)	1.9 (0.0 to 9.9)
Vomiting:Mild	1.7 (0.0 to 9.1)	3.3 (0.7 to 9.2)	1.6 (0.0 to 8.4)	1.9 (0.0 to 9.9)
Vomiting:Moderate	0.0 (0.0 to 6.1)	0.0 (0.0 to 3.9)	1.6 (0.0 to 8.4)	0.0 (0.0 to 6.6)
Vomiting:Severe	0.0 (0.0 to 6.1)	0.0 (0.0 to 3.9)	0.0 (0.0 to 5.6)	0.0 (0.0 to 6.6)
Diarrhea:Any	10.2 (3.8 to 20.8)	13.0 (6.9 to 21.7)	4.7 (1.0 to 13.1)	5.6 (1.2 to 15.4)
Diarrhea:Mild	8.5 (2.8 to 18.7)	12.0 (6.1 to 20.4)	3.1 (0.4 to 10.8)	5.6 (1.2 to 15.4)
Diarrhea:Moderate	1.7 (0.0 to 9.1)	1.1 (0.0 to 5.9)	1.6 (0.0 to 8.4)	0.0 (0.0 to 6.6)
Diarrhea:Severe	0.0 (0.0 to 6.1)	0.0 (0.0 to 3.9)	0.0 (0.0 to 5.6)	0.0 (0.0 to 6.6)
Headache:Any	50.8 (37.5 to 64.1)	47.8 (37.3 to 58.5)	56.3 (43.3 to 68.6)	48.1 (34.3 to 62.2)
Headache:Mild	30.5 (19.2 to 43.9)	28.3 (19.4 to 38.6)	35.9 (24.3 to 48.9)	22.2 (12.0 to 35.6)
Headache:Moderate	20.3 (11.0 to 32.8)	18.5 (11.1 to 27.9)	20.3 (11.3 to 32.2)	25.9 (15.0 to 39.7)
Headache:Severe	0.0 (0.0 to 6.1)	1.1 (0.0 to 5.9)	0.0 (0.0 to 5.6)	0.0 (0.0 to 6.6)
Fatigue:Any	62.7 (49.1 to 75.0)	60.9 (50.1 to 70.9)	62.5 (49.5 to 74.3)	51.9 (37.8 to 65.7)
Fatigue:Mild	27.1 (16.4 to 40.3)	27.2 (18.4 to 37.4)	35.9 (24.3 to 48.9)	24.1 (13.5 to 37.6)
Fatigue:Moderate	32.2 (20.6 to 45.6)	31.5 (22.2 to 42.0)	23.4 (13.8 to 35.7)	24.1 (13.5 to 37.6)
Fatigue:Severe	3.4 (0.4 to 11.7)	2.2 (0.3 to 7.6)	3.1 (0.4 to 10.8)	3.7 (0.5 to 12.7)
Chills:Any	23.7 (13.6 to 36.6)	31.5 (22.2 to 42.0)	20.3 (11.3 to 32.2)	18.5 (9.3 to 31.4)
Chills:Mild	13.6 (6.0 to 25.0)	20.7 (12.9 to 30.4)	12.5 (5.6 to 23.2)	9.3 (3.1 to 20.3)
Chills:Moderate	10.2 (3.8 to 20.8)	9.8 (4.6 to 17.8)	7.8 (2.6 to 17.3)	7.4 (2.1 to 17.9)
Chills:Severe	0.0 (0.0 to 6.1)	1.1 (0.0 to 5.9)	0.0 (0.0 to 5.6)	1.9 (0.0 to 9.9)
Muscle pain:Any	22.0 (12.3 to 34.7)	29.3 (20.3 to 39.8)	18.8 (10.1 to 30.5)	24.1 (13.5 to 37.6)
Muscle pain: Mild	16.9 (8.4 to 29.0)	15.2 (8.6 to 24.2)	7.8 (2.6 to 17.3)	14.8 (6.6 to 27.1)
Muscle pain:Moderate	5.1 (1.1 to 14.1)	13.0 (6.9 to 21.7)	7.8 (2.6 to 17.3)	5.6 (1.2 to 15.4)

Muscle pain:Severe	0.0 (0.0 to 6.1)	1.1 (0.0 to 5.9)	3.1 (0.4 to 10.8)	3.7 (0.5 to 12.7)
Joint pain:Any	11.9 (4.9 to 22.9)	16.3 (9.4 to 25.5)	14.1 (6.6 to 25.0)	18.5 (9.3 to 31.4)
Joint pain:Mild	8.5 (2.8 to 18.7)	9.8 (4.6 to 17.8)	7.8 (2.6 to 17.3)	7.4 (2.1 to 17.9)
Joint pain:Moderate	3.4 (0.4 to 11.7)	6.5 (2.4 to 13.7)	4.7 (1.0 to 13.1)	9.3 (3.1 to 20.3)
Joint pain:Severe	0.0 (0.0 to 6.1)	0.0 (0.0 to 3.9)	1.6 (0.0 to 8.4)	1.9 (0.0 to 9.9)
Use of antipyretic medication	10.2 (3.8 to 20.8)	14.1 (7.7 to 23.0)	7.8 (2.6 to 17.3)	13.0 (5.4 to 24.9)

End point values	Group 6: rLP2086 (0- and 4-Month Schedule)			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C	3.1 (0.1 to 16.2)			
Fever 38.0 to <38.5 degrees C	3.1 (0.1 to 16.2)			
Fever 38.5 to <39.0 degrees C	0.0 (0.0 to 10.9)			
Fever 39.0 to 40.0 degrees C	0.0 (0.0 to 10.9)			
Fever >40.0 degrees C	0.0 (0.0 to 10.9)			
Vomiting:Any	0.0 (0.0 to 10.9)			
Vomiting:Mild	0.0 (0.0 to 10.9)			
Vomiting:Moderate	0.0 (0.0 to 10.9)			
Vomiting:Severe	0.0 (0.0 to 10.9)			
Diarrhea:Any	18.8 (7.2 to 36.4)			
Diarrhea:Mild	18.8 (7.2 to 36.4)			
Diarrhea:Moderate	0.0 (0.0 to 10.9)			
Diarrhea:Severe	0.0 (0.0 to 10.9)			
Headache:Any	37.5 (21.1 to 56.3)			
Headache:Mild	25.0 (11.5 to 43.4)			
Headache:Moderate	12.5 (3.5 to 29.0)			
Headache:Severe	0.0 (0.0 to 10.9)			
Fatigue:Any	65.6 (46.8 to 81.4)			
Fatigue:Mild	31.3 (16.1 to 50.0)			

Fatigue:Moderate	31.3 (16.1 to 50.0)			
Fatigue:Severe	3.1 (0.1 to 16.2)			
Chills:Any	28.1 (13.7 to 46.7)			
Chills:Mild	18.8 (7.2 to 36.4)			
Chills:Moderate	9.4 (2.0 to 25.0)			
Chills:Severe	0.0 (0.0 to 10.9)			
Muscle pain:Any	15.6 (5.3 to 32.8)			
Muscle pain: Mild	6.3 (0.8 to 20.8)			
Muscle pain:Moderate	9.4 (2.0 to 25.0)			
Muscle pain:Severe	0.0 (0.0 to 10.9)			
Joint pain:Any	21.9 (9.3 to 40.0)			
Joint pain:Mild	12.5 (3.5 to 29.0)			
Joint pain:Moderate	9.4 (2.0 to 25.0)			
Joint pain:Severe	0.0 (0.0 to 10.9)			
Use of antipyretic medication	6.3 (0.8 to 20.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Newly Diagnosed Chronic Medical Condition (NDCMC) and Medically Attended Adverse Event (MAE) From Visit 7 to Visit 8 (Booster Vaccination Phase)

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Newly Diagnosed Chronic Medical Condition (NDCMC) and Medically Attended Adverse Event (MAE) From Visit 7 to Visit 8 (Booster Vaccination Phase) ^[3]
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End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. AEs included both non-serious AEs and SAEs. An NDCMC was defined as a disease or medical condition, that was not identified previously and that was expected to be persistent or otherwise long-lasting in its effects. The investigator determined if the AE was an NDCMC. An MAE was defined as a non-serious AE that resulted in an evaluation at a medical facility. Booster stage safety population included all subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety data was available.

End point type	Primary
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End point timeframe:

From Visit 7 to Visit 8

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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0-and 2-Month Schedule)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	92	64	54
Units: percentage of subjects				
number (confidence interval 95%)				
AE	6.8 (1.9 to 16.5)	8.7 (3.8 to 16.4)	12.5 (5.6 to 23.2)	3.7 (0.5 to 12.7)
SAE	0.0 (0.0 to 6.1)	1.1 (0.0 to 5.9)	0.0 (0.0 to 5.6)	1.9 (0.0 to 9.9)
NDCMC	0.0 (0.0 to 6.1)	0.0 (0.0 to 3.9)	0.0 (0.0 to 5.6)	0.0 (0.0 to 6.6)
MAE	5.1 (1.1 to 14.1)	4.3 (1.2 to 10.8)	4.7 (1.0 to 13.1)	0.0 (0.0 to 6.6)

End point values	Group 6: rLP2086 (0-and 4-Month Schedule)			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (confidence interval 95%)				
AE	12.5 (3.5 to 29.0)			
SAE	0.0 (0.0 to 10.9)			
NDCMC	0.0 (0.0 to 10.9)			
MAE	3.1 (0.1 to 16.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) and Medically Attended Adverse Event (MAE) From Visit 8 to Visit 9 (Booster Follow-up Phase)

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) and Medically Attended Adverse Event (MAE) From Visit 8 to Visit 9 (Booster Follow-up Phase) ^[4]
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End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. An MAE was defined as a non-serious AE that resulted in an evaluation at a medical

facility. Booster stage safety population included all subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety data was available.

End point type	Primary
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End point timeframe:

From Visit 8 to Visit 9

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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0-and 2-Month Schedule)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	92	64	54
Units: percentage of subjects				
number (confidence interval 95%)				
SAE	1.7 (0.0 to 9.1)	0.0 (0.0 to 3.9)	3.1 (0.4 to 10.8)	0.0 (0.0 to 6.6)
MAE	28.8 (17.8 to 42.1)	12.0 (6.1 to 20.4)	10.9 (4.5 to 21.2)	11.1 (4.2 to 22.6)

End point values	Group 6: rLP2086 (0-and 4-Month Schedule)			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (confidence interval 95%)				
SAE	0.0 (0.0 to 10.9)			
MAE	21.9 (9.3 to 40.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) and Medically Attended Adverse Event (MAE) From Visit 7 to Visit 9

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) and Medically Attended Adverse Event (MAE) From Visit 7 to Visit 9 ^[5]
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End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. An MAE was defined as a non-serious AE that resulted in an evaluation at a medical facility. Booster stage safety population included all subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety data was available.

End point type	Primary			
End point timeframe:				
From Visit 7 to Visit 9 (From booster vaccination through 6 months after booster 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: Only descriptive data was planned to be analyzed for this endpoint.				
End point values	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0-and 2-Month Schedule)
	Subject group type	Reporting group	Reporting group	Reporting group
	Number of subjects analysed	59	92	64
	Units: percentage of subjects			
	number (confidence interval 95%)			
	SAE	1.7 (0.0 to 9.1)	1.1 (0.0 to 5.9)	3.1 (0.4 to 10.8)
MAE	32.2 (20.6 to 45.6)	15.2 (8.6 to 24.2)	15.6 (7.8 to 26.9)	11.1 (4.2 to 22.6)

End point values	Group 6: rLP2086 (0-and 4-Month Schedule)			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (confidence interval 95%)				
SAE	0.0 (0.0 to 10.9)			
MAE	25.0 (11.5 to 43.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Condition (NDCMC) From the 6-Month Safety Telephone call in the Primary Study to Visit 6 (Stage 1)

End point title	Percentage of Subjects With Newly Diagnosed Chronic Medical Condition (NDCMC) From the 6-Month Safety Telephone call in the Primary Study to Visit 6 (Stage 1) ^[6]
End point description:	
An NDCMC was defined as a disease or medical condition, that was not identified previously and that was expected to be persistent or otherwise long-lasting in its effects. The investigator determined if the AE was an NDCMC. Stage 1 safety population included all subjects who had at least 1 blood draw in the study.	
End point type	Primary
End point timeframe:	
Visit 1 to Visit 6 (6 months after last primary dose to 48 months after last primary dose in primary	

study)

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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Group 1: MCV4+Tdap +Saline (0-, 2-, and 6-Month Schedule)	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0- and 6-Month Schedule)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	101	277	116
Units: percentage of subjects				
number (confidence interval 95%)	5.7 (1.6 to 14.0)	5.0 (1.6 to 11.2)	2.2 (0.8 to 4.7)	2.6 (0.5 to 7.4)

End point values	Group 5: rLP2086 (0- and 2-Month Schedule)	Group 6: rLP2086 (0- and 4-Month Schedule)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	46		
Units: percentage of subjects				
number (confidence interval 95%)	2.3 (0.3 to 8.1)	2.2 (0.1 to 11.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition (NDCMC) From Visit 8 to Visit 10

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition (NDCMC) From Visit 8 to Visit 10 ^[7]
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End point description:

An NDCMC was defined as a disease or medical condition, that was not identified previously and that was expected to be persistent or otherwise long-lasting in its effects. The investigator determined if the AE was an NDCMC. Booster stage safety population included all subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety data was available.

End point type	Primary
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End point timeframe:

From Visit 8 to Visit 10 (From 1 month after booster vaccination through 12 months after booster vaccination)

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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0-and 2-Month Schedule)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	92	64	54
Units: percentage of subjects				
number (confidence interval 95%)	1.7 (0.0 to 9.1)	2.2 (0.3 to 7.6)	0.0 (0.0 to 5.6)	0.0 (0.0 to 6.6)

End point values	Group 6: rLP2086 (0-and 4-Month Schedule)			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (confidence interval 95%)	0.0 (0.0 to 10.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition (NDCMC) From Visit 7 to Visit 10

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition (NDCMC) From Visit 7 to Visit 10 ^[8]
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End point description:

An NDCMC was defined as a disease or medical condition, that was not identified previously and that was expected to be persistent or otherwise long-lasting in its effects. The investigator determined if the AE was an NDCMC. Booster stage safety population included all subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety data was available.

End point type	Primary
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End point timeframe:

From Visit 7 to Visit 10 (From booster vaccination through 12 months after booster vaccination)

Notes:

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

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0-and 2-Month Schedule)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	92	64	54
Units: percentage of subjects				
number (confidence interval 95%)	1.7 (0.0 to 9.1)	2.2 (0.3 to 7.6)	0.0 (0.0 to 5.6)	0.0 (0.0 to 6.6)

End point values	Group 6: rLP2086 (0- and 4-Month Schedule)			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (confidence interval 95%)	0.0 (0.0 to 10.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Condition (NDCMC) From Visit 8 to Visit 11

End point title	Percentage of Subjects With Newly Diagnosed Chronic Medical Condition (NDCMC) From Visit 8 to Visit 11 ^[9]
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End point description:

An NDCMC was defined as a disease or medical condition, that was not identified previously and that was expected to be persistent or otherwise long-lasting in its effects. The investigator determined if the AE was an NDCMC. Booster stage safety population included all subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety data was available. 'Number of subjects analyzed'= subjects who were in the safety population for the specified analysis interval.

End point type	Primary
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End point timeframe:

From Visit 8 to Visit 11 (From 1 month after booster vaccination through 26 months after booster vaccination)

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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Group 2: rLP2086 (0-, 1- , and 6-Month Schedule)	Group 3: rLP2086 (0-, 2- , and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0- and 2-Month Schedule)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[10]	37	49	0 ^[11]
Units: percentage of subjects				
number (confidence interval 95%)	(to)	5.4 (0.7 to 18.2)	0.0 (0.0 to 7.3)	(to)

Notes:

[10] - None of the subject analyzed for the specified time point.

[11] - None of the subject analyzed for the specified time point.

End point values	Group 6: rLP2086 (0- and 4-Month Schedule)			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[12]			
Units: percentage of subjects				
number (confidence interval 95%)	(to)			

Notes:

[12] - None of the subject analyzed for the specified time point.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Condition (NDCMC) From Visit 7 to Visit 11

End point title	Percentage of Subjects With Newly Diagnosed Chronic Medical Condition (NDCMC) From Visit 7 to Visit 11 ^[13]
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End point description:

An NDCMC was defined as a disease or medical condition, that was not identified previously and that was expected to be persistent or otherwise long-lasting in its effects. The investigator determined if the AE was an NDCMC. Booster stage safety population included all subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety data was available. 'Number of subjects analyzed'= subjects who were in the safety population for the specified analysis interval.

End point type	Primary
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End point timeframe:

From Visit 7 to Visit 11 (From booster vaccination through 26 months after booster vaccination)

Notes:

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

Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0-and 2-Month Schedule)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[14]	37	49	0 ^[15]
Units: percentage of subjects				
number (confidence interval 95%)	(to)	5.4 (0.7 to 18.2)	0.0 (0.0 to 7.3)	(to)

Notes:

[14] - None of the subject analyzed for the specified time point.

[15] - None of the subject analyzed for the specified time point.

End point values	Group 6: rLP2086 (0-and 4-Month Schedule)			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[16]			
Units: percentage of subjects				
number (confidence interval 95%)	(to)			

Notes:

[16] - None of the subject analyzed for the specified time point.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Immediate Adverse Event (AE) After Booster Vaccination

End point title	Percentage of Subjects With at Least 1 Immediate Adverse Event (AE) After Booster Vaccination ^[17]
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End point description:

Immediate AE was defined as AEs occurring within the first 30 minutes after investigational product administration. Booster stage safety population included all subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety data was available.

End point type	Primary
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End point timeframe:

Within 30 days after booster vaccination

Notes:

[17] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0-and 2-Month Schedule)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	92	64	54
Units: percentage of subjects				
number (confidence interval 95%)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)

End point values	Group 6: rLP2086 (0-and 4-Month Schedule)			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of subjects				
number (confidence interval 95%)	0.0 (0.0 to 0.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Days Subjects Missed Work or School Due to AE From Visit 7 Through Visit 9

End point title	Number of Days Subjects Missed Work or School Due to AE From Visit 7 Through Visit 9 ^[18]
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End point description:

Booster stage safety population included all subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety data was available.

End point type	Primary
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End point timeframe:

From Visit 7 Through Visit 9 (From booster vaccination through 6 months after booster vaccination)

Notes:

[18] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)	Group 5: rLP2086 (0-and 2-Month Schedule)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	92	64	54
Units: days	12	12	8	3

End point values	Group 6: rLP2086 (0-and 4-Month Schedule)			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: days	6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs: Recorded from Booster vaccination through visit 7 to 11 (Month 26). Subjects recorded local reactions and systemic events in e-diary within 7 days after booster vaccination. NSAEs: Recorded from Booster vaccination through visit 7 to 11 (Month 26).

Adverse event reporting additional description:

AEs were reported for those subjects who had received the booster vaccination (Bivalent rLP2086) and for whom safety information was available for disclosure.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)
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Reporting group description:

Subjects who received bivalent rLP2086 vaccine on 0-, 1-, and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Reporting group title	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)
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Reporting group description:

Subjects who received bivalent rLP2086 vaccine on 0-, 2-, and 6-month schedule in primary study B1971010, B1971012 and B1971015, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Reporting group title	Group 4: rLP2086 (0-and 6-Month Schedule)
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Reporting group description:

Subjects who received bivalent rLP2086 vaccine on 0- and 6-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Reporting group title	Group 5: rLP2086 (0- and 2-Month Schedule)
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Reporting group description:

Subjects who received bivalent rLP2086 vaccine on 0- and 2-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Reporting group title	Group 6: rLP2086 (0- and 4-Month Schedule)
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Reporting group description:

Subjects who received bivalent rLP2086 vaccine on 0- and 4-month schedule in primary study B1971012, received intramuscular injection of 120 mcg of bivalent rLP2086 vaccine at Visit 7 (approximately Month 48) in booster stage of this study.

Serious adverse events	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 59 (1.69%)	1 / 92 (1.09%)	2 / 64 (3.13%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			

Meniscus injury			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	0 / 64 (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
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 59 (0.00%)	0 / 92 (0.00%)	0 / 64 (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			
Depression			
subjects affected / exposed	0 / 59 (0.00%)	0 / 92 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (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
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 92 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 5: rLP2086 (0- and 2-Month Schedule)	Group 6: rLP2086 (0- and 4-Month Schedule)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 54 (1.85%)	0 / 32 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 54 (1.85%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group 2: rLP2086 (0-, 1-, and 6-Month Schedule)	Group 3: rLP2086 (0-, 2-, and 6-Month Schedule)	Group 4: rLP2086 (0-and 6-Month Schedule)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 59 (94.92%)	90 / 92 (97.83%)	62 / 64 (96.88%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Peripheral artery thrombosis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0

General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 59 (0.00%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Withdrawal syndrome			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Chills			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 59 (23.73%)	29 / 92 (31.52%)	13 / 64 (20.31%)
occurrences (all)	14	29	13
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	37 / 59 (62.71%)	56 / 92 (60.87%)	40 / 64 (62.50%)
occurrences (all)	37	56	40
Injection site erythema (redness)			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 59 (20.34%)	19 / 92 (20.65%)	13 / 64 (20.31%)
occurrences (all)	12	19	13
Injection site pain (tenderness at injection site)			
alternative assessment type: Systematic			
subjects affected / exposed	54 / 59 (91.53%)	86 / 92 (93.48%)	57 / 64 (89.06%)
occurrences (all)	54	86	57
Injection site swelling (swelling)			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 59 (18.64%)	19 / 92 (20.65%)	11 / 64 (17.19%)
occurrences (all)	11	19	11
Pyrexia (fever)			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 59 (5.08%)	1 / 92 (1.09%)	3 / 64 (4.69%)
occurrences (all)	3	1	3
Immune system disorders			
Mite allergy			

subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 92 (1.09%) 1	0 / 64 (0.00%) 0
Seasonal allergy subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 92 (1.09%) 1	0 / 64 (0.00%) 0
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 92 (1.09%) 1	0 / 64 (0.00%) 0
Testicular pain subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Gastrointestinal somatic symptom disorder subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 92 (1.09%) 1	0 / 64 (0.00%) 0
Generalised anxiety disorder subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Persistent depressive disorder subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 92 (1.09%) 1	0 / 64 (0.00%) 0
Investigations Borrelia test positive subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Injury, poisoning and procedural complications Animal bite			

subjects affected / exposed	1 / 59 (1.69%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	1	1	0
Fall			
subjects affected / exposed	1 / 59 (1.69%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	1	1	0
Head injury			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	1 / 64 (1.56%)
occurrences (all)	0	1	1
Joint injury			
subjects affected / exposed	0 / 59 (0.00%)	0 / 92 (0.00%)	1 / 64 (1.56%)
occurrences (all)	0	0	1
Laceration			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	1 / 59 (1.69%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	1	1	0
Muscle injury			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	0 / 59 (0.00%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Neck injury			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Road traffic accident			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Vasoplegia syndrome			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Wrist fracture			

subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 92 (1.09%) 1	0 / 64 (0.00%) 0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Cardiac arrest			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Brain injury			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Disturbance in attention			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	0	2	0
Migraine			
subjects affected / exposed	0 / 59 (0.00%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	30 / 59 (50.85%)	44 / 92 (47.83%)	36 / 64 (56.25%)
occurrences (all)	30	44	36
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Myopia			

subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2	1 / 92 (1.09%) 1	0 / 64 (0.00%) 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Gastric ulcer			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Impaired gastric emptying			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Oesophageal varices haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 59 (10.17%)	12 / 92 (13.04%)	3 / 64 (4.69%)
occurrences (all)	6	12	3
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 59 (1.69%)	3 / 92 (3.26%)	2 / 64 (3.13%)
occurrences (all)	1	3	2
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 59 (0.00%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Psoriasis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 92 (0.00%)	1 / 64 (1.56%)
occurrences (all)	0	0	1

Rash subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	0 / 92 (0.00%) 0	1 / 64 (1.56%) 1
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia alternative assessment type: Systematic subjects affected / exposed occurrences (all) Myalgia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1 7 / 59 (11.86%) 7 13 / 59 (22.03%) 13	1 / 92 (1.09%) 1 15 / 92 (16.30%) 15 27 / 92 (29.35%) 27	0 / 64 (0.00%) 0 9 / 64 (14.06%) 9 12 / 64 (18.75%) 12
Infections and infestations Body tinea subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Cervicitis subjects affected / exposed occurrences (all) Chlamydial infection subjects affected / exposed occurrences (all) Conjunctivitis subjects affected / exposed occurrences (all) Cystitis	0 / 59 (0.00%) 0 0 / 59 (0.00%) 0 0 / 59 (0.00%) 0 1 / 59 (1.69%) 1 1 / 59 (1.69%) 1	1 / 92 (1.09%) 1 0 / 92 (0.00%) 0 0 / 92 (0.00%) 0 0 / 92 (0.00%) 0 0 / 92 (0.00%) 0	0 / 64 (0.00%) 0 1 / 64 (1.56%) 1 0 / 64 (0.00%) 0 0 / 64 (0.00%) 0 0 / 64 (0.00%) 0

subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	1 / 64 (1.56%)
occurrences (all)	0	1	1
Genitourinary chlamydia infection			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Impetigo			
subjects affected / exposed	0 / 59 (0.00%)	0 / 92 (0.00%)	1 / 64 (1.56%)
occurrences (all)	0	0	1
Infection			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	2	0	0
Laryngitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 59 (0.00%)	1 / 92 (1.09%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	3 / 59 (5.08%)	2 / 92 (2.17%)	5 / 64 (7.81%)
occurrences (all)	3	2	5
Oral candidiasis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	1 / 59 (1.69%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Otitis media acute			
subjects affected / exposed	0 / 59 (0.00%)	0 / 92 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			

subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	0 / 92 (0.00%) 0	1 / 64 (1.56%) 1
Pneumonia subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Rhinitis subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Tonsillitis subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	1 / 92 (1.09%) 2	2 / 64 (3.13%) 2
Tooth infection subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Tracheitis subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	2 / 92 (2.17%) 2	0 / 64 (0.00%) 0
Infectious mononucleosis subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	1 / 92 (1.09%) 1	0 / 64 (0.00%) 0
Metabolism and nutrition disorders Electrolyte imbalance subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0

Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0
Vitamin K deficiency subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	0 / 92 (0.00%) 0	0 / 64 (0.00%) 0

Non-serious adverse events	Group 5: rLP2086 (0- and 2-Month Schedule)	Group 6: rLP2086 (0- and 4-Month Schedule)	
Total subjects affected by non-serious adverse events subjects affected / exposed	53 / 54 (98.15%)	31 / 32 (96.88%)	
Vascular disorders			
Hypertension subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Hypotension subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Peripheral artery thrombosis subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
General disorders and administration site conditions			
Influenza like illness subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	1 / 32 (3.13%) 1	
Withdrawal syndrome subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Chills alternative assessment type: Systematic subjects affected / exposed occurrences (all)	10 / 54 (18.52%) 10	9 / 32 (28.13%) 9	
Fatigue alternative assessment type: Systematic subjects affected / exposed occurrences (all)	28 / 54 (51.85%) 28	21 / 32 (65.63%) 21	
Injection site erythema (redness)			

<p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>15 / 54 (27.78%)</p> <p>15</p>	<p>2 / 32 (6.25%)</p> <p>2</p>	
<p>Injection site pain (tenderness at injection site)</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>48 / 54 (88.89%)</p> <p>48</p>	<p>27 / 32 (84.38%)</p> <p>27</p>	
<p>Injection site swelling (swelling)</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>8 / 54 (14.81%)</p> <p>8</p>	<p>3 / 32 (9.38%)</p> <p>3</p>	
<p>Pyrexia (fever)</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 54 (1.85%)</p> <p>1</p>	<p>1 / 32 (3.13%)</p> <p>1</p>	
<p>Immune system disorders</p> <p>Mite allergy</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 54 (0.00%)</p> <p>0</p>	<p>0 / 32 (0.00%)</p> <p>0</p>	
<p>Seasonal allergy</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 54 (0.00%)</p> <p>0</p>	<p>0 / 32 (0.00%)</p> <p>0</p>	
<p>Reproductive system and breast disorders</p> <p>Dysmenorrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 54 (0.00%)</p> <p>0</p>	<p>0 / 32 (0.00%)</p> <p>0</p>	
<p>Testicular pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 54 (0.00%)</p> <p>0</p>	<p>0 / 32 (0.00%)</p> <p>0</p>	
<p>Psychiatric disorders</p> <p>Depression</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 54 (0.00%)</p> <p>0</p>	<p>0 / 32 (0.00%)</p> <p>0</p>	
<p>Gastrointestinal somatic symptom disorder</p>			

subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Generalised anxiety disorder subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Insomnia subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Persistent depressive disorder subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Investigations Borrelia test positive subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Injury, poisoning and procedural complications Animal bite subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Fall subjects affected / exposed occurrences (all)	2 / 54 (3.70%) 2	0 / 32 (0.00%) 0	
Head injury subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Joint injury subjects affected / exposed occurrences (all)	1 / 54 (1.85%) 1	0 / 32 (0.00%) 0	
Laceration subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Ligament sprain subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Limb injury			

subjects affected / exposed	0 / 54 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Muscle injury			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Muscle strain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	2	
Neck injury			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Road traffic accident			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Vasoplegia syndrome			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Wrist fracture			
subjects affected / exposed	2 / 54 (3.70%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Cardiac arrest			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Brain injury			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Disturbance in attention			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Dizziness			

subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Migraine subjects affected / exposed occurrences (all)	1 / 54 (1.85%) 1	1 / 32 (3.13%) 1	
Syncope subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Headache alternative assessment type: Systematic subjects affected / exposed occurrences (all)	26 / 54 (48.15%) 26	12 / 32 (37.50%) 12	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Eye disorders Myopia subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Gastric ulcer subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Impaired gastric emptying subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Nausea subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Oesophageal varices haemorrhage subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	

Diarrhoea alternative assessment type: Systematic subjects affected / exposed occurrences (all)	3 / 54 (5.56%) 3	6 / 32 (18.75%) 6	
Vomiting alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 54 (1.85%) 1	0 / 32 (0.00%) 0	
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	1 / 32 (3.13%) 1	
Eczema subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Psoriasis subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 32 (0.00%) 0	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 54 (1.85%) 1	0 / 32 (0.00%) 0	
Arthralgia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	10 / 54 (18.52%) 10	7 / 32 (21.88%) 7	
Myalgia alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	13 / 54 (24.07%) 13	5 / 32 (15.63%) 5	
Infections and infestations			
Body tinea			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Cervicitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Chlamydial infection			
subjects affected / exposed	1 / 54 (1.85%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Cystitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 54 (1.85%)	1 / 32 (3.13%)	
occurrences (all)	1	1	
Genitourinary chlamydia infection			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Impetigo			
subjects affected / exposed	1 / 54 (1.85%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Infection			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 54 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	

Laryngitis		
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0
Lower respiratory tract infection viral		
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0
Nasopharyngitis		
subjects affected / exposed	1 / 54 (1.85%)	0 / 32 (0.00%)
occurrences (all)	1	0
Oral candidiasis		
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0
Oral herpes		
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0
Otitis media acute		
subjects affected / exposed	0 / 54 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	1
Pharyngitis		
subjects affected / exposed	0 / 54 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	1
Pneumonia		
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0
Rhinitis		
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0
Sinusitis		
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0
Tonsillitis		
subjects affected / exposed	0 / 54 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	2
Tooth infection		
subjects affected / exposed	1 / 54 (1.85%)	0 / 32 (0.00%)
occurrences (all)	1	0

Tracheitis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Infectious mononucleosis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Hyperkalaemia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	
Vitamin K deficiency			
subjects affected / exposed	0 / 54 (0.00%)	0 / 32 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 March 2012	Addition of the benefit-risk assessment in the protocol.
19 December 2013	Updation of requirement to report serious adverse events back to the primary studies after the active reporting phase, Addition of Section 7.1.2 on the Luminex assay for antigen detection for MCV4, collection of newly diagnosed chronic medical conditions.
08 January 2015	Addition of a booster dose (booster stage), primary safety objective/endpoints describing the safety profile of bivalent rLP2086 booster vaccination. Updation of safety reporting requirements to reflect receipt of the booster dose.
18 April 2017	Extension of booster stage follow-up duration from 12 months to 26 months, Addition of an additional blood draw visit (Visit 11) to assess immune response 26 months after the booster dose, Updation of the primary and objectives and corresponding endpoint relating to immunogenicity assessment for the booster stage follow-up at 26 months, primary safety endpoint relating to the booster stage follow-up at 26 months. Addition of Visit 11 to the adverse event, Visit 11 to data analysis for immunogenicity and safety endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Immunogenicity data will be posted when it is available.

Notes: