



Clinical trial results:

Final Report: A Phase 3, Randomized, Placebo-Controlled, Observer-Blinded, Trial to Assess the Safety, Tolerability, and Immunogenicity of Bivalent rLP2086 Vaccine When Administered as a 3-Dose Regimen in Healthy Young Adults Aged greater than or equal to (\geq) 18 to less than ($<$) 26 Years

Summary

EudraCT number	2009-014492-46
Trial protocol	FI PL DK ES
Global end of trial date	13 February 2015

Results information

Result version number	v1 (current)
This version publication date	03 August 2016
First version publication date	03 August 2016

Trial information

Trial identification

Sponsor protocol code	B1971016
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01352845
WHO universal trial number (UTN)	-
Other trial identifiers	Alias: 6108A1-2004

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc, 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc, 001 800-718-1021, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 November 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immune response as measured by serum bactericidal assay using human complement (hSBA) performed with 4 primary *Neisseria meningitidis* serogroup B (MnB) test strains, 2 expressing a lipoprotein 2086 vaccine (LP2086) subfamily A protein and 2 expressing a LP2086 subfamily B protein, measured 1 month after the third vaccination with bivalent (recombinant lipoprotein) rLP2086.

To evaluate the safety profile of bivalent rLP2086 compared to a control (saline), as measured by local reactions, systemic events, adverse events (AEs), serious adverse events (SAEs), newly diagnosed chronic medical conditions, medically attended adverse events, and immediate AEs.

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 Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 May 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 361
Country: Number of subjects enrolled	Denmark: 451
Country: Number of subjects enrolled	Finland: 454
Country: Number of subjects enrolled	Poland: 83
Country: Number of subjects enrolled	Spain: 300
Country: Number of subjects enrolled	United States: 1644
Worldwide total number of subjects	3293
EEA total number of subjects	1288

Notes:

Subjects enrolled per age group

In utero	0
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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)	3293
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 3304 subjects were randomized in this study, out of which 3293 subjects received vaccination.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Group 1 rLP2086
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Arm description:

Recombinant lipoprotein 2086 (rLP2086) vaccine on a 0-, 2-, 6- month schedule.

Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 milliliter (mL) of rLP2086 at 0-, 2- and 6- month schedule.

Arm title	Group 2 Saline
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Arm description:

Saline on a 0-, 2-, 6- month schedule.

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

Dosage and administration details:

Subjects received 0.5 mL of saline at 0-, 2- and 6- month schedule.

Number of subjects in period 1	Group 1 rLP2086	Group 2 Saline
Started	2471	822
Completed	1800	619
Not completed	671	203
Adverse event, serious fatal	3	-
Consent withdrawn by subject	48	16

No Longer Willing to Participate	205	58
Adverse event, non-fatal	22	6
Pregnancy	27	7
Unspecified	17	7
Lost to follow-up	313	92
No Longer Meets Eligibility Criteria	24	11
Protocol deviation	12	6

Baseline characteristics

Reporting groups

Reporting group title	Group 1 rLP2086
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Reporting group description:

Recombinant lipoprotein 2086 (rLP2086) vaccine on a 0-, 2-, 6- month schedule.

Reporting group title	Group 2 Saline
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Reporting group description:

Saline on a 0-, 2-, 6- month schedule.

Reporting group values	Group 1 rLP2086	Group 2 Saline	Total
Number of subjects	2471	822	3293
Age categorical Units: Subjects			

Age Continuous Units: Years arithmetic mean standard deviation	21.47 ± 2.14	21.52 ± 2.2	-
Gender, Male/Female Units: Participants			
Female	1452	482	1934
Male	1019	340	1359

End points

End points reporting groups

Reporting group title	Group 1 rLP2086
Reporting group description: Recombinant lipoprotein 2086 (rLP2086) vaccine on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 2 Saline
Reporting group description: Saline on a 0-, 2-, 6- month schedule.	

Primary: Percentage of Subjects with (\geq) 4 Fold Rise in Serum Bactericidal Assay Using Human Complement (hSBA) for 4 Primary Strains and Composite Response (hSBA \geq Lower Limit of Quantification [LLOQ] for all 4 Primary Strains Combined): Group 1

End point title	Percentage of Subjects with (\geq) 4 Fold Rise in Serum Bactericidal Assay Using Human Complement (hSBA) for 4 Primary Strains and Composite Response (hSBA \geq Lower Limit of Quantification [LLOQ] for all 4 Primary Strains Combined): Group 1 ^{[1][2]}
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End point description:

Evaluable immunogenicity population: all eligible subjects randomized, who received correct investigational product, had pre/post vaccination blood drawn at pre-specified time points, had valid and determinate assay results for proposed analysis, received no prohibited treatment or prohibited vaccines, and had no major protocol violations. Here, N signifies subjects with valid and determinate hSBA titers for given strain at specified time point. This outcome measure was planned to be analyzed for Group 1 only.

End point type	Primary
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End point timeframe:

One month after third bivalent rLP2086 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 reported for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data was planned to be analysed only for Group 1 rLP2086.

End point values	Group 1 rLP2086			
Subject group type	Reporting group			
Number of subjects analysed	1723			
Units: Percentage of subjects				
number (confidence interval 95%)				
Composite hSBA response (N=1664)	84.9 (83.1 to 86.6)			
PMB80 [A22] (N=1695)	80.5 (78.6 to 82.4)			
PMB2001 [A56] (N=1642)	90 (88.4 to 91.4)			
PMB2948 [B24] (N=1675)	79.3 (77.3 to 81.2)			
PMB2707 [B44] (N=1696)	79.6 (77.6 to 81.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Pre-specified Local Reactions (LRs) Within 7 Days After First Vaccination

End point title	Percentage of Subjects Reporting Pre-specified Local Reactions (LRs) Within 7 Days After First Vaccination ^[3]
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End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or saline) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary
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End point timeframe:

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

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2425	798		
Units: Percentage of subjects				
number (confidence interval 95%)				
Pain at injection site: Any	84.2 (82.7 to 85.6)	11.8 (9.6 to 14.2)		
Pain at injection site: Mild	42.3 (40.3 to 44.3)	10.7 (8.6 to 13)		
Pain at injection site: Moderate	37.1 (35.1 to 39)	1.1 (0.5 to 2.1)		
Pain at injection site: Severe	4.8 (4 to 5.8)	0 (0 to 0.5)		
Redness: Any	13.8 (12.5 to 15.3)	0.6 (0.2 to 1.5)		
Redness: Mild	5.8 (4.9 to 6.8)	0.5 (0.1 to 1.3)		
Redness: Moderate	7.1 (6.1 to 8.2)	0 (0 to 0.5)		
Redness: Severe	0.9 (0.6 to 1.4)	0.1 (0 to 0.7)		
Swelling: Any	15.5 (14.1 to 17.1)	0.6 (0.2 to 1.5)		
Swelling: Mild	8.5 (7.4 to 9.7)	0.3 (0 to 0.9)		
Swelling: Moderate	6.8 (5.8 to 7.9)	0.3 (0 to 0.9)		
Swelling: Severe	0.2 (0.1 to 0.5)	0.1 (0 to 0.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Pre-specified Local Reactions (LRs) Within 7 Days After Second Vaccination

End point title	Percentage of Subjects Reporting Pre-specified Local Reactions (LRs) Within 7 Days After Second Vaccination ^[4]
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End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary
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End point timeframe:

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

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2076	706		
Units: Percentage of subjects				
number (confidence interval 95%)				
Pain at injection site: Any	79.3 (77.5 to 81.1)	7.8 (5.9 to 10)		
Pain at injection site: Mild	42.2 (40.1 to 44.4)	6.8 (5.1 to 8.9)		
Pain at injection site: Moderate	32.7 (30.7 to 34.8)	1 (0.4 to 2)		
Pain at injection site: Severe	4.4 (3.6 to 5.4)	0 (0 to 0.5)		
Redness: Any	11.8 (10.4 to 13.3)	0.3 (0 to 1)		
Redness: Mild	4.6 (3.7 to 5.6)	0.1 (0 to 0.8)		
Redness: Moderate	6.3 (5.3 to 7.4)	0 (0 to 0.5)		
Redness: Severe	0.9 (0.6 to 1.4)	0.1 (0 to 0.8)		
Swelling: Any	14 (12.6 to 15.6)	0.4 (0.1 to 1.2)		
Swelling: Mild	7.7 (6.6 to 8.9)	0.3 (0 to 1)		
Swelling: Moderate	6 (5 to 7.1)	0.1 (0 to 0.8)		
Swelling: Severe	0.3 (0.1 to 0.7)	0 (0 to 0.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Pre-specified Local Reactions (LRs) Within 7 Days After Third Vaccination

End point title	Percentage of Subjects Reporting Pre-specified Local Reactions (LRs) Within 7 Days After Third Vaccination ^[5]
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End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product (rLP2086 or saline) and for whom safety information was available from third

vaccination until post third-vaccination blood draw.

End point type	Primary
End point timeframe:	
Within 7 days after third 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1823	624		
Units: Percentage of subjects				
number (confidence interval 95%)				
Pain at injection site: Any	80.4 (78.5 to 82.2)	6.7 (4.9 to 9)		
Pain at injection site: Mild	36.1 (33.9 to 38.4)	6.4 (4.6 to 8.6)		
Pain at injection site: Moderate	38.9 (36.6 to 41.2)	0.3 (0 to 1.2)		
Pain at injection site: Severe	5.3 (4.3 to 6.5)	0 (0 to 0.6)		
Redness: Any	17.1 (15.4 to 18.9)	0.2 (0 to 0.9)		
Redness: Mild	6.2 (5.1 to 7.4)	0.2 (0 to 0.9)		
Redness: Moderate	8.6 (7.3 to 9.9)	0 (0 to 0.6)		
Redness: Severe	2.3 (1.7 to 3.1)	0 (0 to 0.6)		
Swelling: Any	16.6 (14.9 to 18.4)	0.3 (0 to 1.2)		
Swelling: Mild	8.8 (7.6 to 10.2)	0 (0 to 0.6)		
Swelling: Moderate	7.2 (6.1 to 8.5)	0.3 (0 to 1.2)		
Swelling: Severe	0.5 (0.2 to 0.9)	0 (0 to 0.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After First Vaccination

End point title	Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After First Vaccination ^[6]
End point description:	
Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or saline) and for whom safety information was available from first vaccination until prior to second vaccination. Here, 'N' signifies subjects with known values reporting specific characteristic.	
End point type	Primary
End point timeframe:	
Within 7 days after first vaccination	

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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2425	798		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C(N=2415, 796)	2.4 (1.8 to 3)	0.6 (0.2 to 1.5)		
Fever 38 to <38.5 degreesC(N=2415, 796)	1.6 (1.1 to 2.2)	0.4 (0.1 to 1.1)		
Fever 38.5 to<39 degrees C(N=2415, 796)	0.7 (0.4 to 1.2)	0 (0 to 0.5)		
Fever 39 to 40 degrees C (N=2415, 796)	0 (0 to 0.2)	0.3 (0 to 0.9)		
Fever >40 degrees C(N=2415, 796)	0 (0 to 0.2)	0 (0 to 0.5)		
Vomiting:Any(N=2425, 798)	2.6 (2 to 3.3)	2.1 (1.2 to 3.4)		
Vomiting:Mild(N=2425, 798)	2.2 (1.6 to 2.8)	2.1 (1.2 to 3.4)		
Vomiting:Moderate(N=2425, 798)	0.4 (0.2 to 0.8)	0 (0 to 0.5)		
Vomiting:Severe(N=2425, 798)	0 (0 to 0.2)	0 (0 to 0.5)		
Diarrhea:Any(N=2425, 798)	12.7 (11.4 to 14.1)	11.8 (9.6 to 14.2)		
Diarrhea:Mild(N=2425, 798)	10.2 (9 to 11.5)	9.8 (7.8 to 12)		
Diarrhea:Moderate(N=2425, 798)	2.4 (1.8 to 3)	1.9 (1.1 to 3.1)		
Diarrhea:Severe(N=2425, 798)	0.2 (0.1 to 0.5)	0.1 (0 to 0.7)		
Headache:Any(N=2425, 798)	43.9 (41.9 to 45.9)	36.2 (32.9 to 39.7)		
Headache:Mild(N=2425, 798)	24.3 (22.6 to 26.1)	22.1 (19.2 to 25.1)		
Headache:Moderate(N=2425, 798)	17.9 (16.4 to 19.5)	13.5 (11.2 to 16.1)		
Headache:Severe(N=2425, 798)	1.6 (1.2 to 2.2)	0.6 (0.2 to 1.5)		
Fatigue:Any(N=2425, 798)	50.9 (48.9 to 52.9)	39.8 (36.4 to 43.3)		
Fatigue:Mild(N=2425, 798)	25.4 (23.7 to 27.2)	23.2 (20.3 to 26.3)		
Fatigue:Moderate(N=2425, 798)	22.1 (20.5 to 23.8)	15.8 (13.3 to 18.5)		
Fatigue:Severe(N=2425, 798)	3.4 (2.7 to 4.2)	0.9 (0.4 to 1.8)		
Chills:Any(N=2425, 798)	18.1 (16.5 to 19.7)	9.8 (7.8 to 12)		
Chills:Mild(N=2425, 798)	12 (10.8 to 13.4)	8.1 (6.3 to 10.3)		
Chills:Moderate(N=2425, 798)	4.9 (4.1 to 5.8)	1.6 (0.9 to 2.8)		
Chills: Severe(N=2425, 798)	1.1 (0.7 to 1.6)	0 (0 to 0.5)		
Muscle pain:Any(N=2425,798)	25.9 (24.1 to 27.6)	14.5 (12.2 to 17.2)		
Muscle pain:Mild(N=2425,798)	13 (11.7 to 14.4)	9.6 (7.7 to 11.9)		
Muscle pain:Moderate(N=2425,798)	11.3 (10 to 12.6)	4.4 (3.1 to 6)		
Muscle pain:Severe(N=2425,798)	1.6 (1.1 to 2.2)	0.5 (0.1 to 1.3)		
Joint pain:Any(N=2425,798)	19.6 (18.1 to 21.3)	10.9 (8.8 to 13.3)		

Joint pain:Mild(N=2425,798)	10.3 (9.1 to 11.6)	6.9 (5.2 to 8.9)		
Joint pain:Moderate(N=2425,798)	7.9 (6.8 to 9)	3.5 (2.3 to 5)		
Joint pain: Severe(N=2425,798)	1.4 (1 to 2)	0.5 (0.1 to 1.3)		
Antipyretic medication(N=2425,798)	13.4 (12.1 to 14.8)	8.9 (7 to 11.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After Second Vaccination

End point title	Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After Second Vaccination ^[7]
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End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination. Here, 'N' signifies subjects with known values reporting specific characteristic.

End point type	Primary
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End point timeframe:

Within 7 days after second 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2076	706		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C(N=2067, 705)	1.2 (0.7 to 1.7)	1 (0.4 to 2)		
Fever 38 to <38.5 degreesC(N=2067, 705)	0.7 (0.4 to 1.1)	0.6 (0.2 to 1.4)		
Fever 38.5 to<39 degrees C(N=2067, 705)	0.4 (0.2 to 0.8)	0.3 (0 to 1)		
Fever 39 to 40 degrees C (N=2067, 705)	0.1 (0 to 0.3)	0.1 (0 to 0.8)		
Fever >40 degrees C(N=2067, 705)	0 (0 to 0.2)	0 (0 to 0.5)		
Vomiting:Any(N=2076, 706)	2.1 (1.5 to 2.8)	1.6 (0.8 to 2.8)		
Vomiting:Mild(N=2076, 706)	1.6 (1.1 to 2.3)	1.3 (0.6 to 2.4)		
Vomiting:Moderate(N=2076, 706)	0.5 (0.2 to 0.9)	0.3 (0 to 1)		
Vomiting:Severe(N=2076, 706)	0 (0 to 0.2)	0 (0 to 0.5)		
Diarrhea:Any(N=2076, 706)	8.6 (7.4 to 9.9)	8.1 (6.2 to 10.3)		
Diarrhea:Mild(N=2076, 706)	6.4 (5.3 to 7.5)	4.7 (3.2 to 6.5)		
Diarrhea:Moderate(N=2076, 706)	1.7 (1.2 to 2.4)	2.8 (1.7 to 4.3)		
Diarrhea:Severe(N=2076, 706)	0.5 (0.3 to 0.9)	0.6 (0.2 to 1.4)		
Headache:Any(N=2076, 706)	33.1 (31.1 to 35.2)	24.9 (21.8 to 28.3)		

Headache:Mild(N=2076, 706)	18.4 (16.8 to 20.1)	13.6 (11.2 to 16.3)		
Headache:Moderate(N=2076, 706)	13.3 (11.9 to 14.8)	10.1 (7.9 to 12.5)		
Headache:Severe(N=2076, 706)	1.4 (1 to 2.1)	1.3 (0.6 to 2.4)		
Fatigue:Any(N=2076, 706)	39.2 (37.1 to 41.3)	27.3 (24.1 to 30.8)		
Fatigue:Mild(N=2076, 706)	20.6 (18.8 to 22.4)	13.9 (11.4 to 16.7)		
Fatigue:Moderate(N=2076, 706)	16.4 (14.8 to 18)	11.5 (9.2 to 14.1)		
Fatigue:Severe(N=2076, 706)	2.2 (1.6 to 2.9)	2 (1.1 to 3.3)		
Chills:Any(N=2076, 706)	12.4 (11 to 13.9)	8.5 (6.5 to 10.8)		
Chills:Mild(N=2076, 706)	8.1 (7 to 9.4)	6.9 (5.2 to 9.1)		
Chills:Moderate(N=2076, 706)	3.5 (2.8 to 4.4)	1.6 (0.8 to 2.8)		
Chills: Severe(N=2076, 706)	0.8 (0.4 to 1.2)	0 (0 to 0.5)		
Muscle pain:Any(N=2076, 706)	15.6 (14 to 17.2)	8.5 (6.5 to 10.8)		
Muscle pain:Mild(N=2076, 706)	7.6 (6.5 to 8.8)	5.8 (4.2 to 7.8)		
Muscle pain:Moderate(N=2076, 706)	7.1 (6.1 to 8.3)	2.3 (1.3 to 3.7)		
Muscle pain:Severe(N=2076, 706)	0.8 (0.5 to 1.3)	0.4 (0.1 to 1.2)		
Joint pain:Any(N=2076, 706)	15.1 (13.6 to 16.7)	6.5 (4.8 to 8.6)		
Joint pain:Mild(N=2076, 706)	8.1 (7 to 9.3)	3.7 (2.4 to 5.3)		
Joint pain:Moderate(N=2076, 706)	6.2 (5.2 to 7.3)	2.5 (1.5 to 4)		
Joint pain: Severe(N=2076, 706)	0.9 (0.5 to 1.4)	0.3 (0 to 1)		
Antipyretic medication(N=2076, 706)	12.3 (10.9 to 13.8)	7.6 (5.8 to 9.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After Third Vaccination

End point title	Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After Third Vaccination ^[8]
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End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product (rLP2086 or saline) and for whom safety information was available from third vaccination until post third-vaccination blood draw. Here, 'N' signifies subjects with known values reporting specific characteristic.

End point type	Primary
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End point timeframe:

Within 7 days after third 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1823	624		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C(N=1814, 621)	2 (1.4 to 2.7)	0.6 (0.2 to 1.6)		
Fever 38 to <38.5 degreesC(N=1814, 621)	1.4 (0.9 to 2)	0.5 (0.1 to 1.4)		
Fever 38.5 to<39 degrees C(N=1814, 621)	0.4 (0.2 to 0.9)	0.2 (0 to 0.9)		
Fever 39 to 40 degrees C (N=1814, 621)	0.1 (0 to 0.4)	0 (0 to 0.6)		
Fever >40 degrees C(N=1814, 621)	0.1 (0 to 0.3)	0 (0 to 0.6)		
Vomiting:Any(N=1823, 624)	2 (1.4 to 2.7)	1.4 (0.7 to 2.7)		
Vomiting:Mild(N=1823, 624)	1.8 (1.2 to 2.5)	1.1 (0.5 to 2.3)		
Vomiting:Moderate(N=1823, 624)	0.2 (0.1 to 0.6)	0.3 (0 to 1.2)		
Vomiting:Severe(N=1823, 624)	0 (0 to 0.2)	0 (0 to 0.6)		
Diarrhea:Any(N=1823, 624)	7.5 (6.3 to 8.8)	6.9 (5 to 9.2)		
Diarrhea:Mild(N=1823, 624)	6.1 (5 to 7.3)	5.3 (3.7 to 7.3)		
Diarrhea:Moderate(N=1823, 624)	1.2 (0.8 to 1.8)	1.3 (0.6 to 2.5)		
Diarrhea:Severe(N=1823, 624)	0.2 (0 to 0.5)	0.3 (0 to 1.2)		
Headache:Any(N=1823, 624)	32.5 (30.4 to 34.7)	21.6 (18.5 to 25.1)		
Headache:Mild(N=1823, 624)	17.6 (15.9 to 19.4)	12.5 (10 to 15.4)		
Headache:Moderate(N=1823, 624)	13.3 (11.8 to 15)	8.3 (6.3 to 10.8)		
Headache:Severe(N=1823, 624)	1.6 (1.1 to 2.3)	0.8 (0.3 to 1.9)		
Fatigue:Any(N=1823, 624)	39.3 (37.1 to 41.6)	24.5 (21.2 to 28.1)		
Fatigue:Mild(N=1823, 624)	18.9 (17.2 to 20.8)	13.1 (10.6 to 16)		
Fatigue:Moderate(N=1823, 624)	18.8 (17 to 20.6)	9.6 (7.4 to 12.2)		
Fatigue:Severe(N=1823, 624)	1.6 (1.1 to 2.3)	1.8 (0.9 to 3.1)		
Chills:Any(N=1823, 624)	12.6 (11.1 to 14.2)	6.4 (4.6 to 8.6)		
Chills:Mild(N=1823, 624)	7.7 (6.5 to 9)	4.3 (2.9 to 6.2)		
Chills:Moderate(N=1823, 624)	4.2 (3.3 to 5.2)	2.1 (1.1 to 3.5)		
Chills: Severe(N=1823, 624)	0.8 (0.4 to 1.3)	0 (0 to 0.6)		
Muscle pain:Any(N=1823, 624)	16.9 (15.2 to 18.7)	7.5 (5.6 to 9.9)		
Muscle pain:Mild(N=1823, 624)	8.9 (7.7 to 10.3)	4.5 (3 to 6.4)		
Muscle pain:Moderate(N=1823, 624)	6.8 (5.7 to 8.1)	2.9 (1.7 to 4.5)		
Muscle pain:Severe(N=1823, 624)	1.2 (0.7 to 1.8)	0.2 (0 to 0.9)		
Joint pain:Any(N=1823, 624)	12.6 (11.1 to 14.2)	5.3 (3.7 to 7.3)		
Joint pain:Mild(N=1823, 624)	6.6 (5.5 to 7.9)	2.9 (1.7 to 4.5)		
Joint pain:Moderate(N=1823, 624)	5.4 (4.4 to 6.5)	2.4 (1.4 to 3.9)		
Joint pain: Severe(N=1823, 624)	0.6 (0.3 to 1.1)	0 (0 to 0.6)		
Antipyretic medication(N=1823, 624)	12.8 (11.3 to 14.5)	6.6 (4.8 to 8.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After First Vaccination

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After First Vaccination ^[9]
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End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or saline) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary
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End point timeframe:

Within 30 days after first 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	8.62 (7.5 to 9.8)	7.3 (5.6 to 9.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Second Vaccination

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Second Vaccination ^[10]
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End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary
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End point timeframe:

Within 30 days after second vaccination

Notes:

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

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

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2169	733		
Units: Percentage of subjects				
number (confidence interval 95%)	10.1 (8.9 to 11.4)	10.1 (8 to 12.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Third Vaccination

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Third Vaccination ^[11]
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End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product (rLP2086 or saline) and for whom safety information was available from third vaccination until post third-vaccination blood draw.

End point type	Primary
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End point timeframe:

Within 30 days after third vaccination

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

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1889	649		
Units: Percentage of subjects				
number (confidence interval 95%)	9.26 (8 to 10.7)	7.24 (5.4 to 9.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After any Vaccination

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After any Vaccination ^[12]
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End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available.

End point type	Primary
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End point timeframe:

Within 30 days after any vaccination

Notes:

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

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

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	21.17 (19.6 to 22.8)	18.86 (16.2 to 21.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE) During the Vaccination Phase

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE) During the Vaccination Phase ^[13]
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End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available.

End point type	Primary
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End point timeframe:

From the first vaccination up to 1 month after the third 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	31.2 (29.4 to 33.1)	31.14 (28 to 34.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After First Vaccination

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After First Vaccination ^[14]
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End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or saline) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary
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End point timeframe:

Within 30 days after first vaccination

Notes:

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

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

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	0.24 (0.1 to 0.5)	0.12 (0 to 0.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Second Vaccination

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Second Vaccination ^[15]
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End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary
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End point timeframe:

Within 30 days after second vaccination

Notes:

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

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

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2169	733		
Units: Percentage of subjects				
number (confidence interval 95%)	0.23 (0.1 to 0.5)	0 (0 to 0.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Third Vaccination

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Third Vaccination ^[16]
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End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product (rLP2086 or saline) and for whom safety information was available from third vaccination until post third-vaccination blood draw.

End point type	Primary
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End point timeframe:

Within 30 days after third vaccination

Notes:

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

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

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1889	649		
Units: Percentage of subjects				
number (confidence interval 95%)	0.11 (0 to 0.4)	0.15 (0 to 0.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After any Vaccination

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After any Vaccination ^[17]
-----------------	---

End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available.

End point type	Primary
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End point timeframe:

Within 30 days after any 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	0.53 (0.3 to 0.9)	0.24 (0 to 0.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) During the Follow-up Phase

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) During the Follow-up Phase ^[18]
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End point description:

Safety population: all subjects who had at least 1 dose of investigational product (rLP2086 or saline) for whom safety information was available from after post-vaccination 3 blood draw to 6 months after last study vaccination.

End point type	Primary
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End point timeframe:

From 1 month after third vaccination up to 6 months after the third 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2067	704		
Units: Percentage of subjects				
number (confidence interval 95%)	0.63 (0.3 to 1.1)	0.71 (0.2 to 1.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) During the Vaccination Phase

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) During the Vaccination Phase ^[19]
-----------------	---

End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available.

End point type	Primary
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End point timeframe:

From the first vaccination up to 1 month after the third vaccination

Notes:

[19] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	0.85 (0.5 to 1.3)	0.73 (0.3 to 1.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Throughout the Study Period

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Throughout the Study Period ^[20]
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End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available.

End point type	Primary
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End point timeframe:

From the first vaccination up to 6 month after the third vaccination

Notes:

[20] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	1.34 (0.9 to 1.9)	1.34 (0.7 to 2.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After First Vaccination

End point title	Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After First Vaccination ^[21]
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End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational

product (rLP2086 or saline) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary
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End point timeframe:

Within 30 days after first vaccination

Notes:

[21] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	3.89 (3.2 to 4.7)	3.77 (2.6 to 5.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After Second Vaccination

End point title	Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After Second Vaccination ^[22]
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End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary
----------------	---------

End point timeframe:

Within 30 days after second vaccination

Notes:

[22] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2169	733		
Units: Percentage of subjects				
number (confidence interval 95%)	4.66 (3.8 to 5.6)	4.91 (3.5 to 6.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After Third Vaccination

End point title	Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After Third Vaccination ^[23]
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End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product (rLP2086 or saline) and for whom safety information was available from third vaccination until until post third-vaccination blood draw.

End point type	Primary
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End point timeframe:

Within 30 days after third vaccination

Notes:

[23] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1889	649		
Units: Percentage of subjects				
number (confidence interval 95%)	5.03 (4.1 to 6.1)	3.85 (2.5 to 5.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After any Vaccination

End point title	Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After any Vaccination ^[24]
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End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available.

End point type	Primary
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End point timeframe:

Within 30 days after any vaccination

Notes:

[24] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	10.93 (9.7 to 12.2)	10.22 (8.2 to 12.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE During the Vaccination Phase

End point title	Percentage of Subjects With at Least 1 Medically Attended AE During the Vaccination Phase ^[25]
-----------------	---

End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available.

End point type	Primary
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End point timeframe:

From the first vaccination up to 1 month after the third vaccination

Notes:

[25] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	19.22 (17.7 to 20.8)	17.76 (15.2 to 20.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE During the Follow-Up Phase

End point title	Percentage of Subjects With at Least 1 Medically Attended AE During the Follow-Up Phase ^[26]
-----------------	---

End point description:

Safety population: all subjects who had at least 1 dose of investigational product (rLP2086 or saline) for whom safety information was available from after post-vaccination 3 blood draw to 6 months after last study vaccination.

End point type	Primary
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End point timeframe:

From 1 month after third vaccination up to 6 months after the third vaccination

Notes:

[26] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2067	704		
Units: Percentage of subjects				
number (confidence interval 95%)	6.97 (5.9 to 8.2)	6.68 (4.9 to 8.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting at Least 1 Medically Attended Adverse Event Throughout the Study Period

End point title	Percentage of Subjects Reporting at Least 1 Medically Attended Adverse Event Throughout the Study Period ^[27]
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End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available.

End point type	Primary
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End point timeframe:

From the first vaccination up to 6 month after the third vaccination

Notes:

[27] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	21.89 (20.3 to 23.6)	21.17 (18.4 to 24.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After First Vaccination

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After First Vaccination ^[28]
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End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or saline) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary
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End point timeframe:

Within 30 days after first vaccination

Notes:

[28] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 0.1)	0 (0 to 0.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After Second Vaccination

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After Second Vaccination ^[29]
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End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary
----------------	---------

End point timeframe:

Within 30 days after second vaccination

Notes:

[29] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2169	733		
Units: Percentage of subjects				
number (confidence interval 95%)	0.23 (0.1 to 0.5)	0 (0 to 0.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After Third Vaccination

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed
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End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product (rLP2086 or saline) and for whom safety information was available from third vaccination until post third-vaccination blood draw.

End point type	Primary
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End point timeframe:

Within 30 days after third vaccination

Notes:

[30] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1889	649		
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 0.2)	0.15 (0 to 0.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After any Vaccination

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After any Vaccination ^[31]
-----------------	---

End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available.

End point type	Primary
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End point timeframe:

Within 30 days after any vaccination

Notes:

[31] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	0.2 (0.1 to 0.5)	0.12 (0 to 0.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition During the Vaccination Phase

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition During the Vaccination Phase ^[32]
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End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available.

End point type	Primary
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End point timeframe:

From the first vaccination up to 1 month after the third vaccination

Notes:

[32] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	0.32 (0.1 to 0.6)	0.24 (0 to 0.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition During the Follow-Up Phase

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition During the Follow-Up Phase ^[33]
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End point description:

Safety population: all subjects who had at least 1 dose of investigational product (rLP2086 or saline) for whom safety information was available from after post third-vaccination blood draw to 6 months after last study vaccination.

End point type	Primary
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End point timeframe:

From 1 month after third vaccination up to 6 months after the third vaccination

Notes:

[33] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2067	704		
Units: Percentage of subjects				
number (confidence interval 95%)	0.1 (0 to 0.3)	0 (0 to 0.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Throughout the Study Period

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Throughout the Study Period ^[34]
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End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available.

End point type	Primary
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End point timeframe:

From the first vaccination up to 6 month after the third vaccination the third vaccination

Notes:

[34] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	0.4 (0.2 to 0.7)	0.24 (0 to 0.9)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects Reporting at Least 1 Immediate Adverse Event (AE) After First Vaccination ^[35]
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End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or saline) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary
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End point timeframe:

Within 30 minutes after first vaccination

Notes:

[35] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2471	822		
Units: Percentage of subjects				
number (confidence interval 95%)	0.4 (0.2 to 0.7)	0.6 (0.2 to 1.4)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects Reporting at Least 1 Immediate Adverse Event (AE) After Second Vaccination ^[36]
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End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary
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End point timeframe:

Within 30 minutes after second vaccination

Notes:

[36] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2169	733		
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 0.3)	0.4 (0.1 to 1.2)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects Reporting at Least 1 Immediate Adverse Event (AE) After Third Vaccination ^[37]
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End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product (rLP2086 or saline) and for whom safety information was available from third vaccination until post third-vaccination blood draw.

End point type	Primary
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End point timeframe:

Within 30 minutes after third vaccination

Notes:

[37] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1889	649		
Units: Percentage of subjects				
number (confidence interval 95%)	0.1 (0 to 0.3)	0 (0 to 0.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Days Subjects Missed School or Work Due to AE During the Vaccination Phase

End point title	Number of Days Subjects Missed School or Work Due to AE During the Vaccination Phase ^[38]
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End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or saline) and had safety data available. Here, number of subjects analyzed signifies subjects that were evaluable for this endpoint.

End point type	Primary
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End point timeframe:

From the first vaccination up to 1 month after the third vaccination

Notes:

[38] - 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 reported for this endpoint.

End point values	Group 1 rLP2086	Group 2 Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	167	63		
Units: Days				
arithmetic mean (standard deviation)	5.6 (± 10.75)	5.6 (± 13.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titers >= LLOQ for 10 Secondary Strains Before First Vaccination and 1 Month After Third Bivalent rLP2086 Vaccination: Group 1

End point title	Percentage of Subjects With hSBA Titers >= LLOQ for 10 Secondary Strains Before First Vaccination and 1 Month After Third Bivalent rLP2086 Vaccination: Group 1 ^[39]
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End point description:

Evaluable immunogenicity population. Here, number of subjects analyzed signifies subjects with valid and determinate hSBA titers for the given strain. Here, N signifies subjects with valid and determinate hSBA titers for the given strain at the specified time point. This outcome measure was planned to be analyzed for Group 1 only.

End point type	Secondary
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End point timeframe:

Before first vaccination, 1 month after third vaccination

Notes:

[39] - 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: Data was planned to be analysed only for Group 1 rLP2086.

End point values	Group 1 rLP2086			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Percentage of subjects				
number (confidence interval 95%)				
PMB3175[A29]:Before Vaccination 1 (N=280)	31.1 (25.7 to 36.9)			
PMB3175[A29]:1 Month after Vaccination 3 (N=283)	99.3 (97.5 to 99.9)			
PMB3010[A06]:Before Vaccination 1 (N=275)	16 (11.9 to 20.9)			
PMB3010[A06]:1 Month after Vaccination 3 (N=275)	92 (88.1 to 94.9)			
PMB3040[A07]:Before Vaccination 1 (N=274)	55.8 (49.7 to 61.8)			
PMB3040[A07]:1 Month after Vaccination 3 (N=277)	95.7 (92.6 to 97.7)			
PMB824[A12]: Before Vaccination 1 (N=278)	5 (2.8 to 8.3)			
PMB824[A12]:1 Month after Vaccination 3 (N=275)	71.3 (65.5 to 76.5)			
PMB1672[A15]:Before Vaccination 1 (N=279)	37.3 (31.6 to 43.2)			
PMB1672[A15]:1 Month after Vaccination 3 (N=279)	91.8 (87.9 to 94.7)			
PMB1989[A19]:Before Vaccination 1 (N=278)	28.8 (23.5 to 34.5)			
PMB1989[A19]:1 Month after Vaccination 3 (N=284)	95.8 (92.7 to 97.8)			
PMB1256[B03]:Before Vaccination 1 (N=277)	11.2 (7.7 to 15.5)			
PMB1256[B03]:1 Month after Vaccination 3 (N=273)	86.4 (81.8 to 90.3)			
PMB866[B09]:Before Vaccination 1 (N=277)	23.5 (18.6 to 28.9)			
PMB866[B09]:1 Month after Vaccination 3 (N=274)	77 (71.6 to 81.9)			
PMB431[B15]:Before Vaccination 1 (N=274)	43.8 (37.8 to 49.9)			
PMB431[B15]:1 Month after Vaccination 3 (N=276)	96.7 (93.9 to 98.5)			
PMB648[B16]:Before Vaccination 1 (N=270)	21.9 (17.1 to 27.3)			
PMB648[B16]:1 Month after Vaccination 3 (N=273)	78 (72.6 to 82.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titers $\geq 1:4$, $\geq 1:8$, $\geq 1:16$, $\geq 1:32$, $\geq 1:64$, $\geq 1:128$ for Each of the 10 Secondary Strains Before First Vaccination and 1 Month After the Third Bivalent rLP2086 Vaccination: Group 1

End point title	Percentage of Subjects With hSBA Titers $\geq 1:4$, $\geq 1:8$, $\geq 1:16$, $\geq 1:32$, $\geq 1:64$, $\geq 1:128$ for Each of the 10 Secondary Strains Before First Vaccination and 1 Month After the Third Bivalent rLP2086 Vaccination: Group 1 ^[40]
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End point description:

Evaluable immunogenicity population. Here, number of subjects analyzed signifies subjects with valid and determinate hSBA titers for the given strain. Here, N signifies subjects with valid and determinate hSBA titers for the given strain at the specified time point. This outcome measure was planned to be analyzed for Group 1 only.

End point type	Secondary
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End point timeframe:

Before first vaccination, 1 month after third vaccination (Vac)

Notes:

[40] - 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: Data was planned to be analysed only for Group 1 rLP2086.

End point values	Group 1 rLP2086			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Percentage of subjects				
number (confidence interval 95%)				
Before Vaccination 1: PMB3175[A29] 1:4 (N=280)	32.9 (27.4 to 38.7)			
1 month after Vac 3: PMB3175[A29] 1:4 (N=283)	99.3 (97.5 to 99.9)			
Before Vaccination 1: PMB3175[A29] 1:8 (N=280)	31.1 (25.7 to 36.9)			
1 month after Vac 3: PMB3175[A29] 1:8 (N=283)	99.3 (97.5 to 99.9)			
Before Vaccination 1: PMB3175[A29] 1:16 (N=280)	27.9 (22.7 to 33.5)			
1 month after Vac 3: PMB3175[A29] 1:16 (N=283)	98.9 (96.9 to 99.8)			
Before Vaccination 1: PMB3175[A29] 1:32 (N=280)	16.1 (12 to 20.9)			
1 month after Vac 3: PMB3175[A29] 1:32 (N=283)	96.8 (94 to 98.5)			
Before Vaccination 1: PMB3175[A29] 1:64 (N=280)	5.7 (3.3 to 9.1)			
1 month after Vac 3: PMB3175[A29] 1:64 (N=283)	80.9 (75.8 to 85.3)			

Before Vaccination 1: PMB3175[A29] 1:128 (N=280)	2.1 (0.8 to 4.6)			
1 month after Vac 3: PMB3175[A29] 1:128 (N=283)	53 (47 to 58.9)			
Before Vaccination 1: PMB3010[A06] 1:4 (N=275)	18.9 (14.5 to 24)			
1 month after Vac 3: PMB3010[A06] 1:4 (N=275)	92.4 (88.6 to 95.2)			
Before Vaccination 1: PMB3010[A06] 1:8 (N=275)	17.5 (13.2 to 22.5)			
1 month after Vac 3: PMB3010[A06] 1:8 (N=275)	92.4 (88.6 to 95.2)			
Before Vaccination 1: PMB3010[A06] 1:16 (N=275)	16 (11.9 to 20.9)			
1 month after Vac 3: PMB3010[A06] 1:16 (N=275)	92 (88.1 to 94.9)			
Before Vaccination 1: PMB3010[A06] 1:32 (N=275)	10.5 (7.2 to 14.8)			
1 month after Vac 3: PMB3010 [A06] 1:32 (N=275)	86.2 (81.5 to 90)			
Before Vaccination 1: PMB3010[A06] 1:64 (N=275)	6.5 (3.9 to 10.1)			
1 month after Vac 3: PMB3010[A06] 1:64 (N=275)	70.5 (64.8 to 75.9)			
Before Vaccination 1: PMB3010[A06] 1:128 (N=275)	2.5 (1 to 5.2)			
1 month after Vac 3: PMB3010[A06] 1:128 (N=275)	41.8 (35.9 to 47.9)			
Before Vaccination 1: PMB3040[A07] 1:4 (N=274)	55.8 (49.7 to 61.8)			
1 month after Vac 3: PMB3040[A07] 1:4 (N=277)	95.7 (92.6 to 97.7)			
Before Vaccination 1: PMB3040[A07] 1:8 (N=274)	55.8 (49.7 to 61.8)			
1 month after Vac 3: PMB3040[A07] 1:8 (N=277)	95.7 (92.6 to 97.7)			
Before Vaccination 1: PMB3040[A07] 1:16 (N=274)	55.5 (49.4 to 61.5)			
1 month after Vac 3: PMB3040[A07] 1:16 (N=277)	95.7 (92.6 to 97.7)			
Before Vaccination 1: PMB3040[A07] 1:32 (N=274)	42.7 (36.8 to 48.8)			
1 month after Vac 3: PMB3040[A07] 1:32 (N=277)	92.4 (88.6 to 95.2)			
Before Vaccination 1: PMB3040[A07] 1:64 (N=274)	21.2 (16.5 to 26.5)			
1 month after Vac 3: PMB3040[A07] 1:64 (N=277)	72.9 (67.3 to 78.1)			
Before Vaccination 1: PMB3040[A07] 1:128 (N=274)	4 (2 to 7.1)			
1 month after Vac 3: PMB3040[A07] 1:128 (N=277)	29.2 (24 to 35)			
Before Vaccination 1: PMB824[A12] 1:4 (N=278)	10.4 (7.1 to 14.6)			
1 month after Vac 3: PMB824[A12] 1:4 (N=275)	73.8 (68.2 to 78.9)			
Before Vaccination 1: PMB824[A12] 1:8 (N=278)	8.3 (5.3 to 12.2)			
1 month after Vac 3: PMB824[A12] 1:8 (N=275)	73.5 (67.8 to 78.6)			
Before Vaccination 1: PMB824[A12] 1:16 (N=278)	5 (2.8 to 8.3)			

1 month after Vac 3: PMB824[A12] 1:16 (N=275)	71.3 (65.5 to 76.5)			
Before Vaccination 1: PMB824[A12] 1:32 (N=278)	2.2 (0.8 to 4.6)			
1 month after Vac 3: PMB824[A12] 1:32 (N=275)	46.5 (40.5 to 52.6)			
Before Vaccination 1: PMB824[A12] 1:64 (N=278)	0 (0 to 1.3)			
1 month after Vac 3: PMB824[A12] 1:64 (N=275)	15.6 (11.6 to 20.5)			
Before Vaccination 1: PMB824[A12] 1:128 (N=278)	0 (0 to 1.3)			
1 month after Vac 3: PMB824[A12] 1:128 (N=275)	3.3 (1.5 to 6.1)			
Before Vaccination 1: PMB1672[A15] 1:4 (N=279)	39.4 (33.7 to 45.4)			
1 month after Vac 3: PMB1672[A15] 1:4 (N=279)	91.8 (87.9 to 94.7)			
Before Vaccination 1: PMB1672[A15] 1:8 (N=279)	37.3 (31.6 to 43.2)			
1 month after Vac 3: PMB1672[A15] 1:8 (N=279)	91.8 (87.9 to 94.7)			
Before Vaccination 1: PMB1672[A15] 1:16 (N=279)	33.3 (27.8 to 39.2)			
1 month after Vac 3: PMB1672[A15] 1:16 (N=279)	91.4 (87.5 to 94.4)			
Before Vaccination 1: PMB1672[A15] 1:32 (N=279)	20.4 (15.9 to 25.6)			
1 month after Vac 3: PMB1672[A15] 1:32 (N=279)	82.4 (77.5 to 86.7)			
Before Vaccination 1: PMB1672[A15] 1:64 (N=279)	7.2 (4.4 to 10.9)			
1 month after Vac 3: PMB1672[A15] 1:64 (N=279)	54.5 (48.4 to 60.4)			
Before Vaccination 1: PMB1672[A15] 1:128 (N=279)	1.8 (0.6 to 4.1)			
1 month after Vac 3: PMB1672[A15] 1:128 (N=279)	19 (14.6 to 24.1)			
Before Vaccination 1: PMB1989[A19] 1:4 (N=278)	39.2 (33.4 to 45.2)			
1 month after Vac 3: PMB1989[A19] 1:4 (N=284)	96.1 (93.2 to 98.1)			
Before Vaccination 1: PMB1989[A19] 1:8 (N=278)	37.1 (31.4 to 43)			
1 month after Vac 3: PMB1989[A19] 1:8 (N=284)	96.1 (93.2 to 98.1)			
Before Vaccination 1: PMB1989[A19] 1:16 (N=278)	28.8 (23.5 to 34.5)			
1 month after Vac 3: PMB1989[A19] 1:16 (N=284)	95.8 (92.7 to 97.8)			
Before Vaccination 1: PMB1989[A19] 1:32 (N=278)	18.3 (14 to 23.4)			
1 month after Vac 3: PMB1989[A19] 1:32 (N=284)	92.3 (88.5 to 95.1)			
Before Vaccination 1: PMB1989[A19] 1:64 (N=278)	9 (5.9 to 13)			
1 month after Vac 3: PMB1989[A19] 1:64 (N=284)	77.5 (72.2 to 82.2)			
Before Vaccination 1: PMB1989[A19] 1:128 (N=278)	9 (5.9 to 13)			
1 month after Vac 3: PMB1989[A19] 1:128 (N=284)	49.6 (43.7 to 55.6)			

Before Vaccination 1: PMB1256[B03] 1:4 (N=277)	13 (9.3 to 17.5)			
1 month after Vac 3: PMB1256[B03] 1:4 (N=273)	86.8 (82.2 to 90.6)			
Before Vaccination 1: PMB1256[B03] 1:8 (N=277)	11.2 (7.7 to 15.5)			
1 month after Vac 3: PMB1256[B03] 1:8 (N=273)	86.4 (81.8 to 90.3)			
Before Vaccination 1: PMB1256[B03] 1:16 (N=277)	10.1 (6.8 to 14.3)			
1 month after Vac 3: PMB1256[B03] 1:16 (N=273)	85.3 (80.6 to 89.3)			
Before Vaccination 1: PMB1256[B03] 1:32 (N=277)	7.6 (4.8 to 11.4)			
1 month after Vac 3: PMB1256[B03] 1:32 (N=273)	78.4 (73 to 83.1)			
Before Vaccination 1: PMB1256[B03] 1:64 (N=277)	4.7 (2.5 to 7.9)			
1 month after Vac 3: PMB1256[B03] 1:64 (N=273)	56.4 (50.3 to 62.4)			
Before Vaccination 1: PMB1256[B03] 1:128 (N=277)	1.1 (0.2 to 3.1)			
1 month after Vac 3: PMB1256[B03] 1:128 (N=273)	30.8 (25.3 to 36.6)			
Before Vaccination 1: PMB866[B09] 1:4 (N=277)	24.5 (19.6 to 30.1)			
1 month after Vac 3: PMB866[B09] 1:4 (N=274)	78.5 (73.1 to 83.2)			
Before Vaccination 1: PMB866[B09] 1:8 (N=277)	23.5 (18.6 to 28.9)			
1 month after Vac 3: PMB866[B09] 1:8 (N=274)	77 (71.6 to 81.9)			
Before Vaccination 1: PMB866[B09] 1:16 (N=277)	18.8 (14.3 to 23.9)			
1 month after Vac 3: PMB866[B09] 1:16 (N=274)	73.4 (67.7 to 78.5)			
Before Vaccination 1: PMB866[B09] 1:32 (N=277)	11.9 (8.3 to 16.3)			
1 month after Vac 3: PMB866[B09] 1:32 (N=274)	52.6 (46.5 to 58.6)			
Before Vaccination 1: PMB866[B09] 1:64 (N=277)	4.7 (2.5 to 7.9)			
1 month after Vac 3: PMB866[B09] 1:64 (N=274)	27.7 (22.5 to 33.4)			
Before Vaccination 1: PMB866[B09] 1:128 (N=277)	1.1 (0.2 to 3.1)			
1 month after Vac 3: PMB866[B09] 1:128 (N=274)	12.8 (9.1 to 17.3)			
Before Vaccination 1: PMB431[B15] 1:4 (N=274)	44.9 (38.9 to 51)			
1 month after Vac 3: PMB431[B15] 1:4 (N=276)	97.1 (94.4 to 98.7)			
Before Vaccination 1: PMB431[B15] 1:8 (N=274)	43.8 (37.8 to 49.9)			
1 month after Vac 3: PMB431[B15] 1:8 (N=276)	96.7 (93.9 to 98.5)			
Before Vaccination 1: PMB431[B15] 1:16 (N=274)	41.2 (35.4 to 47.3)			
1 month after Vac 3: PMB431[B15] 1:16 (N=276)	96.7 (93.9 to 98.5)			
Before Vaccination 1: PMB431[B15] 1:32 (N=274)	23.7 (18.8 to 29.2)			

1 month after Vac 3: PMB431[B15] 1:32 (N=276)	84.4 (79.6 to 88.5)			
Before Vaccination 1: PMB431[B15] 1:64 (N=274)	8 (5.1 to 11.9)			
1 month after Vac 3: PMB431[B15] 1:64 (N=276)	56.5 (50.4 to 62.5)			
Before Vaccination 1: PMB431[B15] 1:128 (N=274)	1.5 (0.4 to 3.7)			
1 month after Vac 3: PMB431[B15] 1:128 (N=276)	22.5 (17.7 to 27.9)			
Before Vaccination 1: PMB648[B16] 1:4 (N=270)	24.4 (19.4 to 30)			
1 month after Vac 3: PMB648[B16] 1:4 (N=273)	79.1 (73.8 to 83.8)			
Before Vaccination 1: PMB648[B16] 1:8 (N=270)	21.9 (17.1 to 27.3)			
1 month after Vac 3: PMB648[B16] 1:8 (N=273)	78 (72.6 to 82.8)			
Before Vaccination 1: PMB648[B16] 1:16 (N=270)	18.9 (14.4 to 24.1)			
1 month after Vac 3: PMB648[B16] 1:16 (N=273)	76.6 (71.1 to 81.5)			
Before Vaccination 1: PMB648[B16] 1:32 (N=270)	11.9 (8.2 to 16.3)			
1 month after Vac 3: PMB648[B16] 1:32 (N=273)	61.2 (55.1 to 67)			
Before Vaccination 1: PMB648[B16] 1:64 (N=270)	7.4 (4.6 to 11.2)			
1 month after Vac 3: PMB648[B16] 1:64 (N=273)	34.4 (28.8 to 40.4)			
Before Vaccination 1: PMB648[B16] 1:128 (N=270)	1.9 (0.6 to 4.3)			
1 month after Vac 3: PMB648[B16] 1:128 (N=273)	16.8 (12.6 to 21.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers (GMTs) for Each of the 10 Secondary Strains Before First Vaccination and 1 Month After the Third Bivalent rLP2086 Vaccination: Group 1

End point title	hSBA Geometric Mean Titers (GMTs) for Each of the 10 Secondary Strains Before First Vaccination and 1 Month After the Third Bivalent rLP2086 Vaccination: Group 1 ^[41]
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End point description:

Evaluable immunogenicity population. Here, number of subjects analyzed signifies subjects with valid and determinate hSBA titers for the given strain. Here, N signifies subjects with valid and determinate assay results for the given antigen or strain. This outcome measure was planned to be analyzed for Group 1 only.

End point type	Secondary
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End point timeframe:

Before first vaccination, 1 month after third vaccination

Notes:

[41] - 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.

End point values	Group 1 rLP2086			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Titers				
geometric mean (confidence interval 95%)				
PMB3175[A29]:Before Vaccination 1 (N=280)	7.1 (6.4 to 8)			
PMB3175[A29]:1 Month after Vaccination 3 (N=283)	96.3 (86.9 to 106.9)			
PMB3010[A06]:Before Vaccination 1 (N=275)	10.3 (9.5 to 11.2)			
PMB3010[A06]:1 Month after Vaccination 3 (N=275)	69.9 (61.8 to 79.1)			
PMB3040[A07]:Before Vaccination 1 (N=274)	13.9 (12 to 16)			
PMB3040[A07]:1 Month after Vaccination 3 (N=277)	60.4 (54.6 to 66.8)			
PMB824[A12]: Before Vaccination 1 (N=278)	8.4 (8.2 to 8.6)			
PMB824[A12]:1 Month after Vaccination 3 (N=275)	20.6 (18.8 to 22.6)			
PMB1672[A15]:Before Vaccination 1 (N=279)	8 (7.1 to 9)			
PMB1672[A15]:1 Month after Vaccination 3 (N=279)	43.1 (38.4 to 48.4)			
PMB1989[A19]:Before Vaccination 1 (N=278)	12.1 (11.1 to 13.3)			
PMB1989[A19]:1 Month after Vaccination 3 (N=284)	87.3 (77.7 to 98)			
PMB1256[B03]:Before Vaccination 1 (N=277)	5.1 (4.7 to 5.6)			
PMB1256[B03]:1 Month after Vaccination 3 (N=273)	49.8 (42.2 to 58.7)			
PMB866[B09]:Before Vaccination 1 (N=277)	6.1 (5.5 to 6.7)			
PMB866[B09]:1 Month after Vaccination 3 (N=274)	23.3 (19.9 to 27.1)			
PMB431[B15]:Before Vaccination 1 (N=274)	9.1 (8.1 to 10.3)			
PMB431[B15]:1 Month after Vaccination 3 (N=276)	49.4 (44.6 to 54.8)			
PMB648[B16]:Before Vaccination 1 (N=270)	6.2 (5.5 to 6.9)			
PMB648[B16]:1 Month after Vaccination 3 (N=273)	26.5 (22.8 to 30.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Composite hSBA Titer \geq Lower Limit

of Quantitation for all 4 Primary Strains Before First Vaccination and 1 Month After Second Bivalent rLP2086 Vaccination: Group 1

End point title	Percentage of Subjects Achieving Composite hSBA Titer >=Lower Limit of Quantitation for all 4 Primary Strains Before First Vaccination and 1 Month After Second Bivalent rLP2086 Vaccination: Group 1 ^[42]
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End point description:

Evaluable immunogenicity population. Here, N signifies subjects valid and determinate hSBA results on all 4 strains at the given time point. This outcome measure was planned to be analyzed for Group 1 only.

End point type	Secondary
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End point timeframe:

Before vaccination 1, 1 Month after Vaccination 2

Notes:

[42] - 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: Data was planned to be analysed only for Group 1 rLP2086.

End point values	Group 1 rLP2086			
Subject group type	Reporting group			
Number of subjects analysed	1723			
Units: Percentage of subjects				
number (confidence interval 95%)				
Before First Vaccination (N=1612)	7.3 (6 to 8.6)			
1 Month after Vaccination 2 (N=1620)	64.5 (62.1 to 66.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving at Least a 4-Fold Increase in hSBA Titer for Each of the 4 Primary Strains Before First Vaccination to 1 Month After the Second Bivalent rLP2086 Vaccination: Group 1

End point title	Percentage of Subjects Achieving at Least a 4-Fold Increase in hSBA Titer for Each of the 4 Primary Strains Before First Vaccination to 1 Month After the Second Bivalent rLP2086 Vaccination: Group 1 ^[43]
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End point description:

Evaluable immunogenicity population. Here, N signifies subjects with valid and determinate hSBA titers for the given strain at both the specified time point. This outcome measure was planned to be analyzed for Group 1 only.

End point type	Secondary
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End point timeframe:

One month after second Bivalent rLP2086 vaccination

Notes:

[43] - 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: Data was planned to be analysed only for Group 1 rLP2086.

End point values	Group 1 rLP2086			
Subject group type	Reporting group			
Number of subjects analysed	1723			
Units: Percentage of subjects				
number (confidence interval 95%)				
PMB80[A22] (N=1679)	66.9 (64.6 to 69.2)			
PMB2001[A56] (N=1637)	85.9 (84.1 to 87.5)			
PMB2948[B24] (N=1658)	67.9 (65.6 to 70.2)			
PMB2707[B44] (N=1686)	55.5 (53.1 to 57.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titers

$\geq 1:4, \geq 1:8, \geq 1:16, \geq 1:32, \geq 1:64, \geq 1:128$ for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination:

End point title	Percentage of Subjects With hSBA Titers $\geq 1:4, \geq 1:8, \geq 1:16, \geq 1:32, \geq 1:64, \geq 1:128$ for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination: Group 1 ^[44]
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End point description:

Results for PMB80[A22] 1:16, PMB2001[A56] 1:8, PMB2948[B24] 1:8 and PMB2707[B44] 1:8 are reported under secondary endpoint 'Percentage of Subjects With hSBA Titers \geq LLOQ for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination: Group 1'. Evaluable immunogenicity population. Here, N signifies subjects with valid and determinate hSBA titers for the given strain at the specified time point. This outcome measure was planned to be analyzed for Group 1 only.

End point type	Secondary
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End point timeframe:

Before Vaccination (Vac) 1, 1 Month after Vac 2, 3

Notes:

[44] - 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: Data was planned to be analysed only for Group 1 rLP2086.

End point values	Group 1 rLP2086			
Subject group type	Reporting group			
Number of subjects analysed	1723			
Units: Percentage of subjects				
number (confidence interval 95%)				
Before Vac 1: PMB80[A22] 1:4 (N=1704)	42.1 (39.7 to 44.5)			
1 month after Vac 2: PMB80[A22] 1:4 (N=1697)	86.2 (84.5 to 87.8)			
1 month after Vac 3: PMB80[A22] 1:4 (N=1714)	94.3 (93.1 to 95.3)			
Before Vac 1: PMB80[A22] 1:8 (N=1704)	38.8 (36.5 to 41.2)			

1 month after Vac 2: PMB80[A22] 1:8 (N=1697)	85.7 (83.9 to 87.3)			
1 month after Vac 3: PMB80[A22] 1:8 (N=1714)	94.1 (92.9 to 95.2)			
Before Vac 1: PMB80[A22] 1:32 (N=1704)	19.7 (17.8 to 21.6)			
1 month after Vac 2: PMB80[A22] 1:32 (N=1697)	71.2 (69 to 73.3)			
1 month after Vac 3: PMB80[A22] 1:32 (N=1714)	85.5 (83.8 to 87.2)			
Before Vac 1: PMB80[A22] 1:64 (N=1704)	9.6 (8.3 to 11.1)			
1 month after Vac 2: PMB80[A22] 1:64 (N=1697)	49.9 (47.4 to 52.3)			
1 month after Vac 3: PMB80[A22] 1:64 (N=1714)	64.4 (62.1 to 66.7)			
Before Vac 1: PMB80[A22] 1:128 (N=1704)	3.4 (2.6 to 4.4)			
1 month after Vac 2: PMB80[A22] 1:128 (N=1697)	29.9 (27.8 to 32.2)			
1 month after Vac 3: PMB80[A22] 1:128 (N=1714)	41.7 (39.4 to 44.1)			
Before Vac 1: PMB2001[A56] 1:4 (N=1657)	35.9 (33.6 to 38.3)			
1 month after Vac 2: PMB2001[A56] 1:4 (N=1701)	97.8 (97 to 98.5)			
1 month after Vac 3: PMB2001[A56] 1:4 (N=1708)	99.4 (98.9 to 99.7)			
Before Vac 1: PMB2001[A56] 1:16 (N=1657)	30.4 (28.2 to 32.7)			
1 month after Vac 2: PMB2001[A56] 1:16 (N=1701)	97.1 (96.1 to 97.8)			
1 month after Vac 3: PMB2001[A56] 1:16 (N=1708)	99.2 (98.7 to 99.6)			
Before Vac 1: PMB2001[A56]] 1:32 (N=1657)	24.4 (22.3 to 26.5)			
1 month after Vac 2: PMB2001[A56] 1:32 (N=1701)	92.8 (91.4 to 94)			
1 month after Vac 3: PMB2001[A56] 1:32 (N=1708)	97.2 (96.4 to 98)			
Before Vac 1: PMB2001[A56] 1:64 (N=1657)	16.4 (14.6 to 18.2)			
1 month after Vac 2 :PMB2001[A56] 1:64 (N=1701)	80.8 (78.9 to 82.7)			
1 month after Vac 3 :PMB2001[A56] 1:64 (N=1708)	90.5 (89 to 91.9)			
Before Vac 1: PMB2001[A56] 1:128 (N=1657)	7.1 (5.9 to 8.5)			
1 month after Vac 2: PMB2001[A56] 1:128 (N=1701)	56.6 (54.2 to 58.9)			
1 month after Vac 3: PMB2001[A56] 1:128 (N=1708)	73.7 (71.5 to 75.7)			
Before Vac 1: PMB2948[B24] 1:4 (N=1696)	35 (32.7 to 37.3)			
1 month after Vac 2: PMB2948[B24] 1:4 (N=1685)	87.2 (85.5 to 88.7)			
1 month after Vac 3: PMB2948[B24] 1:4 (N=1702)	95.8 (94.8 to 96.7)			
Before Vac 1: PMB2948[B24] 1:16 (N=1696)	29.5 (27.3 to 31.7)			
1 month after Vac 2: PMB2948[B24] 1:16 (N=1685)	83.7 (81.9 to 85.5)			

1 month after Vac 3: PMB2948[B24] 1:16 (N=1702)	93.2 (91.9 to 94.3)			
Before Vac 1: PMB2948[B24] 1:32 (N=1696)	18.1 (16.3 to 20)			
1 month after Vac 2: PMB2948[B24] 1:32 (N=1685)	65.6 (63.3 to 67.8)			
1 month after Vac 3: PMB2948[B24] 1:32 (N=1702)	75.1 (73 to 77.2)			
Before Vac 1: PMB2948[B24] 1:64 (N=1696)	8.4 (7.1 to 9.8)			
1 month after Vac 2: PMB2948[B24] 1:64 (N=1685)	40.4 (38 to 42.7)			
1 month after Vac 3: PMB2948[B24] 1:64 (N=1702)	48.8 (46.4 to 51.2)			
Before Vac 1: PMB2948[B24] 1:128 (N=1696)	3.3 (2.5 to 4.3)			
1 month after Vac 2: PMB2948[B24] 1:128 (N=1685)	22.8 (20.9 to 24.9)			
1 month after Vac 3: PMB2948[B24] 1:128 (N=1702)	27.8 (25.7 to 30)			
Before Vac 1: PMB2707[B44] 1:4 (N=1716)	14.5 (12.8 to 16.2)			
1 month after Vac 2: PMB2707[B44] 1:4 (N=1693)	71.5 (69.3 to 73.7)			
1 month after Vac 3: PMB2707[B44] 1:4 (N=1703)	89.7 (88.1 to 91.1)			
Before Vac 1: PMB2707[B44] 1:16 (N=1716)	7.8 (6.5 to 9.1)			
1 month after Vac 2: PMB2707[B44] 1:16 (N=1693)	61 (58.6 to 63.3)			
1 month after Vac 3: PMB2707[B44] 1:16 (N=1703)	83.3 (81.4 to 85)			
Before Vac 1: PMB2707[B44] 1:32 (N=1716)	4.3 (3.4 to 5.4)			
1 month after Vac 2: PMB2707[B44] 1:32 (N=1693)	41.9 (39.6 to 44.3)			
1 month after Vac 3: PMB2707[B44] 1:32 (N=1703)	67.1 (64.8 to 69.3)			
Before Vac 1: PMB2707[B44] 1:64 (N=1716)	2.3 (1.6 to 3.1)			
1 month after Vac 2: PMB2707[B44] 1:64 (N=1693)	30.3 (28.1 to 32.6)			
1 month after Vac 3: PMB2707[B44] 1:64 (N=1703)	49.8 (47.4 to 52.2)			
Before Vac 1: PMB2707[B44] 1:128 (N=1716)	0.8 (0.4 to 1.3)			
1 month after Vac 2: PMB2707[B44] 1:128 (N=1693)	21 (19.1 to 23)			
1 month after Vac 3: PMB2707[B44] 1:128 (N=1703)	32.1 (29.9 to 34.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers (GMTs) for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination: Group 1

End point title	hSBA Geometric Mean Titers (GMTs) for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination: Group 1 ^[45]
End point description:	
Evaluable immunogenicity population. Here, N signifies subjects with valid and determinate hSBA titers for the given strain at the specified time point. This outcome measure was planned to be analyzed for Group 1 only.	
End point type	Secondary
End point timeframe:	
Before Vaccination (Vac) 1, 1 Month after Vac 2, 3	

Notes:

[45] - 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: Data was planned to be analysed only for Group 1 rLP2086.

End point values	Group 1 rLP2086			
Subject group type	Reporting group			
Number of subjects analysed	1723			
Units: Titer				
geometric mean (confidence interval 95%)				
PMB80[A22]: Before Vac 1 (N=1704)	12.8 (12.3 to 13.3)			
PMB80[A22]: 1 Month after Vac 2 (N=1697)	49 (46.2 to 52.1)			
PMB80[A22]: 1 Month after Vac 3 (N=1714)	74.3 (70.2 to 78.6)			
PMB2001[A56]: Before Vac 1 (N=1657)	8.8 (8.3 to 9.3)			
PMB2001[A56]: 1 Month after Vac 2 (N=1701)	114.3 (107.9 to 121)			
PMB2001[A56]: 1 Month after Vac 3 (N=1708)	176.7 (167.8 to 186.1)			
PMB2948[B24]: Before Vac 1 (N=1696)	7.6 (7.3 to 8)			
PMB2948[B24]: 1 Month after Vac 2 (N=1685)	35.8 (33.7 to 38.2)			
PMB2948[B24]: 1 Month after Vac 3 (N=1702)	49.5 (46.8 to 52.4)			
PMB2707[B44]: Before Vac 1 (N=1716)	4.8 (4.7 to 4.9)			
PMB2707[B44]: 1 Month after Vac 2 (N=1693)	22.6 (20.9 to 24.4)			
PMB2707[B44]: 1 Month after Vac 3 (N=1703)	47.6 (44.2 to 51.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving at Least a 3-Fold Increase in hSBA Titer for 4 Primary Test Strains Before First Vaccination to 1 Month After Third Bivalent rLP2086 Vaccination

End point title	Percentage of Subjects Achieving at Least a 3-Fold Increase in hSBA Titer for 4 Primary Test Strains Before First Vaccination to 1 Month After Third Bivalent rLP2086 Vaccination ^[46]
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End point description:

Data was not reported because 3-fold rise analyses was not performed as per change in planned analysis.

End point type	Secondary
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End point timeframe:

One month after third bivalent rLP2086 vaccination

Notes:

[46] - 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: Data was planned to be analysed only for Group 1 rLP2086.

End point values	Group 1 rLP2086			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[47]			
Units: Percentage of subjects				
number (confidence interval 95%)	(to)			

Notes:

[47] - Data not reported because 3-fold rise analyses was not performed as per change in planned analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving at Least a 2-Fold Increase in hSBA Titer for 4 Primary Test Strains Before First Vaccination to 1 Month After the Third Bivalent rLP2086 Vaccination: Group 1

End point title	Percentage of Subjects Achieving at Least a 2-Fold Increase in hSBA Titer for 4 Primary Test Strains Before First Vaccination to 1 Month After the Third Bivalent rLP2086 Vaccination: Group 1 ^[48]
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End point description:

Evaluable immunogenicity population. Here, N signifies subjects with valid and determinate hSBA titers for the given strain at the specified time point. This outcome measure was planned to be analyzed for Group 1 only.

End point type	Secondary
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End point timeframe:

One month after third bivalent rLP2086 vaccination

Notes:

[48] - 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: Data was planned to be analysed only for Group 1 rLP2086.

End point values	Group 1 rLP2086			
Subject group type	Reporting group			
Number of subjects analysed	1723			
Units: Percentage of subjects				
number (confidence interval 95%)				
PMB80[A22]: 1 Month after Vac 3 (N=1695)	89 (87.4 to 90.4)			
PMB2001[A56]: 1 Month after Vac 3 (N=1642)	95.3 (94.2 to 96.3)			

PMB2948[B24]: 1 Month after Vac 3 (N=1675)	87.1 (85.4 to 88.7)			
PMB2707[B44]: 1 Month after Vac 3(N=1696)	81.8 (79.9 to 83.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titers \geq LLOQ for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination: Group 1

End point title	Percentage of Subjects With hSBA Titers \geq LLOQ for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination: Group 1 ^[49]
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End point description:

Evaluable immunogenicity population. Here, N signifies subjects with valid and determinate hSBA titers for the given strain at the specified time point. This outcome measure was planned to be analyzed for Group 1 only.

End point type	Secondary
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End point timeframe:

Before Vaccination (Vac) 1, 1 Month after Vac 2, 3

Notes:

[49] - 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: Data was planned to be analysed only for Group 1 rLP2086.

End point values	Group 1 rLP2086			
Subject group type	Reporting group			
Number of subjects analysed	1723			
Units: Percentage of subjects				
number (confidence interval 95%)				
Before Vac 1: PMB80[A22] 1:16 (N=1704)	33.6 (31.3 to 35.9)			
1 month after Vac 2: PMB80[A22] 1:16 (N=1697)	84.7 (82.9 to 86.4)			
1 month after Vac 3: PMB80[A22] 1:16 (N=1714)	93.5 (92.2 to 94.6)			
Before Vac 1: PMB2001[A56] 1:8 (N=1657)	32.2 (29.9 to 34.5)			
1 month after Vac 2: PMB2001[A56] 1:8 (N=1701)	97.4 (96.5 to 98.1)			
1 month after Vac 3: PMB2001[A56] 1:8 (N=1708)	99.4 (98.9 to 99.7)			
Before Vac 1: PMB2948[B24] 1:8 (N=1696)	33.1 (30.9 to 35.4)			
1 month after Vac 2: PMB2948[B24] 1:8 (N=1685)	86.5 (84.7 to 88.1)			
1 month after Vac 3: PMB2948[B24] 1:8 (N=1702)	95.1 (93.9 to 96)			
Before Vac 1: PMB2707[B44] 1:8 (N=1716)	11 (9.6 to 12.6)			
1 month after Vac 2: PMB2707[B44] 1:8 (N=1693)	68.3 (66.1 to 70.6)			

1 month after Vac 3: PMB2707[B44] 1:8 (N=1703)	87.4 (85.8 to 89)			
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs/SAEs: recorded from first vaccination through 6 months after third vaccination. Subjects recorded pre-specified reactogenicity events (local reactions, systemic events) in electronic diary within 7 days after first, second and third vaccination.

Adverse event reporting additional description:

All AEs collected on case report form are shown below as having been collected via non-systematic assessment. All events reported via electronic diary (reactogenicity events) are shown below as having been collected via systematic assessment. Reactogenicity events are grouped by all severities and doses combined.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Group 1 rLP2086
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Reporting group description:

Recombinant lipoprotein 2086 (rLP2086) vaccine on a 0-, 2-, 6- month schedule.

Reporting group title	Group 2 Saline
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Reporting group description:

Saline on a 0-, 2-, 6- month schedule.

Serious adverse events	Group 1 rLP2086	Group 2 Saline	
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 2471 (1.34%)	11 / 822 (1.34%)	
number of deaths (all causes)	3	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	2 / 2471 (0.08%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			

subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 2471 (0.00%)	2 / 822 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign intracranial hypertension			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dystonia			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 2471 (0.00%)	1 / 822 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	2 / 2471 (0.08%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abortion spontaneous			
subjects affected / exposed	4 / 2471 (0.16%)	1 / 822 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ectopic pregnancy			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperemesis gravidarum			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 2471 (0.12%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	0 / 2471 (0.00%)	1 / 822 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 2471 (0.00%)	1 / 822 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			

subjects affected / exposed	0 / 2471 (0.00%)	1 / 822 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 2471 (0.00%)	1 / 822 (0.12%)	
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			
Asthma			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Depression			
subjects affected / exposed	0 / 2471 (0.00%)	1 / 822 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dissociative disorder			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eating disorder			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Suicide attempt			
subjects affected / exposed	0 / 2471 (0.00%)	1 / 822 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 2471 (0.04%)	1 / 822 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	2 / 2471 (0.08%)	1 / 822 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otosalpingitis			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pyelonephritis			
subjects affected / exposed	1 / 2471 (0.04%)	0 / 822 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Group 1 rLP2086	Group 2 Saline	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2193 / 2471 (88.75%)	567 / 822 (68.98%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	31 / 2471 (1.25%)	6 / 822 (0.73%)	
occurrences (all)	32	6	
Ligament sprain			
subjects affected / exposed	22 / 2471 (0.89%)	11 / 822 (1.34%)	
occurrences (all)	23	11	
Nervous system disorders			
Headache			
subjects affected / exposed	55 / 2471 (2.23%)	10 / 822 (1.22%)	
occurrences (all)	62	10	
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	46 / 2471 (1.86%)	6 / 822 (0.73%)	
occurrences (all)	50	7	
Fatigue			
subjects affected / exposed	12 / 2471 (0.49%)	10 / 822 (1.22%)	
occurrences (all)	14	10	
Vomiting - Any (reactogenicity event)			
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed ^[1]	130 / 2438 (5.33%)	37 / 808 (4.58%)	
occurrences (all)	130	37	
Fever >=38.0 degrees C -Any (reactogenicity event)			

alternative dictionary used: Systemic Events 0.0 alternative assessment type: Systematic subjects affected / exposed ^[2] occurrences (all)	108 / 2432 (4.44%) 108	14 / 807 (1.73%) 14	
Diarrhea-Any (reactogenicity event) alternative dictionary used: Systemic Events 0.0 alternative assessment type: Systematic subjects affected / exposed ^[3] occurrences (all)	497 / 2438 (20.39%) 497	158 / 808 (19.55%) 158	
Headache - Any (reactogenicity event) alternative dictionary used: Systemic Events 0.0 alternative assessment type: Systematic subjects affected / exposed ^[4] occurrences (all)	1440 / 2438 (59.06%) 1440	391 / 808 (48.39%) 391	
Fatigue -Any (reactogenicity event) alternative dictionary used: Systemic Events 0.0 alternative assessment type: Systematic subjects affected / exposed ^[5] occurrences (all)	1576 / 2438 (64.64%) 1576	411 / 808 (50.87%) 411	
Chills - Any (reactogenicity event) alternative dictionary used: Systemic Events 0.0 alternative assessment type: Systematic subjects affected / exposed ^[6] occurrences (all)	697 / 2438 (28.59%) 697	133 / 808 (16.46%) 133	
Muscle pain -Any (reactogenicity event) alternative dictionary used: Systemic Events 0.0 alternative assessment type: Systematic subjects affected / exposed ^[7] occurrences (all)	916 / 2438 (37.57%) 916	170 / 808 (21.04%) 170	
Joint pain -Any (reactogenicity event) alternative dictionary used: Systemic Events 0.0			

alternative assessment type: Systematic subjects affected / exposed ^[8] occurrences (all)	723 / 2438 (29.66%) 723	136 / 808 (16.83%) 136	
Skin and subcutaneous tissue disorders Redness -Any (reactogenicity event) alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed ^[9] occurrences (all)	537 / 2438 (22.03%) 537	8 / 808 (0.99%) 8	
Pain at injection site - Any (reactogenicity event) alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed ^[10] occurrences (all)	2184 / 2438 (89.58%) 2184	147 / 808 (18.19%) 147	
Swelling -Any (reactogenicity event) alternative dictionary used: Local Reactions 0.0 alternative assessment type: Systematic subjects affected / exposed ^[11] occurrences (all)	612 / 2438 (25.10%) 612	8 / 808 (0.99%) 8	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Pharyngitis	98 / 2471 (3.97%) 112 77 / 2471 (3.12%) 89 45 / 2471 (1.82%) 49 33 / 2471 (1.34%) 35	29 / 822 (3.53%) 31 33 / 822 (4.01%) 37 10 / 822 (1.22%) 12 12 / 822 (1.46%) 13	

subjects affected / exposed	37 / 2471 (1.50%)	10 / 822 (1.22%)	
occurrences (all)	41	11	
Tonsillitis			
subjects affected / exposed	19 / 2471 (0.77%)	11 / 822 (1.34%)	
occurrences (all)	23	13	
Bronchitis			
subjects affected / exposed	12 / 2471 (0.49%)	10 / 822 (1.22%)	
occurrences (all)	13	10	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification:

Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 September 2012	1) Events were to be reported throughout the study from the signing of the ICD up to the study end (Visit 6:final telephone contact). 2) Non-serious AEs were to be reported from the signing of the ICD to up to Visit 5 (postvaccination 3 blood draw).
24 January 2013	1) Serious adverse events occurring to a subject after the active reporting period has ended should be reported to the sponsor if the investigator becomes aware of them; at a minimum, all serious events that the investigator believed had at least a reasonable possibility of being related to study drug were to be reported to the sponsor.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported