# 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 (>=) 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 |

### 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, easured 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 |

| | |
|---|---|
| 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 | Investigator, Monitor, Data analyst, Assessor, Subject |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Group 1 rLP2086 |

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 |

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 |
| 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. | |

| Reporting group values | Group 1 rLP2086 | Group 2 Saline | Total |
|---|---|---|---|
| Number of subjects | 2471 | 822 | 3293 |
| Age categorical<br>Units: Subjects | | | |
| Age Continuous \|<br>Units: Years | | | |
| arithmetic mean | 21.47 | 21.52 | |
| standard deviation | ± 2.14 | ± 2.2 | - |
| Gender, Male/Female<br>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 (>=) 4 Fold Rise in Serum Bactericidal Assay Using Human Complement (hSBA) for 4 Primary Strains and Composite Response (hSBA >= Lower Limit of Quantification [LLOQ] for all 4 Primary Strains Combined): Group 1

| | |
|---|---|
| End point title | Percentage of Subjects with (>=) 4 Fold Rise in Serum Bactericidal Assay Using Human Complement (hSBA) for 4 Primary Strains and Composite Response (hSBA >= Lower Limit of Quantification [LLOQ] for all 4 Primary Strains Combined): Group 1[1][2] |

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 |

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 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] |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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:

[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] |
|---|---|

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 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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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:

[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] |
|---|---|

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 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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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 |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

| | |
|---|---|
| | Chronic Medical Condition Within 30 Days After Third Vaccination[30] |

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 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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

End point description:

Safety population: all subjectts 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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 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] |
|---|---|

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 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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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 >=1:4, >=1:8, >=1:16, >=1:32, >=1:64, >=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 >=1:4, >=1:8, >=1:16, >=1:32, >=1:64, >=1:128 for Each of the 10 Secondary Strains Before First Vaccination and 1 Month After the Third Bivalent rLP2086 Vaccination: Group 1[40] |
|---|---|

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 |
|---|---|

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] |

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 |

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.

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: 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 >=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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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 >=1:4,>=1:8,>=1:16,>=1:32,>=1:64,>=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 >=1:4,>=1:8,>=1:16,>=1:32,>=1:64,>=1:128 for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination: Group 1[44] |
|---|---|

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 >=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 |
|---|---|

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] |
|---|---|

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 |
|---|---|

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] |
|---|---|

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:

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 >=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 >=LLOQ for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination: Group 1[49] |

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:

[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) | | | |

## 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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18.0 |

### 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.

| 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 | |
| Fever >=38.0 degrees C -Any (reactogenicity event) | | | |
| alternative dictionary used: Systemic Events 0.0 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[1] | 108 / 2432 (4.44%) | 14 / 807 (1.73%) | |
| occurrences (all) | 108 | 14 | |
| Vomiting - Any (reactogenicity event) | | | |

| | | | |
|---|---|---|---|
| alternative dictionary used: Systemic Events 0.0 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[2] | 130 / 2438 (5.33%) | 37 / 808 (4.58%) | |
| occurrences (all) | 130 | 37 | |
| Diarrhea-Any (reactogenicity event) | | | |
| alternative dictionary used: Systemic Events 0.0 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[3] | 497 / 2438 (20.39%) | 158 / 808 (19.55%) | |
| occurrences (all) | 497 | 158 | |
| Headache - Any (reactogenicity event) | | | |
| alternative dictionary used: Systemic Events 0.0 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[4] | 1440 / 2438 (59.06%) | 391 / 808 (48.39%) | |
| occurrences (all) | 1440 | 391 | |
| Fatigue -Any (reactogenicity event) | | | |
| alternative dictionary used: Systemic Events 0.0 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[5] | 1576 / 2438 (64.64%) | 411 / 808 (50.87%) | |
| occurrences (all) | 1576 | 411 | |
| Chills - Any (reactogenicity event) | | | |
| alternative dictionary used: Systemic Events 0.0 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[6] | 697 / 2438 (28.59%) | 133 / 808 (16.46%) | |
| occurrences (all) | 697 | 133 | |
| Muscle pain -Any (reactogenicity event) | | | |
| alternative dictionary used: Systemic Events 0.0 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[7] | 916 / 2438 (37.57%) | 170 / 808 (21.04%) | |
| occurrences (all) | 916 | 170 | |
| Joint pain -Any (reactogenicity event) | | | |
| alternative dictionary used: Systemic Events 0.0 | | | |

| | | | |
|---|---|---|---|
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[8] | 723 / 2438 (29.66%) | 136 / 808 (16.83%) | |
| occurrences (all) | 723 | 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] | 537 / 2438 (22.03%) | 8 / 808 (0.99%) | |
| occurrences (all) | 537 | 8 | |
| Pain at injection site - Any (reactogenicity event) | | | |
| alternative dictionary used: Local Reactions 0.0 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[10] | 2184 / 2438 (89.58%) | 147 / 808 (18.19%) | |
| occurrences (all) | 2184 | 147 | |
| Swelling -Any (reactogenicity event) | | | |
| alternative dictionary used: Local Reactions 0.0 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[11] | 612 / 2438 (25.10%) | 8 / 808 (0.99%) | |
| occurrences (all) | 612 | 8 | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 98 / 2471 (3.97%) | 29 / 822 (3.53%) | |
| occurrences (all) | 112 | 31 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 77 / 2471 (3.12%) | 33 / 822 (4.01%) | |
| occurrences (all) | 89 | 37 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 45 / 2471 (1.82%) | 10 / 822 (1.22%) | |
| occurrences (all) | 49 | 12 | |
| Pharyngitis | | | |
| subjects affected / exposed | 37 / 2471 (1.50%) | 10 / 822 (1.22%) | |
| occurrences (all) | 41 | 11 | |
| Gastroenteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 33 / 2471 (1.34%) | 12 / 822 (1.46%) | |
| occurrences (all) | 35 | 13 | |
| 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