# Clinical trial results:
# A Phase 2, Randomized, Placebo-Controlled, Single-blind Trial to Assess the Safety, Tolerability, and Immunogenicity of Bivalent rLP2086 Vaccine When Administered in Either 2- or 3-Dose Regimens in Healthy Subjects Aged 11 to <19 Years

## Summary

| | |
|---|---|
| EudraCT number | 2009-014493-18 |
| Trial protocol | SE CZ ES PL DE FI DK |
| Global end of trial date | 18 September 2012 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 29 June 2016 |
| First version publication date | 01 August 2015 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | B1971012 (6108A1-2003-EU) |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01299480 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Clinical Trials.gov Call Center, Pfizer Inc., 001 800-718-1021, ClinicalTrials.govCallCenter@pfizer.com |
| Scientific contact | Clinical Trials.gov Call Center, Pfizer Inc., 001 800-718-1021, ClinicalTrials.govCallCenter@pfizer.com |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-001037-PIP02-11 |
| 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 | 03 December 2013 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 18 September 2012 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Co-Primary Objectives:

To assess the immune response as measured by serum bactericidal assay performed with MnB strains expressing LP2086 subfamily A and B proteins, measured 1 month after the third vaccination with bivalent rLP2086 vaccine among group 1 subjects.

To assess the immune response as measured by serum bactericidal assay performed with MnB strains expressing LP2086 subfamily A and B proteins, measured 1 month after the third vaccination with bivalent rLP2086 vaccine among group 2 subjects.

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 March 2011 |
| 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 | Poland: 239 |
| Country: Number of subjects enrolled | Spain: 176 |
| Country: Number of subjects enrolled | Sweden: 133 |
| Country: Number of subjects enrolled | Czech Republic: 330 |
| Country: Number of subjects enrolled | Denmark: 302 |
| Country: Number of subjects enrolled | Finland: 368 |
| Country: Number of subjects enrolled | Germany: 164 |
| Worldwide total number of subjects | 1712 |
| EEA total number of subjects | 1712 |

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) | 220 |
| Adolescents (12-17 years) | 1325 |
| Adults (18-64 years) | 167 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 1714 subjects were enrolled in this study. Of these, 1 subject was not randomized but was vaccinated with Saline at Injection 1. This subject was included in safety population and not intent-to-treat population.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Group 1:rLP2086(0-, 1-, 6-Month) + Saline(2-Month) |

Arm description:

Randomized to receive rLP2086 on a 0-, 1-, 6- month and 0.9% normal saline on a 2- month schedule.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bivalent Recombinant lipoprotein 2086 (rLP2086) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received rLP2086 120 mcg on a 0-, 1-, 6- month schedule.

| | |
|---|---|
| Investigational medicinal product name | Saline (0.9% sodium chloride) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received 0.9% saline on a 2- month schedule.

| | |
|---|---|
| **Arm title** | Group 2:rLP2086(0-, 2-, 6-Month) +Saline(1-Month) |

Arm description:

Randomized to receive rLP2086 on a 0-, 2-, 6- month and 0.9% normal saline on a 1- month schedule.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bivalent Recombinant lipoprotein 2086 (rLP2086) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received rLP2086 120 mcg on a 0-, 2-, 6- month schedule.

| | |
|---|---|
| Investigational medicinal product name | Saline (0.9% sodium chloride) |
| Investigational medicinal product code | |
| Other name | |

| | |
|---|---|
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received 0.9% saline on a 1- month schedule.

| **Arm title** | Group 3:rLP2086(0-, 6-Month) +Saline(1-, 2-Month) |
|---|---|

Arm description:

Randomized to receive rLP2086 on a 0-, 6- month and 0.9% normal saline on a 1-, 2- month schedule.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bivalent Recombinant lipoprotein 2086 (rLP2086) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received rLP2086 120 mcg on a 0-, 6- month schedule.

| | |
|---|---|
| Investigational medicinal product name | Saline (0.9% sodium chloride) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received 0.9% saline on a 1-, 2-month schedule.

| **Arm title** | Group 4:rLP2086(0-, 2-Month) + Saline(1-, 6-Month) |
|---|---|

Arm description:

Randomized to receive rLP2086 on a 0-, 2- month and 0.9% normal saline on a 1-, 6- month schedule.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bivalent Recombinant lipoprotein 2086 (rLP2086) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received rLP2086 120 mcg on a 0-, 2- month schedule.

| | |
|---|---|
| Investigational medicinal product name | Saline (0.9% sodium chloride) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received 0.9% saline on a 1-, 6-month schedule.

| **Arm title** | Group 5:rLP2086(2-, 6-Month) + Saline(0-, 1-Month) |
|---|---|

Arm description:

Randomized to receive rLP2086 on a 2-, 6- month and 0.9% normal saline on a 0-, 1- month schedule.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bivalent Recombinant lipoprotein 2086 (rLP2086) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

| | |
|---|---|
| Dosage and administration details:<br>Subjects received rLP2086 on a 2-, 6- month schedule. | |
| Investigational medicinal product name | Saline (0.9% sodium chloride) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received 0.9% saline on a 0-, 1-month schedule.

| **Number of subjects in period 1** | Group 1:rLP2086(0-, 1-, 6-Month) + Saline(2-Month) | Group 2:rLP2086(0-, 2-, 6-Month) +Saline(1-Month) | Group 3:rLP2086(0-, 6-Month) +Saline(1-, 2-Month) |
|---|---|---|---|
| Started | 427 | 430 | 426 |
| Randomized and Treated | 427 | 430 | 426 |
| Completed | 385 | 395 | 386 |
| Not completed | 42 | 35 | 40 |
| Withdrawal due to pregnancy | - | 1 | 1 |
| Consent withdrawn by subject | 3 | 4 | 7 |
| Physician decision | 1 | 1 | - |
| Adverse event | 6 | 4 | 5 |
| Treated but not randomized | - | - | - |
| No longer willing to participate | 19 | 17 | 14 |
| Unspecified | 3 | 2 | 3 |
| Protocol Violation | 7 | 5 | 8 |
| Lost to follow-up | 3 | 1 | 2 |

| **Number of subjects in period 1** | Group 4:rLP2086(0-, 2-Month) + Saline(1-, 6-Month) | Group 5:rLP2086(2-, 6-Month) + Saline(0-, 1-Month) |
|---|---|---|
| Started | 285 | 144 |
| Randomized and Treated | 285 | 143 |
| Completed | 261 | 123 |
| Not completed | 24 | 21 |
| Withdrawal due to pregnancy | - | - |
| Consent withdrawn by subject | 3 | 4 |
| Physician decision | 2 | - |
| Adverse event | 4 | - |
| Treated but not randomized | - | 1 |
| No longer willing to participate | 13 | 10 |
| Unspecified | - | 3 |
| Protocol Violation | 1 | 1 |
| Lost to follow-up | 1 | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Overall Study |
| Reporting group description: | |
| Baseline characteristics are represented for safety population. | |

| Reporting group values | Overall Study | Total | |
|---|---|---|---|
| Number of subjects | 1712 | 1712 | |
| Age categorical | | | |
| Some subjects randomized to receive vaccination as per Groups 1, 2 or 4 schedules actually received vaccination as per Group 3 schedule. One subject was not randomized but received Saline at Injection 1 and was included in Group 5. Subjects have been presented as per actual administration schedule received. | | | |
| Units: Subjects | | | |
| 11- less than (<) 14 years | 627 | 627 | |
| 14 - <19 years | 1085 | 1085 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 870 | 870 | |
| Male | 842 | 842 | |

| Subject analysis sets | |
|---|---|
| Subject analysis set title | Group 1:rLP2086(0 -,1-,6- Month) +Saline(2-Month):Safety |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Randomized to receive rLP2086 on a 0-, 1-, 6-month and 0.9% normal saline on a 2- month schedule. | |
| Subject analysis set title | Group 2:rLP2086(0-,2-,6-Month)+Saline(1- Month):Safety |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Randomized to receive rLP2086 on a 0-, 2-, 6-month and 0.9% normal saline on a 1- month schedule. | |
| Subject analysis set title | Group 3: rLP2086(0-, 6-Month) +Saline(1-,2-Month):Safety |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Randomized to receive rLP2086 on a 0-, 6- month and 0.9% normal saline on a 1-, 2- month schedule. | |
| Subject analysis set title | Group 4:rLP2086(0-,2- Month) +Saline(1-,6-Month):Safety |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Randomized to receive rLP2086 on a 0-, 2- month and 0.9% normal saline on a 1-, 6- month schedule. | |
| Subject analysis set title | Group 5:rLP2086(2-,6- Month)+ Saline(0-,1- Month): Safety |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Randomized to receive rLP2086 on a 2-, 6- month and 0.9% normal saline on a 0-, 1- month schedule. | |

| Reporting group values | Group 1:rLP2086(0 -,1-,6- Month) +Saline(2-Month):Safety | Group 2:rLP2086(0-,2-,6-Month)+Saline(1-Month):Safety | Group 3: rLP2086(0-, 6-Month) +Saline(1-,2-Month):Safety |
|---|---|---|---|
| Number of subjects | 426 | 414 | 451 |

| | | | |
|---|---|---|---|
| Age categorical | | | |
| Some subjects randomized to receive vaccination as per Groups 1, 2 or 4 schedules actually received vaccination as per Group 3 schedule. One subject was not randomized but received Saline at Injection 1 and was included in Group 5. Subjects have been presented as per actual administration schedule received. | | | |
| Units: Subjects | | | |
| 11- less than (<) 14 years | 155 | 154 | 164 |
| 14 - <19 years | 271 | 260 | 287 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 212 | 217 | 227 |
| Male | 214 | 197 | 224 |

| **Reporting group values** | Group 4:rLP2086(0-,2- Month) +Saline(1-,6-Month):Safety | Group 5:rLP2086(2-,6- Month)+ Saline(0-,1-Month): Safety | |
|---|---|---|---|
| Number of subjects | 277 | 144 | |
| Age categorical | | | |
| Some subjects randomized to receive vaccination as per Groups 1, 2 or 4 schedules actually received vaccination as per Group 3 schedule. One subject was not randomized but received Saline at Injection 1 and was included in Group 5. Subjects have been presented as per actual administration schedule received. | | | |
| Units: Subjects | | | |
| 11- less than (<) 14 years | 101 | 53 | |
| 14 - <19 years | 176 | 91 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 135 | 79 | |
| Male | 142 | 65 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Group 1:rLP2086(0-, 1-, 6-Month) + Saline(2-Month) |
| Reporting group description: Randomized to receive rLP2086 on a 0-, 1-, 6- month and 0.9% normal saline on a 2- month schedule. | |
| Reporting group title | Group 2:rLP2086(0-, 2-, 6-Month) +Saline(1-Month) |
| Reporting group description: Randomized to receive rLP2086 on a 0-, 2-, 6- month and 0.9% normal saline on a 1- month schedule. | |
| Reporting group title | Group 3:rLP2086(0-, 6-Month) +Saline(1-, 2-Month) |
| Reporting group description: Randomized to receive rLP2086 on a 0-, 6- month and 0.9% normal saline on a 1-, 2- month schedule. | |
| Reporting group title | Group 4:rLP2086(0-, 2-Month) + Saline(1-, 6-Month) |
| Reporting group description: Randomized to receive rLP2086 on a 0-, 2- month and 0.9% normal saline on a 1-, 6- month schedule. | |
| Reporting group title | Group 5:rLP2086(2-, 6-Month) + Saline(0-, 1-Month) |
| Reporting group description: Randomized to receive rLP2086 on a 2-, 6- month and 0.9% normal saline on a 0-, 1- month schedule. | |
| Subject analysis set title | Group 1:rLP2086(0 -,1-,6- Month) +Saline(2-Month):Safety |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Randomized to receive rLP2086 on a 0-, 1-, 6-month and 0.9% normal saline on a 2- month schedule. | |
| Subject analysis set title | Group 2:rLP2086(0-,2-,6-Month)+Saline(1- Month):Safety |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Randomized to receive rLP2086 on a 0-, 2-, 6-month and 0.9% normal saline on a 1- month schedule. | |
| Subject analysis set title | Group 3: rLP2086(0-, 6-Month) +Saline(1-,2-Month):Safety |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Randomized to receive rLP2086 on a 0-, 6- month and 0.9% normal saline on a 1-, 2- month schedule. | |
| Subject analysis set title | Group 4:rLP2086(0-,2- Month) +Saline(1-,6-Month):Safety |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Randomized to receive rLP2086 on a 0-, 2- month and 0.9% normal saline on a 1-, 6- month schedule. | |
| Subject analysis set title | Group 5:rLP2086(2-,6- Month)+ Saline(0-,1- Month): Safety |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Randomized to receive rLP2086 on a 2-, 6- month and 0.9% normal saline on a 0-, 1- month schedule. | |

### Primary: Percentage of Subjects Achieving Serum Bactericidal Assay Using Human Complement (hSBA) Titer Greater Than or Equal to (>=) Lower Limit of Quantitation: Group 1 and 2 Subjects

| | |
|---|---|
| End point title | Percentage of Subjects Achieving Serum Bactericidal Assay Using Human Complement (hSBA) Titer Greater Than or Equal to (>=) Lower Limit of Quantitation: Group 1 and 2 Subjects[1][2] |
| End point description: | |
| End point type | Primary |
| End point timeframe: 1 month after Injection 4 | |

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: Statistical Analysis has been provided in the form of attachment.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was planned to be reported for reporting group Group 1: rLP2086(0-, 1-, 6-Month) + Saline(2-Month) and Group 2: rLP2086(0-, 2-, 6-Month) +Saline(1-Month) only.

| **End point values** | Group 1:rLP2086(0-, 1-, 6-Month) + Saline(2-Month) | Group 2:rLP2086(0-, 2-, 6-Month) +Saline(1-Month) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 365 | 360 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| PMB80 [A22] 1:8 (N=360,357) | 91.7 | 95 | | |
| PMB2001 [A56] 1:8 (N=362, 359) | 99.4 | 98.9 | | |
| PMB2948 [B24] 1:8 (N=354, 354) | 89 | 88.4 | | |
| PMB2707 [B44] 1:8 (N=356, 352) | 88.5 | 86.1 | | |

| **Attachments (see zip file)** | Statistical Analysis for Primary Endpoint/Statistical Analysis for |
|---|---|

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects Reporting At Least 1 Adverse Event (AE)

| End point title | Percentage of Subjects Reporting At Least 1 Adverse Event (AE)[3] |
|---|---|

End point description:

Some subjects randomized to receive vaccination as per Groups 1, 2 or 4 schedules actually received vaccination as per Group 3 schedule. One subject was not randomized but received Saline at Injection 1 and was included in Group 5. Subjects have been presented as per actual administration schedule received.

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

End point timeframe:

Injection 1 up to 1 month after Injection 4

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(0 -,1-,6- Month) +Saline(2-Month):Safety | Group 2:rLP2086(0-,2-,6-Month)+Saline(1- | Group 3: rLP2086(0-, 6-Month) +Saline(1-,2-Month):Safety | Group 4:rLP2086(0-,2- Month) +Saline(1-,6-Month):Safety |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 426 | 414 | 451 | 277 |
| Units: percentage of subjects | | | | |
| number (not applicable) | 36.9 | 35.7 | 35.5 | 35.7 |

| End point values | Group 5:rLP2086(2-,6- Month)+ Saline(0-,1-Month): Safety | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 144 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 37.5 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects Achieving hSBA Titer >=LLOQ: Group 3 Subjects

| End point title | Percentage of Subjects Achieving hSBA Titer >=LLOQ: Group 3 Subjects[4] |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

1 month after Injection 4

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The endpoint was planned to be reported for reporting group Group 3:rLP2086(0-, 6-Month) +Saline(1-, 2-Month) only.

| End point values | Group 3:rLP2086(0-, 6-Month) +Saline(1-, 2- | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 371 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| PMB80 [A22] 1:8 (N=369) | 93.5 | | | |
| PMB2001 [A56] 1: 8 (N=370) | 98.4 | | | |
| PMB2948 [B24] 1:8 (N=359) | 81.1 | | | |
| PMB2707 [B44] 1:8 (N=356) | 77.5 | | | |

| Attachments (see zip file) | Statistical Analysis for Secondary Endpoint/Statistical analysis |
|---|---|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Serum Bactericidal Assay Using Human Complement (hSBA) Geometric Mean Titers (GMTs)

| End point title | Serum Bactericidal Assay Using Human Complement (hSBA) Geometric Mean Titers (GMTs) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Before Injection (Inj) 1, 1 Month (M) after (aft) Injection 2, 3, 4

| End point values | Group 1:rLP2086(0-, 1-, 6-Month) + Saline(2-Month) | Group 2:rLP2086(0-, 2-, 6-Month) +Saline(1-Month) | Group 3:rLP2086(0-, 6-Month) +Saline(1-, 2- | Group 4:rLP2086(0-, 2-Month) + Saline(1-, 6-Month) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 365 | 360 | 371 | 241 |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Before Inj1: PMB80 [A22]; N=356,352,364,235,108 | 7.1 (6.41 to 7.87) | 6.3 (5.72 to 6.95) | 6.4 (5.84 to 7.02) | 6.4 (5.66 to 7.22) |
| 1M aft Inj2: PMB80 [A22]; N=351,345,351,224,110 | 24.4 (21.25 to 27.94) | 10.7 (9.44 to 12.09) | 12 (10.58 to 13.6) | 13.3 (11.21 to 15.76) |
| 1M aft Inj3: PMB80 [A22]; N=332,344,340,238,102 | 17.7 (15.28 to 20.47) | 32.9 (29.34 to 36.92) | 10.3 (9.09 to 11.68) | 37.1 (32.23 to 42.76) |
| 1M aft Inj4: PMB80 [A22]; N=360,357,369,234,111 | 55.1 (48.87 to 62.07) | 56.3 (50.91 to 62.27) | 48.4 (43.45 to 53.86) | 14.2 (12.08 to 16.73) |
| Before Inj1: PMB2001 [A56]; N=350,348,355,231,107 | 6.8 (6.06 to 7.64) | 6.1 (5.54 to 6.77) | 6.7 (6 to 7.48) | 6.3 (5.54 to 7.15) |
| 1M aft Inj2: PMB2001 [A56]; N=353,329,335,218,102 | 77.3 (68.54 to 87.12) | 17 (14.56 to 19.96) | 18.5 (15.81 to 21.63) | 17.7 (14.45 to 21.58) |
| 1M aft Inj3: PMB2001 [A56]; N=329,339,320,240,102 | 48.3 (41.96 to 55.5) | 94.6 (84.64 to 105.68) | 15.1 (12.89 to 17.74) | 104.9 (93.16 to 118.05) |
| 1M aft Inj4: PMB2001 [A56]; N=362,359,370,228,113 | 152.9 (137.23 to 170.47) | 155.6 (140.39 to 172.38) | 125.6 (112.59 to 140.17) | 26.5 (22.24 to 31.58) |
| Before Inj1: PMB2948 [B24]; N=362,356,369,241,112 | 5.3 (4.93 to 5.75) | 5.1 (4.77 to 5.52) | 5 (4.7 to 5.38) | 4.9 (4.49 to 5.24) |
| 1M aft Inj2: PMB2948 [B24]; N=344,345,352,223,110 | 13.8 (12.15 to 15.57) | 8.2 (7.38 to 9.21) | 9.2 (8.2 to 10.28) | 9.8 (8.39 to 11.35) |
| 1M aft Inj3: PMB2948 [B24]; N=328,337,340,237,102 | 11 (9.61 to 12.5) | 14.9 (13.2 to 16.73) | 7.5 (6.75 to 8.35) | 17.7 (15.24 to 20.49) |
| 1M aft Inj4: PMB2948 [B24]; N=354,354,359,228,110 | 29.1 (25.88 to 32.66) | 25.6 (23.03 to 28.45) | 20.6 (18.38 to 23.18) | 8 (7.01 to 9.24) |
| Before Inj1: PMB2707 [B44]; N=363,357,370,241,113 | 4.4 (4.18 to 4.54) | 4.5 (4.24 to 4.67) | 4.5 (4.26 to 4.7) | 4.6 (4.28 to 4.9) |
| 1M aft Inj2: PMB2707 [B44]; N=341,345,349,225,111 | 13.1 (11.29 to 15.11) | 5.5 (5.04 to 6.01) | 5.7 (5.19 to 6.3) | 5.9 (5.19 to 6.74) |
| 1M aft Inj3: PMB2707 [B44]; N=333,331,341,234,105 | 8.4 (7.4 to 9.6) | 15.5 (13.51 to 17.87) | 5.2 (4.78 to 5.68) | 19.1 (16.03 to 22.78) |
| 1M aft Inj4: PMB2707 [B44]; N=356,352,356,230,111 | 40.3 (35.16 to 46.11) | 35 (30.63 to 39.91) | 22.5 (19.6 to 25.72) | 6.2 (5.52 to 7.07) |

| End point values | Group 5:rLP2086(2-, 6-Month) + Saline(0-, 1-Month) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 113 | | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Before Inj1: PMB80 [A22]; N=356,352,364,235,108 | 6.8 (5.59 to 8.3) | | | |
| 1M aft Inj2: PMB80 [A22]; N=351,345,351,224,110 | 7.1 (5.86 to 8.48) | | | |
| 1M aft Inj3: PMB80 [A22]; N=332,344,340,238,102 | 16 (12.15 to 21.06) | | | |
| 1M aft Inj4: PMB80 [A22]; N=360,357,369,234,111 | 39.6 (32.31 to 48.46) | | | |
| Before Inj1: PMB2001 [A56]; N=350,348,355,231,107 | 6.2 (5.1 to 7.47) | | | |
| 1M aft Inj2: PMB2001 [A56]; N=353,329,335,218,102 | 6.8 (5.52 to 8.36) | | | |
| 1M aft Inj3: PMB2001 [A56]; N=329,339,320,240,102 | 26.8 (19.48 to 36.92) | | | |
| 1M aft Inj4: PMB2001 [A56]; N=362,359,370,228,113 | 111.8 (92.73 to 134.9) | | | |
| Before Inj1: PMB2948 [B24]; N=362,356,369,241,112 | 5.1 (4.51 to 5.82) | | | |
| 1M aft Inj2: PMB2948 [B24]; N=344,345,352,223,110 | 5.3 (4.7 to 6.08) | | | |
| 1M aft Inj3: PMB2948 [B24]; N=328,337,340,237,102 | 12.6 (10.01 to 15.89) | | | |
| 1M aft Inj4: PMB2948 [B24]; N=354,354,359,228,110 | 14.7 (12.01 to 18.1) | | | |
| Before Inj1: PMB2707 [B44]; N=363,357,370,241,113 | 4.4 (4.04 to 4.76) | | | |
| 1M aft Inj2: PMB2707 [B44]; N=341,345,349,225,111 | 4.4 (4.04 to 4.77) | | | |
| 1M aft Inj3: PMB2707 [B44]; N=333,331,341,234,105 | 6.8 (5.45 to 8.55) | | | |
| 1M aft Inj4: PMB2707 [B44]; N=356,352,356,230,111 | 17.8 (14.12 to 22.42) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects Achieving hSBA Titer >=LLOQ

| End point title | Percentage of Subjects Achieving hSBA Titer >=LLOQ |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:
Before Injection 1, 1 Month after Injection 2, 3, 4

| **End point values** | Group 1:rLP2086(0-, 1-, 6-Month) + Saline(2-Month) | Group 2:rLP2086(0-, 2-, 6-Month) +Saline(1-Month) | Group 3:rLP2086(0-, 6-Month) +Saline(1-, 2- | Group 4:rLP2086(0-, 2-Month) + Saline(1-, 6-Month) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 365 | 360 | 371 | 241 |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Before Inj1: PMB80[A22] 1:8; N=356,352,364,235,108 | 28.1 | 21.9 | 24.7 | 22.6 |
| 1M aft Inj2:PMB80[A22]1:8; N=351,345,351,224,110 | 74.6 | 46.7 | 51.3 | 52.2 |
| 1M aft Inj3:PMB80[A22]1:8; N=332,344,340,238,102 | 63 | 88.7 | 44.7 | 90.8 |
| 1M aft Inj4:PMB80[A22]1:8; N=360,357,369,234,111 | 91.7 | 95 | 93.5 | 57.7 |
| Before Inj1:PMB2001[A56]1:8; N=350,348,355,231,107 | 20.9 | 18.7 | 21.7 | 19 |
| 1M aft Inj2:PMB2001[A56]1:8; N=353,329,335,218,102 | 96.6 | 56.2 | 58.8 | 56 |
| 1M aft Inj3;PMB2001[A56]1:8; N=329,339,320,240,102 | 89.1 | 97.9 | 50.6 | 100 |
| 1M aft Inj4:PMB2001[A56]1:8; N=362,359,370,228,113 | 99.4 | 98.9 | 98.4 | 76.8 |
| Before Inj1:PMB2948[B24]1:8; N=362,356,369,241,112 | 16.3 | 13.8 | 13 | 11.2 |
| 1M aft Inj2:PMB2948[B24]1:8; N=344,345,352,223,110 | 62.2 | 39.4 | 43.8 | 45.3 |
| 1M aft Inj3:PMB2948[B24]1:8; N=328,337,340,237,102 | 50.6 | 70.3 | 35.6 | 73 |
| 1M aft Inj4:PMB2948[B24]1:8; N=354,354,359,228,110 | 89 | 88.4 | 81.1 | 35.5 |
| Before Inj1:PMB2707[B44]1:8; N=363,357,370,241,113 | 5.2 | 6.2 | 6.2 | 7.5 |
| 1M aft Inj2:PMB2707[B44]1:8; N=341,345,349,225,111 | 54 | 15.7 | 17.8 | 18.2 |
| 1M aft Inj3:PMB2707[B44]1:8; N=333,331,341,234,105 | 35.4 | 61.9 | 12.6 | 70.1 |
| 1M aft Inj4:PMB2707[B44]1:8; N=356,352,356,230,111 | 88.5 | 86.1 | 77.5 | 23.9 |

| **End point values** | Group 5:rLP2086(2-, 6-Month) + Saline(0-, 1-Month) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 113 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |

| | | | | |
|---|---|---|---|---|
| Before Inj1: PMB80[A22] 1:8; N=356,352,364,235,108 | 25 | | | |
| 1M aft Inj2:PMB80[A22]1:8; N=351,345,351,224,110 | 28.2 | | | |
| 1M aft Inj3:PMB80[A22]1:8; N=332,344,340,238,102 | 55.9 | | | |
| 1M aft Inj4:PMB80[A22]1:8; N=360,357,369,234,111 | 91.9 | | | |
| Before Inj1:PMB2001[A56]1:8; N=350,348,355,231,107 | 17.8 | | | |
| 1M aft Inj2:PMB2001[A56]1:8; N=353,329,335,218,102 | 22.5 | | | |
| 1M aft Inj3;PMB2001[A56]1:8; N=329,339,320,240,102 | 67.6 | | | |
| 1M aft Inj4:PMB2001[A56]1:8; N=362,359,370,228,113 | 99.1 | | | |
| Before Inj1:PMB2948[B24]1:8; N=362,356,369,241,112 | 14.3 | | | |
| 1M aft Inj2:PMB2948[B24]1:8; N=344,345,352,223,110 | 18.2 | | | |
| 1M aft Inj3:PMB2948[B24]1:8; N=328,337,340,237,102 | 56.9 | | | |
| 1M aft Inj4:PMB2948[B24]1:8; N=354,354,359,228,110 | 69.1 | | | |
| Before Inj1:PMB2707[B44]1:8; N=363,357,370,241,113 | 4.4 | | | |
| 1M aft Inj2:PMB2707[B44]1:8; N=341,345,349,225,111 | 4.5 | | | |
| 1M aft Inj3:PMB2707[B44]1:8; N=333,331,341,234,105 | 23.8 | | | |
| 1M aft Inj4:PMB2707[B44]1:8; N=356,352,356,230,111 | 73 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Serum Bactericidal Assay Using Human Complement (hSBA) Titer >= Prespecified Titer Level

| End point title | Percentage of Subjects With Serum Bactericidal Assay Using Human Complement (hSBA) Titer >= Prespecified Titer Level |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Before Injection 1, 1 Month after Injection 2, 3, 4

| End point values | Group 1:rLP2086(0-, 1-, 6-Month) + Saline(2-Month) | Group 2:rLP2086(0-, 2-, 6-Month) +Saline(1-Month) | Group 3:rLP2086(0-, 6-Month) +Saline(1-, 2- | Group 4:rLP2086(0-, 2-Month) + Saline(1-, 6-Month) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 365 | 360 | 371 | 241 |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Before Inj1:PMB80[A22] 1:4; N=356,352,364,235,108 | 28.9 | 23.9 | 26.4 | 23.8 |
| Before Inj1:PMB80[A22] 1:16; N=356,352,364,235,108 | 27.2 | 20.5 | 22.8 | 22.1 |
| Before Inj1:PMB80[A22] 1:32; N=356,352,364,235,108 | 18.3 | 14.5 | 13.5 | 13.2 |
| Before Inj1:PMB80[A22] 1:64; N=356,352,364,235,108 | 7.6 | 6.5 | 4.7 | 6.8 |
| Before Inj1:PMB80[A22]1:128; N=356,352,364,235,108 | 1.4 | 2.3 | 1.6 | 2.6 |
| 1M aft Inj2:PMB80[A22] 1:4; N=351,345,351,224,110 | 74.9 | 47.8 | 51.3 | 52.2 |
| 1M aft Inj2:PMB80[A22] 1:16; N=351,345,351,224,110 | 73.5 | 45.8 | 50.7 | 51.8 |
| 1M aft Inj2:PMB80[A22] 1:32; N=351,345,351,224,110 | 58.4 | 28.7 | 34.5 | 37.9 |
| 1M aft Inj2:PMB80[A22] 1:64; N=351,345,351,224,110 | 30.8 | 14.5 | 14.5 | 19.6 |
| 1M aft Inj2:PMB80[A22]1:128; N=351,345,351,224,110 | 14.8 | 5.2 | 5.7 | 8.5 |
| 1M aft Inj3:PMB80[A22] 1:4; N=332,344,340,238,102 | 63.6 | 88.7 | 45.6 | 90.8 |
| 1M aft Inj3:PMB80[A22]1:16; N=332,344,340,238,102 | 62.3 | 88.1 | 42.4 | 90.8 |
| 1M aft Inj3:PMB80[A22]1:32; N=332,344,340,238,102 | 47.3 | 69.5 | 30.6 | 70.6 |
| 1M aft Inj3:PMB80[A22]1:64; N=332,344,340,238,102 | 22.3 | 35.8 | 12.4 | 39.1 |
| 1M aft Inj3:PMB80[A22]1:128; N=332,344,340,238,102 | 11.7 | 14.8 | 4.4 | 19.7 |
| 1M aft Inj4:PMB80[A22] 1:4; N=360,357,369,234,111 | 91.9 | 95 | 94 | 58.1 |
| 1M aft Inj4:PMB80[A22] 1:16; N=360,357,369,234,111 | 91.4 | 95 | 93.2 | 56 |
| 1M aft Inj4:PMB80[A22] 1:32; N=360,357,369,234,111 | 84.2 | 86.6 | 81.8 | 38 |
| 1M aft Inj4:PMB80[A22] 1:64;N=360,357,369,234,111 | 61.9 | 63.9 | 53.9 | 19.2 |
| 1M aft Inj4:PMB80[A22]1:128; N=360,357,369,234,111 | 31.7 | 32.5 | 25.7 | 8.5 |
| Before Inj1:PMB2001[A56] 1:4;N=350,348,355,231,107 | 25.1 | 22.1 | 25.1 | 25.5 |
| Before Inj1:PMB2001[A56]1:16;N=350,348,35 | 20 | 18.1 | 20.3 | 19 |
| Before Inj1:PMB2001[A56]1:32;N=350,348,35 | 18 | 14.1 | 17.2 | 15.6 |
| Before Inj1:PMB2001[A56]1:64;N=350,348,35 | 11.7 | 7.5 | 10.7 | 8.7 |
| Before Inj1: PMB2001 1:128;N=350,348,355,231,107 | 4.3 | 2.3 | 3.7 | 2.6 |
| 1M aft Inj2:PMB2001[A56] 1:4;N=353,329,335,218,102 | 96.6 | 61.4 | 63.3 | 60.1 |

| | | | | |
|---|---|---|---|---|
| 1M aft Inj2:PMB2001[A56]1:16;N=353,329,33 | 96.3 | 55 | 57.9 | 55.5 |
| 1M aft Inj2:PMB2001[A56]1:32;N=353,329,33 | 87.8 | 48 | 50.1 | 47.2 |
| 1M aft Inj2:PMB2001[A56]1:64;N=353,329,33 | 72.8 | 27.4 | 31 | 29.8 |
| 1M aft Inj2:PMB2001 1:128;N=353,329,335,218,102 | 41.1 | 14.3 | 14.9 | 15.6 |
| 1M aft Inj3:PMB2001[A56] 1:4;N=329,339,320,240,102 | 91.5 | 98.5 | 54.4 | 100 |
| 1M aft Inj3:PMB2001[A56]1:16;N=329,339,32 | 87.8 | 97.9 | 50 | 99.2 |
| 1M aft Inj3:PMB2001[A56]1:32;N=329,339,32 | 79.9 | 94.1 | 43.8 | 95 |
| 1M aft Inj3:PMB2001[A56]1:64;N=329,339,32 | 52.9 | 79.1 | 28.4 | 81.7 |
| 1M aft Inj3:PMB2001 1:128;N=329,339,320,240,102 | 26.7 | 50.4 | 13.1 | 57.1 |
| 1M aft Inj4:PMB2001[A56] 1:4;N=362,359,370,228,113 | 99.7 | 99.2 | 98.9 | 79.8 |
| 1M aft Inj4:PMB2001[A56]1:16;N=362,359,37 | 99.2 | 98.9 | 98.4 | 74.6 |
| 1M aft Inj4:PMB2001[A56]1:32;N=362,359,37 | 95.3 | 96.1 | 94.6 | 59.6 |
| 1M aft Inj4:PMB2001[A56]1:64;N=362,359,37 | 87.8 | 91.1 | 83.8 | 34.2 |
| 1M aft Inj4:PMB2001 1:128;N=362,359,370,228,113 | 72.4 | 73.5 | 65.9 | 15.8 |
| Before Inj1:PMB2948[B24]1:4;N=362,356,369 | 18.5 | 15.4 | 14.4 | 13.3 |
| Before Inj1:PMB2948[B24]1:16;N=362,356,36 | 12.7 | 11.5 | 10.8 | 8.7 |
| Before Inj1:PMB2948[B24]1:32;N=362,356,36 | 7.2 | 6.2 | 6 | 5 |
| Before Inj1:PMB2948[B24]1:64;N=362,356,36 | 2.8 | 3.1 | 2.2 | 2.1 |
| Before Inj1:PMB2948 1:128;N=362,356,369,241,112 | 1.4 | 0.8 | 0.5 | 0.8 |
| 1M aft Inj2:PMB2948[B24]1:4;N=344,345,352 | 66.3 | 42.3 | 45.7 | 47.1 |
| 1M aft Inj2:PMB2948[B24]1:16;N=344,345,35 | 57.6 | 32.8 | 39.5 | 40.4 |
| 1M aft Inj2:PMB2948[B24]1:32;N=344,345,35 | 34.9 | 18.6 | 23.3 | 24.7 |
| 1M aft Inj2:PMB2948[B24]1:64;N=344,345,35 | 14 | 9 | 8.8 | 11.7 |
| 1M aft Inj2:PMB2948 1:128;N=344,345,352,223,110 | 6.1 | 3.5 | 2.6 | 4.5 |
| 1M aft Inj3:PMB2948[B24]1:4;N=328,337,340 | 52.1 | 72.1 | 37.6 | 75.5 |
| 1M aft Inj3:PMB2948[B24]1:16;N=328,337,34 | 45.1 | 63.5 | 29.7 | 67.1 |
| 1M aft Inj3:PMB2948[B24]1:32;N=328,337,34 | 23.8 | 32 | 15.9 | 43.5 |
| 1M aft Inj3:PMB2948[B24]1:64;N=328,337,34 | 15.5 | 13.6 | 5 | 19.4 |
| 1M aft Inj3:PMB2948 1:128;N=328,337,340,237,102 | 6.7 | 6.5 | 2.6 | 8.4 |
| 1M aft Inj4:PMB2948[B24]1:4;N=354,354,359 | 90.1 | 90.1 | 83 | 38.2 |
| 1M aft Inj4:PMB2948[B24]1:16;N=354,354,35 | 82.8 | 83.6 | 73.8 | 32.9 |

| | | | | |
|---|---|---|---|---|
| 1M aft Inj4:PMB2948[B24]1:32;N=354,354,35 | 60.7 | 56.2 | 47.1 | 18 |
| 1M aft Inj4:PMB2948[B24]1:64;N=354,354,35 | 33.3 | 26.6 | 22.6 | 10.5 |
| 1M aft Inj4:PMB2948 1:128;N=354,354,359,228,110 | 13 | 10.5 | 7.2 | 3.1 |
| Before Inj1:PMB2707[B44]1:4;N=363,357,370 | 7.7 | 7.8 | 7.8 | 8.3 |
| Before Inj1:PMB2707[B44]1:16;N=363,357,37 | 3.6 | 5 | 4.9 | 6.6 |
| Before Inj1:PMB2707[B44]1:32;N=363,357,37 | 3 | 2.5 | 3.5 | 2.9 |
| Before Inj1:PMB2707[B44]1:64;N=363,357,37 | 0.6 | 1.4 | 1.4 | 1.2 |
| Before Inj1:PMB2707 1:128;N=363,357,370,241,113 | 0 | 0.3 | 0.3 | 0.8 |
| 1M aftInj2:PMB2707[B44]1:4;N=341,345,3 | 57.5 | 17.7 | 20.6 | 20.4 |
| 1M aft Inj2:PMB2707[B44]1:16;N=341,345,34 | 47.2 | 13.6 | 14 | 14.2 |
| 1M aft Inj2:PMB2707[B44]1:32;N=341,345,34 | 32 | 9.9 | 8.3 | 9.8 |
| 1M aft Inj2:PMB2707[B44]1:64;N=341,345,34 | 18.8 | 4.1 | 5.2 | 6.2 |
| 1M aft Inj2:PMB2707 1:128;N=341,345,349,225,111 | 10 | 1.7 | 3.7 | 4 |
| 1M aft Inj3:PMB2707[B44]1:4;N=333,331,341 | 39 | 65.9 | 15.5 | 73.5 |
| 1M aft Inj3:PMB2707[B44]1:16;N=333,331,34 | 30.3 | 58.6 | 10.9 | 64.5 |
| 1M aft Inj3:PMB2707[B44]1:32;N=333,331,34 | 18.6 | 39 | 5.9 | 42.3 |
| 1M aft Inj3:PMB2707[B44]1:64;N=333,331,34 | 11.4 | 22.7 | 3.8 | 24.4 |
| 1M aft Inj3:PMB2707 1:128;N=333,331,341,234,105 | 6.3 | 7.9 | 2.6 | 14.1 |
| 1M aft Inj4:PMB2707[B44]1:4;N=356,352,356 | 89.3 | 87.8 | 78.9 | 26.1 |
| 1M aft Inj4:PMB2707[B44]1:16;N=356,352,35 | 84.8 | 83.8 | 70.8 | 19.1 |
| 1M aft Inj4:PMB2707[B44]1:32;N=356,352,35 | 68.5 | 65.3 | 49.2 | 10 |
| 1M aft Inj4:PMB2707[B44]1:64;N=356,352,35 | 46.6 | 42.3 | 27.8 | 5.2 |
| 1M aft Inj4:PMB2707 1:128;N=356,352,356,230,111 | 27.5 | 22.7 | 13.8 | 3.9 |

| **End point values** | Group 5:rLP2086(2-, 6-Month) + Saline(0-, 1-Month) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 113 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Before Inj1:PMB80[A22] 1:4; N=356,352,364,235,108 | 25.9 | | | |

| | | | | |
|---|---|---|---|---|
| Before Inj1:PMB80[A22] 1:16; N=356,352,364,235,108 | 24.1 | | | |
| Before Inj1:PMB80[A22] 1:32; N=356,352,364,235,108 | 15.7 | | | |
| Before Inj1:PMB80[A22] 1:64; N=356,352,364,235,108 | 7.4 | | | |
| Before Inj1:PMB80[A22]1:128; N=356,352,364,235,108 | 1.9 | | | |
| 1M aft Inj2:PMB80[A22] 1:4; N=351,345,351,224,110 | 29.1 | | | |
| 1M aft Inj2:PMB80[A22] 1:16; N=351,345,351,224,110 | 27.3 | | | |
| 1M aft Inj2:PMB80[A22] 1:32; N=351,345,351,224,110 | 18.2 | | | |
| 1M aft Inj2:PMB80[A22] 1:64; N=351,345,351,224,110 | 6.4 | | | |
| 1M aft Inj2:PMB80[A22]1:128; N=351,345,351,224,110 | 0.9 | | | |
| 1M aft Inj3:PMB80[A22] 1:4; N=332,344,340,238,102 | 55.9 | | | |
| 1M aft Inj3:PMB80[A22]1:16; N=332,344,340,238,102 | 55.9 | | | |
| 1M aft Inj3:PMB80[A22]1:32; N=332,344,340,238,102 | 45.1 | | | |
| 1M aft Inj3:PMB80[A22]1:64; N=332,344,340,238,102 | 22.5 | | | |
| 1M aft Inj3:PMB80[A22]1:128; N=332,344,340,238,102 | 14.7 | | | |
| 1M aft Inj4:PMB80[A22] 1:4; N=360,357,369,234,111 | 91.9 | | | |
| 1M aft Inj4:PMB80[A22] 1:16; N=360,357,369,234,111 | 91 | | | |
| 1M aft Inj4:PMB80[A22] 1:32; N=360,357,369,234,111 | 74.8 | | | |
| 1M aft Inj4:PMB80[A22] 1:64;N=360,357,369,234,111 | 42.3 | | | |
| 1M aft Inj4:PMB80[A22]1:128; N=360,357,369,234,111 | 20.7 | | | |
| Before Inj1:PMB2001[A56] 1:4;N=350,348,355,231,107 | 25.2 | | | |
| Before Inj1:PMB2001[A56]1:16;N=350,348,35 | 16.8 | | | |
| Before Inj1:PMB2001[A56]1:32;N=350,348,35 | 15.9 | | | |
| Before Inj1:PMB2001[A56]1:64;N=350,348,35 | 8.4 | | | |
| Before Inj1: PMB2001 1:128;N=350,348,355,231,107 | 2.8 | | | |
| 1M aft Inj2:PMB2001[A56] 1:4;N=353,329,335,218,102 | 25.5 | | | |
| 1M aft Inj2:PMB2001[A56]1:16;N=353,329,33 | 21.6 | | | |
| 1M aft Inj2:PMB2001[A56]1:32;N=353,329,33 | 17.6 | | | |
| 1M aft Inj2:PMB2001[A56]1:64;N=353,329,33 | 10.8 | | | |
| 1M aft Inj2:PMB2001 1:128;N=353,329,335,218,102 | 2.9 | | | |
| 1M aft Inj3:PMB2001[A56] 1:4;N=329,339,320,240,102 | 72.5 | | | |
| 1M aft Inj3:PMB2001[A56]1:16;N=329,339,32 | 65.7 | | | |

| | | | | |
|---|---|---|---|---|
| 1M aft Inj3:PMB2001[A56]1:32;N=329,339,32 | 55.9 | | | |
| 1M aft Inj3:PMB2001[A56]1:64;N=329,339,32 | 39.2 | | | |
| 1M aft Inj3:PMB2001 1:128;N=329,339,320,240,102 | 22.5 | | | |
| 1M aft Inj4:PMB2001[A56] 1:4;N=362,359,370,228,113 | 99.1 | | | |
| 1M aft Inj4:PMB2001[A56]1:16;N=362,359,37 | 99.1 | | | |
| 1M aft Inj4:PMB2001[A56]1:32;N=362,359,37 | 92.9 | | | |
| 1M aft Inj4:PMB2001[A56]1:64;N=362,359,37 | 85 | | | |
| 1M aft Inj4:PMB2001 1:128;N=362,359,370,228,113 | 60.2 | | | |
| Before Inj1:PMB2948[B24]1:4;N=362,356,369 | 16.1 | | | |
| Before Inj1:PMB2948[B24]1:16;N=362,356,36 | 12.5 | | | |
| Before Inj1:PMB2948[B24]1:32;N=362,356,36 | 4.5 | | | |
| Before Inj1:PMB2948[B24]1:64;N=362,356,36 | 2.7 | | | |
| Before Inj1:PMB2948 1:128;N=362,356,369,241,112 | 1.8 | | | |
| 1M aft Inj2:PMB2948[B24]1:4;N=344,345,352 | 20 | | | |
| 1M aft Inj2:PMB2948[B24]1:16;N=344,345,35 | 14.5 | | | |
| 1M aft Inj2:PMB2948[B24]1:32;N=344,345,35 | 5.5 | | | |
| 1M aft Inj2:PMB2948[B24]1:64;N=344,345,35 | 3.6 | | | |
| 1M aft Inj2:PMB2948 1:128;N=344,345,352,223,110 | 0 | | | |
| 1M aft Inj3:PMB2948[B24]1:4;N=328,337,340 | 57.8 | | | |
| 1M aft Inj3:PMB2948[B24]1:16;N=328,337,34 | 52.9 | | | |
| 1M aft Inj3:PMB2948[B24]1:32;N=328,337,34 | 32.4 | | | |
| 1M aft Inj3:PMB2948[B24]1:64;N=328,337,34 | 15.7 | | | |
| 1M aft Inj3:PMB2948 1:128;N=328,337,340,237,102 | 6.9 | | | |
| 1M aft Inj4:PMB2948[B24]1:4;N=354,354,359 | 70.9 | | | |
| 1M aft Inj4:PMB2948[B24]1:16;N=354,354,35 | 64.5 | | | |
| 1M aft Inj4:PMB2948[B24]1:32;N=354,354,35 | 33.6 | | | |
| 1M aft Inj4:PMB2948[B24]1:64;N=354,354,35 | 12.7 | | | |
| 1M aft Inj4:PMB2948 1:128;N=354,354,359,228,110 | 6.4 | | | |
| Before Inj1:PMB2707[B44]1:4;N=363,357,370 | 7.1 | | | |
| Before Inj1:PMB2707[B44]1:16;N=363,357,37 | 4.4 | | | |
| Before Inj1:PMB2707[B44]1:32;N=363,357,37 | 3.5 | | | |

| | | | | |
|---|---|---|---|---|
| Before Inj1:PMB2707[B44]1:64;N=363,357,37 | 0.9 | | | |
| Before Inj1:PMB2707 1:128;N=363,357,370,241,113 | 0 | | | |
| 1M aftInj2:PMB2707[B44]1:4;N=341,345,3 | 5.4 | | | |
| 1M aft Inj2:PMB2707[B44]1:16;N=341,345,34 | 4.5 | | | |
| 1M aft Inj2:PMB2707[B44]1:32;N=341,345,34 | 3.6 | | | |
| 1M aft Inj2:PMB2707[B44]1:64;N=341,345,34 | 0.9 | | | |
| 1M aft Inj2:PMB2707 1:128;N=341,345,349,225,111 | 0 | | | |
| 1M aft Inj3:PMB2707[B44]1:4;N=333,331,341 | 28.6 | | | |
| 1M aft Inj3:PMB2707[B44]1:16;N=333,331,34 | 21 | | | |
| 1M aft Inj3:PMB2707[B44]1:32;N=333,331,34 | 13.3 | | | |
| 1M aft Inj3:PMB2707[B44]1:64;N=333,331,34 | 7.6 | | | |
| 1M aft Inj3:PMB2707 1:128;N=333,331,341,234,105 | 3.8 | | | |
| 1M aft Inj4:PMB2707[B44]1:4;N=356,352,356 | 73 | | | |
| 1M aft Inj4:PMB2707[B44]1:16;N=356,352,35 | 66.7 | | | |
| 1M aft Inj4:PMB2707[B44]1:32;N=356,352,35 | 39.6 | | | |
| 1M aft Inj4:PMB2707[B44]1:64;N=356,352,35 | 20.7 | | | |
| 1M aft Inj4:PMB2707 1:128;N=356,352,356,230,111 | 9 | | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Percentage of Subjects Achieving At Least 4-fold Increase in hSBA Titer

| End point title | Percentage of Subjects Achieving At Least 4-fold Increase in hSBA Titer |
|---|---|

End point description:

Results were not reported because a decision was made a priori to remove the endpoint as a secondary outcome measure.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

1 month after Injection 2, 3, 4

| **End point values** | Group 1:rLP2086(0-, 1-, 6-Month) + Saline(2-Month) | Group 2:rLP2086(0-, 2-, 6-Month) +Saline(1-Month) | Group 3:rLP2086(0-, 6-Month) +Saline(1-, 2- | Group 4:rLP2086(0-, 2-Month) + Saline(1-, 6-Month) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[5] | 0[6] | 0[7] | 0[8] |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |

Notes:

[5] - Results not reported because the endpoint was removed as a secondary endpoint.

[6] - Results not reported because the endpoint was removed as a secondary endpoint.

[7] - Results not reported because the endpoint was removed as a secondary endpoint.

[8] - Results not reported because the endpoint was removed as a secondary endpoint.

| **End point values** | Group 5:rLP2086(2-, 6-Month) + Saline(0-, 1-Month) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[9] | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |

Notes:

[9] - Results not reported because the endpoint was removed as a secondary endpoint.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AE reported from Injection 1 to 1 month after last administration of investigational product (bivalent rLP2086/saline). SAE reported from Injection 1 to 6 months after last of investigational product (bivalent rLP2086/saline)

Adverse event reporting additional description:

Some subjects randomized to receive vaccination as per Groups 1, 2 or 4 schedules actually received vaccination as per Group 3 schedule. One subject was not randomized but received Saline at Injection 1 and was included in Group 5. Subjects have been presented as per actual administration schedule received.

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 15.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Group 1:rLP2086(0-,1-,6- Month)+Saline(2-Month) |
| Reporting group description: | |
| Randomized to receive rLP2086 and 0.9% normal saline. | |
| Reporting group title | Group 2:rLP2086(0 -,2-,6-Month) +Saline(1-Month) |
| Reporting group description: | |
| Randomized to receive rLP2086 and 0.9% normal saline. | |
| Reporting group title | Group 3: rLP2086(0- ,6-Month) +Saline(1-,2-Month) |
| Reporting group description: | |
| Randomized to receive rLP2086 and 0.9% normal saline. | |
| Reporting group title | Group 4: rLP2086(0-,2-Month) +Saline(1-,6 - Month) |
| Reporting group description: | |
| Randomized to receive rLP2086 and 0.9% normal saline. | |
| Reporting group title | Group 5: rLP2086(2- ,6-Month)+ Saline(0-, 1-Month) |
| Reporting group description: | |
| Randomized to receive rLP2086 and 0.9% normal saline. | |

| Serious adverse events | Group 1:rLP2086(0-,1-,6-Month)+Saline(2- | Group 2:rLP2086(0-,2-,6-Month) +Saline(1-Month) | Group 3: rLP2086(0- ,6-Month) +Saline(1- |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 12 / 426 (2.82%) | 14 / 414 (3.38%) | 7 / 451 (1.55%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal | | | |

| | | | |
|---|---|---|---|
| conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chills | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 1 / 451 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Allergic cough | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Concussion | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 1 / 451 (0.22%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Alcohol poisoning | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 1 / 451 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone contusion | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clavicle fracture | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foreign body | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hand fracture | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Head injury | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Near drowning | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 1 / 451 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Poisoning | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skeletal injury | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 2 / 414 (0.48%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Migraine | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 1 / 451 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Aphthous stomatitis | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Crohn's disease | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 1 / 451 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis contact | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urticaria | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Musculoskeletal and connective tissue disorders | | | |
| Sympathetic posterior cervical syndrome | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 2 / 414 (0.48%) | 1 / 451 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 426 (0.47%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infectious mononucleosis | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Localised infection | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsillitis streptococcal | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urethritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 1 / 451 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 1 / 451 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 0 / 414 (0.00%) | 1 / 451 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Group 4: rLP2086(0-,2-Month) +Saline(1-,6 - | Group 5: rLP2086(2-,6-Month)+ Saline(0-, 1-Month) | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 277 (2.53%) | 3 / 144 (2.08%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chills | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 144 (0.69%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Allergic cough | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Concussion | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alcohol poisoning | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone contusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clavicle fracture | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foreign body | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand fracture | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 144 (0.69%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Near drowning | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Poisoning | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skeletal injury | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 1 / 144 (0.69%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Migraine | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aphthous stomatitis | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Constipation | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Sympathetic posterior cervical syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 144 (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 | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute sinusitis | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious mononucleosis | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Localised infection | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsillitis streptococcal | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethritis | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 0 / 144 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Group 1:rLP2086(0-,1-,6-Month)+Saline(2- | Group 2:rLP2086(0-,2-,6-Month) +Saline(1-Month) | Group 3: rLP2086(0- ,6-Month) +Saline(1- |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 113 / 426 (26.53%) | 115 / 414 (27.78%) | 114 / 451 (25.28%) |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 2 / 426 (0.47%) | 10 / 414 (2.42%) | 3 / 451 (0.67%) |
| occurrences (all) | 2 | 11 | 3 |
| Fall | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 2 / 414 (0.48%) | 4 / 451 (0.89%) |
| occurrences (all) | 1 | 2 | 4 |
| Foot fracture | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 0 / 451 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 13 / 426 (3.05%) | 12 / 414 (2.90%) | 11 / 451 (2.44%) |
| occurrences (all) | 13 | 13 | 11 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Injection site pain | | | |
| subjects affected / exposed | 6 / 426 (1.41%) | 4 / 414 (0.97%) | 3 / 451 (0.67%) |
| occurrences (all) | 6 | 4 | 3 |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 426 (1.64%) | 3 / 414 (0.72%) | 4 / 451 (0.89%) |
| occurrences (all) | 7 | 3 | 4 |
| Fatigue | | | |
| subjects affected / exposed | 5 / 426 (1.17%) | 5 / 414 (1.21%) | 1 / 451 (0.22%) |
| occurrences (all) | 5 | 5 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 2 / 451 (0.44%) |
| occurrences (all) | 1 | 0 | 2 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 4 / 426 (0.94%) | 7 / 414 (1.69%) | 2 / 451 (0.44%) |
| occurrences (all) | 5 | 7 | 2 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 43 / 426 (10.09%) | 32 / 414 (7.73%) | 25 / 451 (5.54%) |
| occurrences (all) | 56 | 33 | 31 |
| Pharyngitis | | | |
| subjects affected / exposed | 20 / 426 (4.69%) | 21 / 414 (5.07%) | 20 / 451 (4.43%) |
| occurrences (all) | 20 | 23 | 26 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 9 / 426 (2.11%) | 14 / 414 (3.38%) | 12 / 451 (2.66%) |
| occurrences (all) | 9 | 15 | 13 |
| Gastroenteritis | | | |
| subjects affected / exposed | 10 / 426 (2.35%) | 10 / 414 (2.42%) | 14 / 451 (3.10%) |
| occurrences (all) | 10 | 12 | 14 |
| Tonsillitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 10 / 426 (2.35%) | 11 / 414 (2.66%) | 9 / 451 (2.00%) |
| occurrences (all) | 13 | 12 | 9 |
| Sinusitis | | | |
| subjects affected / exposed | 7 / 426 (1.64%) | 6 / 414 (1.45%) | 7 / 451 (1.55%) |
| occurrences (all) | 7 | 6 | 8 |
| Bronchitis | | | |
| subjects affected / exposed | 4 / 426 (0.94%) | 5 / 414 (1.21%) | 9 / 451 (2.00%) |
| occurrences (all) | 4 | 5 | 9 |
| Urinary tract infection | | | |
| subjects affected / exposed | 5 / 426 (1.17%) | 4 / 414 (0.97%) | 4 / 451 (0.89%) |
| occurrences (all) | 5 | 4 | 4 |
| Rhinitis | | | |
| subjects affected / exposed | 3 / 426 (0.70%) | 4 / 414 (0.97%) | 3 / 451 (0.67%) |
| occurrences (all) | 3 | 4 | 3 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 3 / 414 (0.72%) | 4 / 451 (0.89%) |
| occurrences (all) | 0 | 3 | 5 |
| Acute tonsillitis | | | |
| subjects affected / exposed | 0 / 426 (0.00%) | 4 / 414 (0.97%) | 1 / 451 (0.22%) |
| occurrences (all) | 0 | 4 | 1 |
| Tracheitis | | | |
| subjects affected / exposed | 1 / 426 (0.23%) | 0 / 414 (0.00%) | 5 / 451 (1.11%) |
| occurrences (all) | 1 | 0 | 5 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 2 / 426 (0.47%) | 1 / 414 (0.24%) | 0 / 451 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |

| **Non-serious adverse events** | Group 4: rLP2086(0-,2-Month) +Saline(1-,6 - | Group 5: rLP2086(2-,6-Month)+ Saline(0-, 1-Month) | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 72 / 277 (25.99%) | 43 / 144 (29.86%) | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 5 / 277 (1.81%) | 0 / 144 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Fall | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 277 (0.36%) | 2 / 144 (1.39%) | |
| occurrences (all) | 1 | 2 | |
| Foot fracture | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 2 / 144 (1.39%) | |
| occurrences (all) | 1 | 2 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 6 / 277 (2.17%) | 6 / 144 (4.17%) | |
| occurrences (all) | 7 | 6 | |
| General disorders and administration site conditions | | | |
| Injection site pain | | | |
| subjects affected / exposed | 6 / 277 (2.17%) | 1 / 144 (0.69%) | |
| occurrences (all) | 6 | 1 | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 277 (1.08%) | 3 / 144 (2.08%) | |
| occurrences (all) | 3 | 3 | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 277 (0.72%) | 2 / 144 (1.39%) | |
| occurrences (all) | 2 | 2 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 2 / 144 (1.39%) | |
| occurrences (all) | 0 | 2 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 2 / 144 (1.39%) | |
| occurrences (all) | 0 | 2 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 277 (0.36%) | 2 / 144 (1.39%) | |
| occurrences (all) | 1 | 2 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 21 / 277 (7.58%) | 8 / 144 (5.56%) | |
| occurrences (all) | 27 | 10 | |
| Pharyngitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 14 / 277 (5.05%) | 7 / 144 (4.86%) | |
| occurrences (all) | 15 | 8 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 6 / 277 (2.17%) | 3 / 144 (2.08%) | |
| occurrences (all) | 6 | 3 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 6 / 277 (2.17%) | 3 / 144 (2.08%) | |
| occurrences (all) | 6 | 3 | |
| Tonsillitis | | | |
| subjects affected / exposed | 8 / 277 (2.89%) | 2 / 144 (1.39%) | |
| occurrences (all) | 8 | 2 | |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 277 (0.72%) | 3 / 144 (2.08%) | |
| occurrences (all) | 2 | 5 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 2 / 144 (1.39%) | |
| occurrences (all) | 0 | 2 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 277 (0.72%) | 1 / 144 (0.69%) | |
| occurrences (all) | 2 | 1 | |
| Rhinitis | | | |
| subjects affected / exposed | 3 / 277 (1.08%) | 2 / 144 (1.39%) | |
| occurrences (all) | 4 | 3 | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 2 / 144 (1.39%) | |
| occurrences (all) | 0 | 2 | |
| Acute tonsillitis | | | |
| subjects affected / exposed | 3 / 277 (1.08%) | 0 / 144 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Tracheitis | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 2 / 144 (1.39%) | |
| occurrences (all) | 0 | 2 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 277 (0.00%) | 2 / 144 (1.39%) | |
| occurrences (all) | 0 | 2 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 19 October 2010 | 1- The study design was changed, with vaccinations given at 0, 1, 2, and 6 months; previously vaccinations were designated to be given at 0, 2, 6, and 12 months.<br>2-The primary objective became 2 coprimary objectives.<br>3- Endpoints have been updated to reflect objectives.<br>4- Inclusion/ exclusion have also been updated.<br>5- Safety section became the current sponsor template text.<br>6- Statistics section updated to reflect the changes in objectives and endpoints.<br>7- Biological sample wording had been clarified.<br>8- Protocol text was updated to match the current template.<br>8- Protocol text was updated to match the current template. |
| 15 July 2011 | 1-Visit windows for Visits 2, 3, and 5 at month 1, month 2 and month 5 updated to 28-132 days, 56-160 days and 105-156 days to allow subjects to continue in the study following the delay of study immunizations due to the study pause.<br>2- Duration of subject participation updated to 17 months and duration of study updated to 20 months.<br>3- Clinical experience has been updated.<br>4- Exclusion criteria added to exclude family members of study site and sponsor personnel.<br>5- Unscheduled telephone contact was added. |
| 23 April 2012 | Protocol text was amended to address following changes in safety reporting:<br>1- Revision of section on ongoing safety reviews performed.<br>2- Text had been amended to address changes in safety reporting exposure during pregnancy.<br>3- Medication errors language was updated to align with sponsor SOP.<br>4- Adverse Event Reporting section was updated due to alignment with sponsor SOP guidance and US FDA Final Rule.<br>5- Active reporting period and necessity to report all SAEs post- active reporting period clarifying language was added to align with sponsor SOP and Final Rule. Vaccine study reporting period language was also added.<br>6- Definition of AE was updated to align under sponsor SOP guidance, including addition of medication error.<br>7- Clarification was added regarding persistent or significant disability/incapacity in serious adverse events section to align under Final Rule definition<br>8- Medical device reporting criteria was clarified to align with EU and US legislation.<br>9- Causality Assessment section was updated to align with sponsor SOP guidance.<br>10- Minor administrative corrections were done. |
| 24 April 2012 | 1- Immunogenicity exploratory objective and endpoints were added to be consistent with Phase 2/3 program.<br>2- Safety endpoints were updated to be consistent with Phase 3 program.<br>3- A clarification was added regarding exploratory analysis which was already performed.<br>4- Language was inserted to confirm sera drawn without prior vaccination which was not be assayed or analyzed. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|
| 01 July 2011 | Injections were temporarily paused during investigation of a suspected unexpected serious adverse reaction (SUSAR). A comprehensive review of the case was performed by Pfizer's risk management committee (RMC), which recommended resumption of study immunization. The external data monitoring committee (EDMC) reviewed the case and agreed with the recommendation of the RMC that vaccinations were safe to resume without change to the benefit-risk profile. Subsequently, a decision was made to resume study immunizations. | 01 November 2011 |

Notes:

## Limitations and caveats

None reported