Clinical trial results:
A Phase 2, Randomized, Controlled, Observer-Blinded Study to Describe the Immunogenicity, Safety, and Tolerability of Neisseria Meningitidis Serogroup B (MnB) Bivalent Recombinant Lipoprotein 2086 Vaccine (Bivalent rLP2086) in Healthy Subjects Aged Greater Than or Equal to (>=) 24 Months to Less Than (<) 10 Years

Summary

EudraCT number	2014-000933-21
Trial protocol	FI
Global end of trial date	01 March 2017

Results information

Result version number	v1 (current)
This version publication date	14 September 2017
First version publication date	14 September 2017

Trial information

Trial identification

Sponsor protocol code	B1971017 (6108K2-3012)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02531698
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 March 2017
Global end of trial reached?	Yes
Global end of trial date	01 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the immune response as measured by serum bactericidal assay using human complement (hSBA) performed with 4 primary MnB test strains, 2 expressing an LP2086 subfamily A protein and 2 expressing an LP2086 subfamily B protein, measured 1 month after the third vaccination with bivalent rLP2086, in healthy subjects aged >=24 months to <4 years and >=4 years to <10 years at study entry and to evaluate the safety profile of bivalent rLP2086 compared to a control (hepatitis A virus [HAV] vaccine), as measured by local reactions, systemic events, adverse event (AEs), Serious AEs (SAEs), newly diagnosed chronic medical conditions (NDCMCs), medically attended AEs (MAEs), and immediate AEs in healthy subjects aged >=24 months to <4 years and >=4 years to <10 years at study entry, and in both age strata combined.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 August 2015
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	Finland: 156
Country: Number of subjects enrolled	Poland: 244
Worldwide total number of subjects	400
EEA total number of subjects	400

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)	400
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Four hundred subjects were enrolled at 14 centers, 6 in Finland and 8 in Poland. The study was conducted from 27 August 2015 to 1 March 2017.

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, Subject, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 bivalent rLP2086 (>=24 months to <4 years)

Arm description:

Subjects from >=24 months to <4 years of age, received intramuscular injection of 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	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 0.5 milliliter (mL) bivalent rLP2086 as intramuscular injection at Months 0, 2, and 6.

Arm title	Group 1 bivalent rLP2086 (>=4 years to <10 years)

Arm description:

Subjects from >=4 years to <10 years of age, received intramuscular injection of 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	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 0.5 mL bivalent rLP2086 as intramuscular injection at Months 0, 2, and 6.

Arm title	Group 2 HAV/Saline (>=24 months to <4 years)

Arm description:

Subjects from >=24 months to <4 years of age, received intramuscular injection of saline on 2- month and HAV vaccine on a 0-, 6- month schedule.

Arm type	Active comparator

Investigational medicinal product name	HAV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 0.5 mL HAV vaccine as intramuscular injection at Months 0 and 6.

Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 0.5 mL saline solution as intramuscular injection at Month 2.

Arm title	Group 2 HAV/Saline (>=4 years to <10 years)

Arm description:

Subjects from >=4 years to <10 years of age, received intramuscular injection of saline on 2- month and HAV vaccine on a 0-, 6- month schedule.

Arm type	Active comparator
Investigational medicinal product name	HAV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 0.5 mL HAV vaccine as intramuscular injection at Months 0 and 6.

Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 0.5 mL saline solution as intramuscular injection at Month 2.

Number of subjects in period 1	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)
Started	145	149	55
Completed	137	146	54
Not completed	8	3	1
Consent withdrawn by subject	4	2	1
Adverse event	2	-	-
Lost to follow-up	1	-	-
Protocol deviation	1	1	-

Number of subjects in period 1	Group 2 HAV/Saline (>=4 years to <10 years)
Started	51

Completed	50
Not completed	1
Consent withdrawn by subject	-
Adverse event	1
Lost to follow-up	-
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1 bivalent rLP2086 (>=24 months to <4 years)
Reporting group description:	
Subjects from >=24 months to <4 years of age, received intramuscular injection of rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 1 bivalent rLP2086 (>=4 years to <10 years)
Reporting group description:	
Subjects from >=4 years to <10 years of age, received intramuscular injection of rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 2 HAV/Saline (>=24 months to <4 years)
Reporting group description:	
Subjects from >=24 months to <4 years of age, received intramuscular injection of saline on 2- month and HAV vaccine on a 0-, 6- month schedule.	
Reporting group title	Group 2 HAV/Saline (>=4 years to <10 years)
Reporting group description:	
Subjects from >=4 years to <10 years of age, received intramuscular injection of saline on 2- month and HAV vaccine on a 0-, 6- month schedule.	

Reporting group values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)
Number of subjects	145	149	55
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	145	149	55
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	2.4	6.1	2.5
standard deviation	± 0.5	± 1.72	± 0.5
Gender, Male/Female			
Units: Subjects			
Female	69	77	35
Male	76	72	20

Reporting group values	Group 2 HAV/Saline (>=4 years to <10 years)	Total	
Number of subjects	51	400	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	51	400	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	6		
standard deviation	± 1.64	-	
Gender, Male/Female Units: Subjects			
Female	27	208	
Male	24	192	

Subject analysis sets	
Subject analysis set title	Group 1 bivalent rLP2086 (>=24 months to <10 years)
Subject analysis set type	Full analysis
Subject analysis set description: Subjects from >=24 months to <10 years of age, received intramuscular injection of rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Subject analysis set title	Group 2 HAV/Saline (>=24 months to <10 years)
Subject analysis set type	Full analysis
Subject analysis set description: Subjects from >=24 months to <10 years of age, received intramuscular injection of saline on 2- month and HAV vaccine on a 0-, 6- month schedule.	

Reporting group values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)	
Number of subjects	294	106	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age Continuous Units: Years			
arithmetic mean	4.3	4.2	
standard deviation	± 2.24	± 2.15	
Gender, Male/Female Units: Subjects			
Female	146	62	
Male	148	44	

End points

End points reporting groups

Reporting group title	Group 1 bivalent rLP2086 (>=24 months to <4 years)
Reporting group description:	
Subjects from >=24 months to <4 years of age, received intramuscular injection of rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 1 bivalent rLP2086 (>=4 years to <10 years)
Reporting group description:	
Subjects from >=4 years to <10 years of age, received intramuscular injection of rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 2 HAV/Saline (>=24 months to <4 years)
Reporting group description:	
Subjects from >=24 months to <4 years of age, received intramuscular injection of saline on 2- month and HAV vaccine on a 0-, 6- month schedule.	
Reporting group title	Group 2 HAV/Saline (>=4 years to <10 years)
Reporting group description:	
Subjects from >=4 years to <10 years of age, received intramuscular injection of saline on 2- month and HAV vaccine on a 0-, 6- month schedule.	
Subject analysis set title	Group 1 bivalent rLP2086 (>=24 months to <10 years)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects from >=24 months to <10 years of age, received intramuscular injection of rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Subject analysis set title	Group 2 HAV/Saline (>=24 months to <10 years)
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects from >=24 months to <10 years of age, received intramuscular injection of saline on 2- month and HAV vaccine on a 0-, 6- month schedule.	

Primary: Percentage of Subjects With hSBA Titers >= Lower Limit of Quantitation (LLOQ) for Each of the 4 Primary MnB Test Strains 1 Month After Vaccination 3

End point title	Percentage of Subjects With hSBA Titers >= Lower Limit of Quantitation (LLOQ) for Each of the 4 Primary MnB Test Strains 1 Month After Vaccination 3[1]
End point description:	
Percentage of subjects achieving hSBA titer >= LLOQ were computed along with corresponding 2-sided 95 percent (%) confidence interval (CIs). LLOQ was 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24) and PMB2707 (B44). Evaluable immunogenicity population included all eligible subjects randomized to study, received scheduled investigational products, had pre and post vaccination blood drawn with valid and determinate assay results and had no important protocol deviation. Here, "n" signifies number of subjects evaluable for the specified test strain.	
End point type	Primary
End point timeframe:	
1 month after Vaccination 3	

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	136	138	52	45
Units: Percentage of subjects				
number (confidence interval 95%)				
PMB80 [A22] (n = 68, 67, 25, 20)	83.8 (72.9 to 91.6)	91 (81.5 to 96.6)	4 (0.1 to 20.4)	10 (1.2 to 31.7)
PMB2001 [A56] (n = 68, 71, 24, 19)	100 (94.7 to 100)	100 (94.9 to 100)	4.2 (0.1 to 21.1)	42.1 (20.3 to 66.5)
PMB2948 [B24] (n = 63, 63, 26, 20)	85.7 (74.6 to 93.3)	92.1 (82.4 to 97.4)	7.7 (0.9 to 25.1)	0 (0 to 16.8)
PMB2707 [B44] (n = 65, 69, 26, 24)	80 (68.2 to 88.9)	78.3 (66.7 to 87.3)	0 (0 to 13.2)	0 (0 to 14.2)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Pre-specified Local Reactions Within 7 Days After Vaccination 1

End point title	Percentage of Subjects Reporting Pre-specified Local Reactions Within 7 Days After Vaccination 1[2]

End point description:

Local reactions included pain at injection site, swelling and redness collected by using an electronic diary (e-diary). Pain was graded as: mild (did not interfere with activity), moderate (interfered with activity) and severe (prevented daily activity). Redness and swelling were graded as: mild (0.5-2.0 centimeter [cm]), moderate (2.5 to 7.0 cm) and severe (>7.0 cm). Vaccination 1 safety population included all subjects who received the first dose of investigational products (rLP2086 or HAV vaccine) on Day 1 (Month 0).

End point type	Primary

End point timeframe:

Within 7 Days after Vaccination 1

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)				
Pain at injection site: Any	51.7 (43.3 to 60.1)	79.9 (72.5 to 86)	10.9 (4.1 to 22.2)	35.3 (22.4 to 49.9)
Pain at injection site: Mild	24.1 (17.4 to 31.9)	40.3 (32.3 to 48.6)	9.1 (3 to 20)	27.5 (15.9 to 41.7)
Pain at injection site: Moderate	24.8 (18 to 32.7)	35.6 (27.9 to 43.8)	1.8 (0 to 9.7)	7.8 (2.2 to 18.9)

Pain at injection site: Severe	2.8 (0.8 to 6.9)	4 (1.5 to 8.6)	0 (0 to 6.5)	0 (0 to 7)
Redness: Any	42.1 (33.9 to 50.5)	39.6 (31.7 to 47.9)	10.9 (4.1 to 22.2)	7.8 (2.2 to 18.9)
Redness: Mild	22.1 (15.6 to 29.7)	13.4 (8.4 to 20)	7.3 (2 to 17.6)	3.9 (0.5 to 13.5)
Redness: Moderate	18.6 (12.6 to 25.9)	18.8 (12.9 to 26)	3.6 (0.4 to 12.5)	3.9 (0.5 to 13.5)
Redness: Severe	1.4 (0.2 to 4.9)	7.4 (3.7 to 12.8)	0 (0 to 6.5)	0 (0 to 7)
Swelling: Any	27.6 (20.5 to 35.6)	34.9 (27.3 to 43.1)	5.5 (1.1 to 15.1)	5.9 (1.2 to 16.2)
Swelling: Mild	11 (6.4 to 17.3)	13.4 (8.4 to 20)	3.6 (0.4 to 12.5)	3.9 (0.5 to 13.5)
Swelling: Moderate	16.6 (10.9 to 23.6)	18.1 (12.3 to 25.3)	1.8 (0 to 9.7)	2 (0 to 10.4)
Swelling: Severe	0 (0 to 2.5)	3.4 (1.1 to 7.7)	0 (0 to 6.5)	0 (0 to 7)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)				
Pain at injection site: Any	66 (60.3 to 71.4)	22.6 (15.1 to 31.8)		
Pain at injection site: Mild	32.3 (27 to 38)	17.9 (11.2 to 26.6)		
Pain at injection site: Moderate	30.3 (25.1 to 35.9)	4.7 (1.5 to 10.7)		
Pain at injection site: Severe	3.4 (1.6 to 6.2)	0 (0 to 3.4)		
Redness: Any	40.8 (35.1 to 46.7)	9.4 (4.6 to 16.7)		
Redness: Mild	17.7 (13.5 to 22.5)	5.7 (2.1 to 11.9)		
Redness: Moderate	18.7 (14.4 to 23.6)	3.8 (1 to 9.4)		
Redness: Severe	4.4 (2.4 to 7.4)	0 (0 to 3.4)		
Swelling: Any	31.3 (26 to 36.9)	5.7 (2.1 to 11.9)		
Swelling: Mild	12.2 (8.7 to 16.5)	3.8 (1 to 9.4)		
Swelling: Moderate	17.3 (13.2 to 22.2)	1.9 (0.2 to 6.6)		
Swelling: Severe	1.7 (0.6 to 3.9)	0 (0 to 3.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Pre-specified Local Reactions Within 7

Days After Vaccination 2

End point title	Percentage of Subjects Reporting Pre-specified Local Reactions Within 7 Days After Vaccination 2[3]

End point description:

Local reactions included pain at injection site, swelling and redness collected by using an e-diary. Pain was graded as: mild (did not interfere with activity), moderate (interfered with activity) and severe (prevented daily activity). Redness and swelling were graded as: mild (0.5-2.0 cm), moderate (2.5 to 7.0 cm) and severe (>7.0 cm). Vaccination 2 safety population included all subjects who received the second dose of investigational products (rLP2086 or saline) on Month 2 visit. Here "number of subjects analyzed (N)" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 Days after Vaccination 2

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	143	148	54	49
Units: Percentage of subjects				
number (confidence interval 95%)				
Pain at injection site: Any	63.6 (55.2 to 71.5)	77.7 (70.1 to 84.1)	5.6 (1.2 to 15.4)	20.4 (10.2 to 34.3)
Pain at injection site: Mild	40.6 (32.4 to 49.1)	39.9 (31.9 to 48.2)	5.6 (1.2 to 15.4)	14.3 (5.9 to 27.2)
Pain at injection site: Moderate	20.3 (14 to 27.8)	36.5 (28.7 to 44.8)	0 (0 to 6.6)	6.1 (1.3 to 16.9)
Pain at injection site: Severe	2.8 (0.8 to 7)	1.4 (0.2 to 4.8)	0 (0 to 6.6)	0 (0 to 7.3)
Redness: Any	36.4 (28.5 to 44.8)	37.8 (30 to 46.2)	5.6 (1.2 to 15.4)	6.1 (1.3 to 16.9)
Redness: Mild	15.4 (9.9 to 22.4)	17.6 (11.8 to 24.7)	5.6 (1.2 to 15.4)	6.1 (1.3 to 16.9)
Redness: Moderate	20.3 (14 to 27.8)	16.2 (10.7 to 23.2)	0 (0 to 6.6)	0 (0 to 7.3)
Redness: Severe	0.7 (0 to 3.8)	4.1 (1.5 to 8.6)	0 (0 to 6.6)	0 (0 to 7.3)
Swelling: Any	27.3 (20.2 to 35.3)	29.7 (22.5 to 37.8)	0 (0 to 6.6)	2 (0.1 to 10.9)
Swelling: Mild	11.9 (7.1 to 18.4)	11.5 (6.8 to 17.8)	0 (0 to 6.6)	2 (0.1 to 10.9)
Swelling: Moderate	14.7 (9.3 to 21.6)	17.6 (11.8 to 24.7)	0 (0 to 6.6)	0 (0 to 7.3)
Swelling: Severe	0.7 (0 to 3.8)	0.7 (0 to 3.7)	0 (0 to 6.6)	0 (0 to 7.3)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	291	103		

Units: Percentage of subjects				
number (confidence interval 95%)				
Pain at injection site: Any	70.8 (65.2 to 76)	12.6 (6.9 to 20.6)		
Pain at injection site: Mild	40.2 (34.5 to 46.1)	9.7 (4.8 to 17.1)		
Pain at injection site: Moderate	28.5 (23.4 to 34.1)	2.9 (0.6 to 8.3)		
Pain at injection site: Severe	2.1 (0.8 to 4.4)	0 (0 to 3.5)		
Redness: Any	37.1 (31.5 to 42.9)	5.8 (2.2 to 12.2)		
Redness: Mild	16.5 (12.4 to 21.3)	5.8 (2.2 to 12.2)		
Redness: Moderate	18.2 (14 to 23.1)	0 (0 to 3.5)		
Redness: Severe	2.4 (1 to 4.9)	0 (0 to 3.5)		
Swelling: Any	28.5 (23.4 to 34.1)	1 (0 to 5.3)		
Swelling: Mild	11.7 (8.2 to 15.9)	1 (0 to 5.3)		
Swelling: Moderate	16.2 (12.1 to 20.9)	0 (0 to 3.5)		
Swelling: Severe	0.7 (0.1 to 2.5)	0 (0 to 3.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Pre-specified Local Reactions Within 7 Days After Vaccination 3

End point title	Percentage of Subjects Reporting Pre-specified Local Reactions Within 7 Days After Vaccination 3[4]

End point description:

Local reactions included pain at injection site, swelling and redness collected by using an e-diary. Pain was graded as: mild (did not interfere with activity), moderate (interfered with activity) and severe (prevented daily activity). Redness and swelling were graded as: mild (0.5-2.0 cm), moderate (2.5 to 7.0 cm) and severe (>7.0 cm). Vaccination 3 safety population included all subjects who received the third dose of investigational product (rLP2086 or HAV vaccine) on Month 6 visit. Here "N" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 Days after Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	139	146	54	50
Units: Percentage of subjects				
number (confidence interval 95%)				

Pain at injection site: Any	54.7 (46 to 63.1)	81.5 (74.2 to 87.4)	9.3 (3.1 to 20.3)	22 (11.5 to 36)
Pain at injection site: Mild	26.6 (19.5 to 34.8)	49.3 (41 to 57.7)	7.4 (2.1 to 17.9)	14 (5.8 to 26.7)
Pain at injection site: Moderate	25.2 (18.2 to 33.2)	28.8 (21.6 to 36.8)	1.9 (0 to 9.9)	8 (2.2 to 19.2)
Pain at injection site: Severe	2.9 (0.8 to 7.2)	3.4 (1.1 to 7.8)	0 (0 to 6.6)	0 (0 to 7.1)
Redness: Any	34.5 (26.7 to 43.1)	35.6 (27.9 to 44)	9.3 (3.1 to 20.3)	10 (3.3 to 21.8)
Redness: Mild	15.8 (10.2 to 23)	17.1 (11.4 to 24.2)	7.4 (2.1 to 17.9)	10 (3.3 to 21.8)
Redness: Moderate	17.3 (11.4 to 24.6)	12.3 (7.5 to 18.8)	1.9 (0 to 9.9)	0 (0 to 7.1)
Redness: Severe	1.4 (0.2 to 5.1)	6.2 (2.9 to 11.4)	0 (0 to 6.6)	0 (0 to 7.1)
Swelling: Any	24.5 (17.6 to 32.5)	30.1 (22.8 to 38.3)	3.7 (0.5 to 12.7)	6 (1.3 to 16.5)
Swelling: Mild	9.4 (5.1 to 15.5)	14.4 (9.1 to 21.1)	1.9 (0 to 9.9)	6 (1.3 to 16.5)
Swelling: Moderate	15.1 (9.6 to 22.2)	14.4 (9.1 to 21.1)	1.9 (0 to 9.9)	0 (0 to 7.1)
Swelling: Severe	0 (0 to 2.6)	1.4 (0.2 to 4.9)	0 (0 to 6.6)	0 (0 to 7.1)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	285	104		
Units: Percentage of subjects				
number (confidence interval 95%)				
Pain at injection site: Any	68.4 (62.7 to 73.8)	15.4 (9.1 to 23.8)		
Pain at injection site: Mild	38.2 (32.6 to 44.2)	10.6 (5.4 to 18.1)		
Pain at injection site: Moderate	27 (21.9 to 32.6)	4.8 (1.6 to 10.9)		
Pain at injection site: Severe	3.2 (1.5 to 5.9)	0 (0 to 3.5)		
Redness: Any	35.1 (29.6 to 40.9)	9.6 (4.7 to 17)		
Redness: Mild	16.5 (12.4 to 21.3)	8.7 (4 to 15.8)		
Redness: Moderate	14.7 (10.8 to 19.4)	1 (0 to 5.2)		
Redness: Severe	3.9 (1.9 to 6.8)	0 (0 to 3.5)		
Swelling: Any	27.4 (22.3 to 32.9)	4.8 (1.6 to 10.9)		
Swelling: Mild	11.9 (8.4 to 16.3)	3.8 (1.1 to 9.6)		
Swelling: Moderate	14.7 (10.8 to 19.4)	1 (0 to 5.2)		
Swelling: Severe	0.7 (0.1 to 2.5)	0 (0 to 3.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 1

End point title	Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 1[5]

End point description:

Systemic reactions included fever, vomiting, diarrhea, headache, fatigue, muscle and joint pain (other than at the injection site) and recorded by using an e-diary. Fever was graded as 38.0 to 38.4 degree Celsius (C), 38.5 to 38.9 degree C, 39.0 to 39.4 degree C, >39.5 to 40.0 degree C and >40.0 degree C. Vomiting was graded as mild (1-2 times in 24 hours), moderate (>2 times in 24 hours) and severe (required intravenous hydration). Diarrhea was graded as mild (2-3 loose stools in 24 hours), moderate (4-5 loose stools in 24 hours) and severe (>=6 loose stools in 24 hours). Headache, fatigue, muscle pain and joint pain were graded as mild (no interference with activity), moderate (some interference with activity) and severe (prevented daily activity). Vaccination 1 safety population included all subjects who received the first dose of investigational products (rLP2086 or HAV vaccine) on Day 1 (Month 0).

End point type	Primary

End point timeframe:

Within 7 Days after Vaccination 1

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees Celsius (C)	21.4 (15 to 29)	11.4 (6.8 to 17.6)	10.9 (4.1 to 22.2)	2 (0 to 10.4)
Fever 38 to <38.5 degrees C	6.9 (3.4 to 12.3)	5.4 (2.3 to 10.3)	7.3 (2 to 17.6)	2 (0 to 10.4)
Fever 38.5 to <39 degrees C	7.6 (3.8 to 13.2)	4.7 (1.9 to 9.4)	3.6 (0.4 to 12.5)	0 (0 to 7)
Fever 39 to <39.5 degrees C	3.4 (1.1 to 7.9)	1.3 (0.2 to 4.8)	0 (0 to 6.5)	0 (0 to 7)
Fever 39.5 to 40 degrees C	2.8 (0.8 to 6.9)	0 (0 to 2.4)	0 (0 to 6.5)	0 (0 to 7)
Fever >40 degrees C	0.7 (0 to 3.8)	0 (0 to 2.4)	0 (0 to 6.5)	0 (0 to 7)
Vomiting: Any	9 (4.9 to 14.8)	2 (0.4 to 5.8)	5.5 (1.1 to 15.1)	2 (0 to 10.4)
Vomiting: Mild	7.6 (3.8 to 13.2)	1.3 (0.2 to 4.8)	5.5 (1.1 to 15.1)	0 (0 to 7)
Vomiting: Moderate	1.4 (0.2 to 4.9)	0.7 (0 to 3.7)	0 (0 to 6.5)	2 (0 to 10.4)
Vomiting: Severe	0 (0 to 2.5)	0 (0 to 2.4)	0 (0 to 6.5)	0 (0 to 7)
Diarrhea: Any	11.7 (7 to 18.1)	6.7 (3.3 to 12)	7.3 (2 to 17.6)	5.9 (1.2 to 16.2)
Diarrhea: Mild	9 (4.9 to 14.8)	5.4 (2.3 to 10.3)	7.3 (2 to 17.6)	5.9 (1.2 to 16.2)
Diarrhea: Moderate	2.1 (0.4 to 5.9)	1.3 (0.2 to 4.8)	0 (0 to 6.5)	0 (0 to 7)
Diarrhea: Severe	0.7 (0 to 3.8)	0 (0 to 2.4)	0 (0 to 6.5)	0 (0 to 7)
Headache: Any	8.3 (4.3 to 14)	28.2 (21.1 to 36.1)	3.6 (0.4 to 12.5)	19.6 (9.8 to 33.1)

Headache: Mild	3.4 (1.1 to 7.9)	15.4 (10 to 22.3)	1.8 (0 to 9.7)	11.8 (4.4 to 23.9)
Headache: Moderate	4.8 (2 to 9.7)	12.1 (7.3 to 18.4)	1.8 (0 to 9.7)	5.9 (1.2 to 16.2)
Headache: Severe	0 (0 to 2.5)	0.7 (0 to 3.7)	0 (0 to 6.5)	2 (0 to 10.4)
Fatigue: Any	55.9 (47.4 to 64.1)	42.3 (34.2 to 50.6)	20 (10.4 to 33)	31.4 (19.1 to 45.9)
Fatigue: Mild	24.1 (17.4 to 31.9)	19.5 (13.4 to 26.7)	9.1 (3 to 20)	19.6 (9.8 to 33.1)
Fatigue: Moderate	27.6 (20.5 to 35.6)	19.5 (13.4 to 26.7)	5.5 (1.1 to 15.1)	11.8 (4.4 to 23.9)
Fatigue: Severe	4.1 (1.5 to 8.8)	3.4 (1.1 to 7.7)	5.5 (1.1 to 15.1)	0 (0 to 7)
Muscle pain : Any	13.1 (8.1 to 19.7)	19.5 (13.4 to 26.7)	1.8 (0 to 9.7)	9.8 (3.3 to 21.4)
Muscle pain : Mild	6.2 (2.9 to 11.5)	11.4 (6.8 to 17.6)	1.8 (0 to 9.7)	7.8 (2.2 to 18.9)
Muscle pain : Moderate	4.8 (2 to 9.7)	7.4 (3.7 to 12.8)	0 (0 to 6.5)	2 (0 to 10.4)
Muscle pain : Severe	2.1 (0.4 to 5.9)	0.7 (0 to 3.7)	0 (0 to 6.5)	0 (0 to 7)
Joint pain: Any	6.2 (2.9 to 11.5)	6.7 (3.3 to 12)	1.8 (0 to 9.7)	7.8 (2.2 to 18.9)
Joint pain: Mild	3.4 (1.1 to 7.9)	3.4 (1.1 to 7.7)	1.8 (0 to 9.7)	7.8 (2.2 to 18.9)
Joint pain: Moderate	2.8 (0.8 to 6.9)	3.4 (1.1 to 7.7)	0 (0 to 6.5)	0 (0 to 7)
Joint pain: Severe	0 (0 to 2.5)	0 (0 to 2.4)	0 (0 to 6.5)	0 (0 to 7)
Antipyretic Medication Use	42.8 (34.6 to 51.2)	31.5 (24.2 to 39.7)	14.5 (6.5 to 26.7)	17.6 (8.4 to 30.9)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees Celsius (C)	16.3 (12.3 to 21.1)	6.6 (2.7 to 13.1)		
Fever 38 to <38.5 degrees C	6.1 (3.7 to 9.5)	4.7 (1.5 to 10.7)		
Fever 38.5 to <39 degrees C	6.1 (3.7 to 9.5)	1.9 (0.2 to 6.6)		
Fever 39 to <39.5 degrees C	2.4 (1 to 4.8)	0 (0 to 3.4)		
Fever 39.5 to 40 degrees C	1.4 (0.4 to 3.4)	0 (0 to 3.4)		
Fever >40 degrees C	0.3 (0 to 1.9)	0 (0 to 3.4)		
Vomiting: Any	5.4 (3.1 to 8.7)	3.8 (1 to 9.4)		
Vomiting: Mild	4.4 (2.4 to 7.4)	2.8 (0.6 to 8)		
Vomiting: Moderate	1 (0.2 to 3)	0.9 (0 to 5.1)		
Vomiting: Severe	0 (0 to 1.2)	0 (0 to 3.4)		
Diarrhea: Any	9.2 (6.1 to 13.1)	6.6 (2.7 to 13.1)		
Diarrhea: Mild	7.1 (4.5 to 10.7)	6.6 (2.7 to 13.1)		
Diarrhea: Moderate	1.7 (0.6 to 3.9)	0 (0 to 3.4)		
Diarrhea: Severe	0.3 (0 to 1.9)	0 (0 to 3.4)		

Headache: Any	18.4 (14.1 to 23.3)	11.3 (6 to 18.9)		
Headache: Mild	9.5 (6.4 to 13.5)	6.6 (2.7 to 13.1)		
Headache: Moderate	8.5 (5.6 to 12.3)	3.8 (1 to 9.4)		
Headache: Severe	0.3 (0 to 1.9)	0.9 (0 to 5.1)		
Fatigue: Any	49 (43.1 to 54.8)	25.5 (17.5 to 34.9)		
Fatigue: Mild	21.8 (17.2 to 26.9)	14.2 (8.1 to 22.3)		
Fatigue: Moderate	23.5 (18.7 to 28.7)	8.5 (4 to 15.5)		
Fatigue: Severe	3.7 (1.9 to 6.6)	2.8 (0.6 to 8)		
Muscle pain : Any	16.3 (12.3 to 21.1)	5.7 (2.1 to 11.9)		
Muscle pain : Mild	8.8 (5.9 to 12.7)	4.7 (1.5 to 10.7)		
Muscle pain : Moderate	6.1 (3.7 to 9.5)	0.9 (0 to 5.1)		
Muscle pain : Severe	1.4 (0.4 to 3.4)	0 (0 to 3.4)		
Joint pain: Any	6.5 (3.9 to 9.9)	4.7 (1.5 to 10.7)		
Joint pain: Mild	3.4 (1.6 to 6.2)	4.7 (1.5 to 10.7)		
Joint pain: Moderate	3.1 (1.4 to 5.7)	0 (0 to 3.4)		
Joint pain: Severe	0 (0 to 1.2)	0 (0 to 3.4)		
Antipyretic Medication Use	37.1 (31.5 to 42.9)	16 (9.6 to 24.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 2

End point title	Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 2[6]

End point description:

Systemic reactions included fever, vomiting, diarrhea, headache, fatigue, muscle and joint pain (other than at the injection site) and recorded by using an e-diary. Fever was graded as 38.0 to 38.4 degree C, 38.5 to 38.9 degree C, 39.0 to 39.4 degree C, >39.5 to 40.0 degree C and >40.0 degree C. Vomiting was graded as mild (1-2 times in 24 hours), moderate (>2 times in 24 hours) and severe (required intravenous hydration). Diarrhea was graded as mild (2-3 loose stools in 24 hours), moderate (4-5 loose stools in 24 hours) and severe (>=6 loose stools in 24 hours). Headache, fatigue, muscle pain and joint pain were graded as mild (no interference with activity), moderate (some interference with activity) and severe (prevented daily activity). Vaccination 2 safety population included all subjects who received the second dose of investigational products (rLP2086 or saline) on Month 2 visit. Here "N" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 Days after Vaccination 2

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	143	148	54	49
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C	15.4 (9.9 to 22.4)	8.8 (4.8 to 14.6)	3.7 (0.5 to 12.7)	2 (0.1 to 10.9)
Fever 38 to <38.5 degrees C	7.7 (3.9 to 13.3)	5.4 (2.4 to 10.4)	3.7 (0.5 to 12.7)	0 (0 to 7.3)
Fever 38.5 to <39 degrees C	2.8 (0.8 to 7)	0.7 (0 to 3.7)	0 (0 to 6.6)	2 (0.1 to 10.9)
Fever 39 to <39.5 degrees C	1.4 (0.2 to 5)	2 (0.4 to 5.8)	0 (0 to 6.6)	0 (0 to 7.3)
Fever 39.5 to 40 degrees C	2.8 (0.8 to 7)	0.7 (0 to 3.7)	0 (0 to 6.6)	0 (0 to 7.3)
Fever >40 degrees C	0.7 (0 to 3.8)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.3)
Vomiting: Any	5.6 (2.4 to 10.7)	4.7 (1.9 to 9.5)	3.7 (0.5 to 12.7)	6.1 (1.3 to 16.9)
Vomiting: Mild	4.2 (1.6 to 8.9)	2.7 (0.7 to 6.8)	1.9 (0 to 9.9)	6.1 (1.3 to 16.9)
Vomiting: Moderate	1.4 (0.2 to 5)	2 (0.4 to 5.8)	1.9 (0 to 9.9)	0 (0 to 7.3)
Vomiting: Severe	0 (0 to 2.5)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.3)
Diarrhea: Any	9.8 (5.5 to 15.9)	6.8 (3.3 to 12.1)	5.6 (1.2 to 15.4)	6.1 (1.3 to 16.9)
Diarrhea: Mild	8.4 (4.4 to 14.2)	6.8 (3.3 to 12.1)	5.6 (1.2 to 15.4)	6.1 (1.3 to 16.9)
Diarrhea: Moderate	0.7 (0 to 3.8)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.3)
Diarrhea: Severe	0.7 (0 to 3.8)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.3)
Headache: Any	11.2 (6.5 to 17.5)	25 (18.3 to 32.8)	1.9 (0 to 9.9)	22.4 (11.8 to 36.6)
Headache: Mild	7.7 (3.9 to 13.3)	12.8 (7.9 to 19.3)	1.9 (0 to 9.9)	18.4 (8.8 to 32)
Headache: Moderate	3.5 (1.1 to 8)	11.5 (6.8 to 17.8)	0 (0 to 6.6)	2 (0.1 to 10.9)
Headache: Severe	0 (0 to 2.5)	0.7 (0 to 3.7)	0 (0 to 6.6)	2 (0.1 to 10.9)
Fatigue: Any	45.5 (37.1 to 54)	41.2 (33.2 to 49.6)	13 (5.4 to 24.9)	14.3 (5.9 to 27.2)
Fatigue: Mild	22.4 (15.8 to 30.1)	19.6 (13.5 to 26.9)	7.4 (2.1 to 17.9)	8.2 (2.3 to 19.6)
Fatigue: Moderate	19.6 (13.4 to 27)	19.6 (13.5 to 26.9)	5.6 (1.2 to 15.4)	6.1 (1.3 to 16.9)
Fatigue: Severe	3.5 (1.1 to 8)	2 (0.4 to 5.8)	0 (0 to 6.6)	0 (0 to 7.3)
Muscle pain: Any	11.2 (6.5 to 17.5)	14.9 (9.6 to 21.6)	0 (0 to 6.6)	4.1 (0.5 to 14)
Muscle pain: Mild	3.5 (1.1 to 8)	10.1 (5.8 to 16.2)	0 (0 to 6.6)	4.1 (0.5 to 14)
Muscle pain: Moderate	7 (3.4 to 12.5)	4.7 (1.9 to 9.5)	0 (0 to 6.6)	0 (0 to 7.3)
Muscle pain: Severe	0.7 (0 to 3.8)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.3)
Joint pain: Any	5.6 (2.4 to 10.7)	8.8 (4.8 to 14.6)	0 (0 to 6.6)	8.2 (2.3 to 19.6)
Joint pain: Mild	1.4 (0.2 to 5)	4.1 (1.5 to 8.6)	0 (0 to 6.6)	8.2 (2.3 to 19.6)
Joint pain: Moderate	2.1 (0.4 to 6)	4.7 (1.9 to 9.5)	0 (0 to 6.6)	0 (0 to 7.3)
Joint pain: Severe	2.1 (0.4 to 6)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.3)
Antipyretic Medication Use	32.9 (25.2 to 41.2)	27 (20.1 to 34.9)	1.9 (0 to 9.9)	10.2 (3.4 to 22.2)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	291	103		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C	12 (8.5 to 16.3)	2.9 (0.6 to 8.3)		
Fever 38 to <38.5 degrees C	6.5 (4 to 10)	1.9 (0.2 to 6.8)		
Fever 38.5 to <39 degrees C	1.7 (0.6 to 4)	1 (0 to 5.3)		
Fever 39 to <39.5 degrees C	1.7 (0.6 to 4)	0 (0 to 3.5)		
Fever 39.5 to 40 degrees C	1.7 (0.6 to 4)	0 (0 to 3.5)		
Fever >40 degrees C	0.3 (0 to 1.9)	0 (0 to 3.5)		
Vomiting: Any	5.2 (2.9 to 8.4)	4.9 (1.6 to 11)		
Vomiting: Mild	3.4 (1.7 to 6.2)	3.9 (1.1 to 9.6)		
Vomiting: Moderate	1.7 (0.6 to 4)	1 (0 to 5.3)		
Vomiting: Severe	0 (0 to 1.3)	0 (0 to 3.5)		
Diarrhea: Any	8.2 (5.4 to 12)	5.8 (2.2 to 12.2)		
Diarrhea: Mild	7.6 (4.8 to 11.2)	5.8 (2.2 to 12.2)		
Diarrhea: Moderate	0.3 (0 to 1.9)	0 (0 to 3.5)		
Diarrhea: Severe	0.3 (0 to 1.9)	0 (0 to 3.5)		
Headache: Any	18.2 (14 to 23.1)	11.7 (6.2 to 19.5)		
Headache: Mild	10.3 (7.1 to 14.4)	9.7 (4.8 to 17.1)		
Headache: Moderate	7.6 (4.8 to 11.2)	1 (0 to 5.3)		
Headache: Severe	0.3 (0 to 1.9)	1 (0 to 5.3)		
Fatigue: Any	43.3 (37.5 to 49.2)	13.6 (7.6 to 21.8)		
Fatigue: Mild	21 (16.4 to 26.1)	7.8 (3.4 to 14.7)		
Fatigue: Moderate	19.6 (15.2 to 24.6)	5.8 (2.2 to 12.2)		
Fatigue: Severe	2.7 (1.2 to 5.3)	0 (0 to 3.5)		
Muscle pain: Any	13.1 (9.4 to 17.5)	1.9 (0.2 to 6.8)		
Muscle pain: Mild	6.9 (4.2 to 10.4)	1.9 (0.2 to 6.8)		
Muscle pain: Moderate	5.8 (3.4 to 9.2)	0 (0 to 3.5)		
Muscle pain: Severe	0.3 (0 to 1.9)	0 (0 to 3.5)		
Joint pain: Any	7.2 (4.5 to 10.8)	3.9 (1.1 to 9.6)		
Joint pain: Mild	2.7 (1.2 to 5.3)	3.9 (1.1 to 9.6)		
Joint pain: Moderate	3.4 (1.7 to 6.2)	0 (0 to 3.5)		
Joint pain: Severe	1 (0.2 to 3)	0 (0 to 3.5)		
Antipyretic Medication Use	29.9 (24.7 to 35.5)	5.8 (2.2 to 12.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 3

End point title	Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 3[7]

End point description:

Systemic reactions included fever, vomiting, diarrhea, headache, fatigue, muscle and joint pain (other than at the injection site) and recorded by using an e-diary. Fever was graded as 38.0 to 38.4 degree C, 38.5 to 38.9 degree C, 39.0 to 39.4 degree C, >39.5 to 40.0 degree C and >40.0 degree C. Vomiting was graded as mild (1-2 times in 24 hours), moderate (>2 times in 24 hours) and severe (required intravenous hydration). Diarrhea was graded as mild (2-3 loose stools in 24 hours), moderate (4-5 loose stools in 24 hours) and severe (>=6 loose stools in 24 hours). Headache, fatigue, muscle pain and joint pain were graded as mild (no interference with activity), moderate (some interference with activity) and severe (prevented daily activity). Vaccination 3 safety population included all subjects who received the third dose of investigational product (rLP2086 or HAV vaccine) on Month 6 visit. Here "N" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 Days after Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	139	146	54	50
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C	11.5 (6.7 to 18)	2.1 (0.4 to 5.9)	9.3 (3.1 to 20.3)	2 (0.1 to 10.6)
Fever 38 to <38.5 degrees C	5 (2 to 10.1)	2.1 (0.4 to 5.9)	3.7 (0.5 to 12.7)	2 (0.1 to 10.6)
Fever 38.5 to <39 degrees C	3.6 (1.2 to 8.2)	0 (0 to 2.5)	3.7 (0.5 to 12.7)	0 (0 to 7.1)
Fever 39 to <39.5 degrees C	2.2 (0.4 to 6.2)	0 (0 to 2.5)	1.9 (0 to 9.9)	0 (0 to 7.1)
Fever 39.5 to 40 degrees C	0.7 (0 to 3.9)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.1)
Fever >40 degrees C	0 (0 to 2.6)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.1)
Vomiting: Any	4.3 (1.6 to 9.2)	2.1 (0.4 to 5.9)	5.6 (1.2 to 15.4)	2 (0.1 to 10.6)
Vomiting: Mild	2.9 (0.8 to 7.2)	1.4 (0.2 to 4.9)	3.7 (0.5 to 12.7)	0 (0 to 7.1)
Vomiting: Moderate	1.4 (0.2 to 5.1)	0.7 (0 to 3.8)	1.9 (0 to 9.9)	2 (0.1 to 10.6)
Vomiting: Severe	0 (0 to 2.6)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.1)

Diarrhea: Any	6.5 (3 to 11.9)	6.2 (2.9 to 11.4)	3.7 (0.5 to 12.7)	2 (0.1 to 10.6)
Diarrhea: Mild	5.8 (2.5 to 11)	4.8 (1.9 to 9.6)	3.7 (0.5 to 12.7)	2 (0.1 to 10.6)
Diarrhea: Moderate	0.7 (0 to 3.9)	0.7 (0 to 3.8)	0 (0 to 6.6)	0 (0 to 7.1)
Diarrhea: Severe	0 (0 to 2.6)	0.7 (0 to 3.8)	0 (0 to 6.6)	0 (0 to 7.1)
Headache: Any	7.2 (3.5 to 12.8)	20.5 (14.3 to 28)	1.9 (0 to 9.9)	12 (4.5 to 24.3)
Headache: Mild	5.8 (2.5 to 11)	15.1 (9.7 to 21.9)	0 (0 to 6.6)	8 (2.2 to 19.2)
Headache: Moderate	1.4 (0.2 to 5.1)	5.5 (2.4 to 10.5)	1.9 (0 to 9.9)	4 (0.5 to 13.7)
Headache: Severe	0 (0 to 2.6)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.1)
Fatigue: Any	36 (28 to 44.5)	30.8 (23.5 to 39)	18.5 (9.3 to 31.4)	16 (7.2 to 29.1)
Fatigue: Mild	16.5 (10.8 to 23.8)	19.9 (13.7 to 27.3)	11.1 (4.2 to 22.6)	12 (4.5 to 24.3)
Fatigue: Moderate	18 (12 to 25.4)	10.3 (5.9 to 16.4)	7.4 (2.1 to 17.9)	4 (0.5 to 13.7)
Fatigue: Severe	1.4 (0.2 to 5.1)	0.7 (0 to 3.8)	0 (0 to 6.6)	0 (0 to 7.1)
Muscle pain: Any	12.9 (7.9 to 19.7)	11.6 (6.9 to 18)	5.6 (1.2 to 15.4)	4 (0.5 to 13.7)
Muscle pain: Mild	7.2 (3.5 to 12.8)	5.5 (2.4 to 10.5)	1.9 (0 to 9.9)	4 (0.5 to 13.7)
Muscle pain: Moderate	5 (2 to 10.1)	6.2 (2.9 to 11.4)	3.7 (0.5 to 12.7)	0 (0 to 7.1)
Muscle pain: Severe	0.7 (0 to 3.9)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.1)
Joint pain: Any	7.2 (3.5 to 12.8)	7.5 (3.8 to 13.1)	0 (0 to 6.6)	6 (1.3 to 16.5)
Joint pain: Mild	2.9 (0.8 to 7.2)	4.8 (1.9 to 9.6)	0 (0 to 6.6)	6 (1.3 to 16.5)
Joint pain: Moderate	3.6 (1.2 to 8.2)	2.7 (0.8 to 6.9)	0 (0 to 6.6)	0 (0 to 7.1)
Joint pain: Severe	0.7 (0 to 3.9)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.1)
Antipyretic Medication Use	25.2 (18.2 to 33.2)	27.4 (20.3 to 35.4)	13 (5.4 to 24.9)	8 (2.2 to 19.2)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	285	104		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C	6.7 (4.1 to 10.2)	5.8 (2.1 to 12.1)		
Fever 38 to <38.5 degrees C	3.5 (1.7 to 6.4)	2.9 (0.6 to 8.2)		
Fever 38.5 to <39 degrees C	1.8 (0.6 to 4)	1.9 (0.2 to 6.8)		
Fever 39 to <39.5 degrees C	1.1 (0.2 to 3)	1 (0 to 5.2)		
Fever 39.5 to 40 degrees C	0.4 (0 to 1.9)	0 (0 to 3.5)		
Fever >40 degrees C	0 (0 to 1.3)	0 (0 to 3.5)		
Vomiting: Any	3.2 (1.5 to 5.9)	3.8 (1.1 to 9.6)		
Vomiting: Mild	2.1 (0.8 to 4.5)	1.9 (0.2 to 6.8)		
Vomiting: Moderate	1.1 (0.2 to 3)	1.9 (0.2 to 6.8)		
Vomiting: Severe	0 (0 to 1.3)	0 (0 to 3.5)		

Diarrhea: Any	6.3 (3.8 to 9.8)	2.9 (0.6 to 8.2)		
Diarrhea: Mild	5.3 (3 to 8.5)	2.9 (0.6 to 8.2)		
Diarrhea: Moderate	0.7 (0.1 to 2.5)	0 (0 to 3.5)		
Diarrhea: Severe	0.4 (0 to 1.9)	0 (0 to 3.5)		
Headache: Any	14 (10.2 to 18.6)	6.7 (2.7 to 13.4)		
Headache: Mild	10.5 (7.2 to 14.7)	3.8 (1.1 to 9.6)		
Headache: Moderate	3.5 (1.7 to 6.4)	2.9 (0.6 to 8.2)		
Headache: Severe	0 (0 to 1.3)	0 (0 to 3.5)		
Fatigue: Any	33.3 (27.9 to 39.1)	17.3 (10.6 to 26)		
Fatigue: Mild	18.2 (13.9 to 23.2)	11.5 (6.1 to 19.3)		
Fatigue: Moderate	14 (10.2 to 18.6)	5.8 (2.1 to 12.1)		
Fatigue: Severe	1.1 (0.2 to 3)	0 (0 to 3.5)		
Muscle pain: Any	12.3 (8.7 to 16.7)	4.8 (1.6 to 10.9)		
Muscle pain: Mild	6.3 (3.8 to 9.8)	2.9 (0.6 to 8.2)		
Muscle pain: Moderate	5.6 (3.2 to 9)	1.9 (0.2 to 6.8)		
Muscle pain: Severe	0.4 (0 to 1.9)	0 (0 to 3.5)		
Joint pain: Any	7.4 (4.6 to 11)	2.9 (0.6 to 8.2)		
Joint pain: Mild	3.9 (1.9 to 6.8)	2.9 (0.6 to 8.2)		
Joint pain: Moderate	3.2 (1.5 to 5.9)	0 (0 to 3.5)		
Joint pain: Severe	0.4 (0 to 1.9)	0 (0 to 3.5)		
Antipyretic Medication Use	26.3 (21.3 to 31.8)	10.6 (5.4 to 18.1)		

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 Vaccination 1

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Vaccination 1[8]

End point description:

SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication. An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. Vaccination 1 safety population included all subjects who received the first dose of investigational products (rLP2086 or HAV vaccine) on Day 1 (Month 0).

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 1

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	0.7 (0 to 3.8)	0 (0 to 2.4)	1.8 (0 to 9.7)	0 (0 to 7)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	0.3 (0 to 1.9)	0.9 (0 to 5.1)		

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 Vaccination 2

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Vaccination 2[9]

End point description:

SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication. An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. Vaccination 2 safety population included all subjects who received the second dose of investigational products (rLP2086 or saline) on Month 2 visit. Here "N" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 2

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	143	148	54	50
Units: Percentage of subjects				

number (confidence interval 95%)	1.4 (0.2 to 5)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.1)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	291	104		
Units: Percentage of subjects				
number (confidence interval 95%)	0.7 (0.1 to 2.5)	0 (0 to 3.5)		

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 Vaccination 3

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Vaccination 3[10]

End point description:

SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication. An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. Vaccination 3 safety population included all subjects who received the third dose of investigational product (rLP2086 or HAV vaccine) on Month 6 visit. Here "N" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	140	147	54	50
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 2.6)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.1)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10	Group 2 HAV/Saline (>=24 months to <10 years)		

	years)			
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	287	104		
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 1.3)	0 (0 to 3.5)		

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 Any Vaccination

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Any Vaccination[11]

End point description:

SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication. An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. Safety population included all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

Within 30 Days after any 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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	2.1 (0.4 to 5.9)	0 (0 to 2.4)	1.8 (0 to 9.7)	0 (0 to 7)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	1 (0.2 to 3)	0.9 (0 to 5.1)		

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[12]

End point description:

SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication. An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. Safety population included all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

From the Vaccination 1 up to 1 month after Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	2.1 (0.4 to 5.9)	0.7 (0 to 3.7)	1.8 (0 to 9.7)	0 (0 to 7)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	1.4 (0.4 to 3.4)	0.9 (0 to 5.1)		

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[13]

End point description:

SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication. An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. Safety population included all subjects who had at least 1 dose of investigational product (rLP2086 or HAV/saline) and had safety data available from after post third-vaccination blood draw to 6 months after last study vaccination. Here "N" signifies number of subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

From 1 month after Vaccination 3 up to 6 months after Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	137	147	54	50
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 2.7)	0.7 (0 to 3.7)	0 (0 to 6.6)	0 (0 to 7.1)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	284	104		
Units: Percentage of subjects				
number (confidence interval 95%)	0.4 (0 to 1.9)	0 (0 to 3.5)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event

	(SAE) Throughout the Study[14]

End point description:

SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication. An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. Safety population included all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

From Vaccination 1 up to 6 months after Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	2.1 (0.4 to 5.9)	1.3 (0.2 to 4.8)	1.8 (0 to 9.7)	0 (0 to 7)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	1.7 (0.6 to 3.9)	0.9 (0 to 5.1)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With at Least 1 Medically Attended Adverse Event (AE) Within 30 Days After Vaccination 1[15]

End point description:

A medically attended AE was defined as a non-serious AE that resulted in an evaluation at a medical facility. Vaccination 1 safety population included all subjects who received the first dose of investigational products (rLP2086 or HAV vaccine) on Day 1 (Month 0).

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 1

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	18.6 (12.6 to 25.9)	8.1 (4.2 to 13.6)	16.4 (7.8 to 28.8)	9.8 (3.3 to 21.4)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	13.3 (9.6 to 17.7)	13.2 (7.4 to 21.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended Adverse Event (AE) Within 30 Days After Vaccination 2

End point title	Percentage of Subjects With at Least 1 Medically Attended Adverse Event (AE) Within 30 Days After Vaccination 2[16]

End point description:

A medically attended AE was defined as a non-serious AE that resulted in an evaluation at a medical facility. Vaccination 2 safety population included all subjects who received the second dose of investigational products (rLP2086 or saline) on Month 2 visit. Here "N" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 2

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	143	148	54	50
Units: Percentage of subjects				
number (confidence interval 95%)	10.5 (6 to 16.7)	13.5 (8.5 to 20.1)	14.8 (6.6 to 27.1)	8 (2.2 to 19.2)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	291	104		
Units: Percentage of subjects				
number (confidence interval 95%)	12 (8.5 to 16.3)	11.5 (6.1 to 19.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended Adverse Event (AE) Within 30 Days After Vaccination 3

End point title	Percentage of Subjects With at Least 1 Medically Attended Adverse Event (AE) Within 30 Days After Vaccination 3[17]

End point description:

A medically attended AE was defined as a non-serious AE that resulted in an evaluation at a medical facility. Vaccination 3 safety population included all subjects who received the third dose of investigational product (rLP2086 or HAV vaccine) on Month 6 visit. Here "N" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	140	147	54	50
Units: Percentage of subjects				
number (confidence interval 95%)	6.4 (3 to 11.9)	4.8 (1.9 to 9.6)	5.6 (1.2 to 15.4)	4 (0.5 to 13.7)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	287	104		
Units: Percentage of subjects				
number (confidence interval 95%)	5.6 (3.2 to 8.9)	4.8 (1.6 to 10.9)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With at Least 1 Medically Attended Adverse Event (AE) Within 30 Days After any Vaccination[18]

End point description:

A medically attended AE was defined as a non-serious AE that resulted in an evaluation at a medical facility. Safety population included all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

Within 30 Days after any 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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	29 (21.7 to 37.1)	22.8 (16.3 to 30.4)	30.9 (19.1 to 44.8)	21.6 (11.3 to 35.3)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		

Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	25.9 (20.9 to 31.3)	26.4 (18.3 to 35.9)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With at Least 1 Medically Attended Adverse Event (AE) During the Vaccination Phase[19]

End point description:

A medically attended AE was defined as a non-serious AE that resulted in an evaluation at a medical facility. Safety population included all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

From the Vaccination 1 up to 1 month after the Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	45.5 (37.2 to 54)	40.9 (33 to 49.3)	41.8 (28.7 to 55.9)	51 (36.6 to 65.2)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	43.2 (37.5 to 49.1)	46.2 (36.5 to 56.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended Adverse Event (AE) During the Follow-up Phase

End point title	Percentage of Subjects With at Least 1 Medically Attended Adverse Event (AE) During the Follow-up Phase[20]

End point description:

A medically attended AE was defined as a non-serious AE that resulted in an evaluation at a medical facility. Safety population included all subjects who had at least 1 dose of investigational product (rLP2086 or HAV/saline) and had safety data available from after post third-vaccination blood draw to 6 months after last study vaccination. Here "N" signifies number of subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

From 1 month after Vaccination 3 up to 6 months after the Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	137	147	54	50
Units: Percentage of subjects				
number (confidence interval 95%)	20.4 (14 to 28.2)	16.3 (10.7 to 23.3)	13 (5.4 to 24.9)	12 (4.5 to 24.3)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	284	104		
Units: Percentage of subjects				
number (confidence interval 95%)	18.3 (14 to 23.3)	12.5 (6.8 to 20.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended Adverse Event (AE) Throughout the Study

End point title	Percentage of Subjects With at Least 1 Medically Attended Adverse Event (AE) Throughout the Study[21]

End point description:

A medically attended AE was defined as a non-serious AE that resulted in an evaluation at a medical facility. Safety population included all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

From the Vaccination 1 up to 6 month after the Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	49 (40.6 to 57.4)	48.3 (40.1 to 56.6)	47.3 (33.7 to 61.2)	52.9 (38.5 to 67.1)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	48.6 (42.8 to 54.5)	50 (40.1 to 59.9)		

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 Vaccination 1

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After Vaccination 1[22]

End point description:

A newly diagnosed chronic medical condition was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Vaccination 1 safety population included all subjects who received the first dose of investigational products (rLP2086 or HAV vaccine) on Day 1 (Month 0).

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 1

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (not applicable)	0	0	0	0

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (not applicable)	0	0		

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 Vaccination 2

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After Vaccination 2[23]

End point description:

A newly diagnosed chronic medical condition was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Vaccination 2 safety population included all subjects who received the second dose of investigational products (rLP2086 or saline) on Month 2 visit.

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 2

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (not applicable)	0	0	0	0

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (not applicable)	0	0		

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 Vaccination 3

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After Vaccination 3[24]

End point description:

A newly diagnosed chronic medical condition was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Vaccination 3 safety population included all subjects who received the third dose of investigational product (rLP2086 or HAV vaccine) on Month 6 visit.

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (not applicable)	0	0	0	0

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (not applicable)	0	0		

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[25]

End point description:

A newly diagnosed chronic medical condition was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Safety population included all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

Within 30 Days after any 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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (not applicable)	0	0	0	0

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		

Units: Percentage of subjects				
number (not applicable)	0	0		

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[26]

End point description:

A newly diagnosed chronic medical condition was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Safety population included all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

From the Vaccination 1 up to 1 month after the Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (not applicable)	0	0	0	0

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (not applicable)	0	0		

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[27]

End point description:

A newly diagnosed chronic medical condition was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Safety population included all subjects who had at least 1 dose of investigational product (rLP2086 or HAV/saline) and had safety data 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 Vaccination 3 up to 6 months after the Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (not applicable)	0	0	0	0

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (not applicable)	0	0		

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

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Throughout the Study[28]

End point description:

A newly diagnosed chronic medical condition was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects.

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

End point type	Primary

End point timeframe:

From the Vaccination 1 up to 6 month after the Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (not applicable)	0	0	0	0

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Vaccination 1[29]

End point description:

AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Vaccination 1 safety population included all subjects who received the first dose of investigational products (rLP2086 or HAV vaccine) on Day 1 (Month 0).

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 1

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	29 (21.7 to 37.1)	19.5 (13.4 to 26.7)	21.8 (11.8 to 35)	13.7 (5.7 to 26.3)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	24.1 (19.4 to 29.5)	17.9 (11.2 to 26.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Vaccination 2

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Vaccination 2[30]

End point description:

AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Vaccination 2 safety population included all subjects who received the second dose of investigational products (rLP2086 or saline) on Month 2 visit. Here "N" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 2

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	143	148	54	50
Units: Percentage of subjects				
number (confidence interval 95%)	19.6 (13.4 to 27)	26.4 (19.5 to 34.2)	27.8 (16.5 to 41.6)	16 (7.2 to 29.1)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	291	104		
Units: Percentage of subjects				
number (confidence interval 95%)	23 (18.3 to 28.3)	22.1 (14.6 to 31.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Vaccination 3

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Vaccination 3[31]

End point description:

AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Vaccination 3 safety population included all subjects who received the third dose of investigational product (rLP2086 or HAV vaccine) on Month 6 visit. Here "N" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 30 Days after Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	140	147	54	50
Units: Percentage of subjects				
number (confidence interval 95%)	12.9 (7.8 to 19.6)	15.6 (10.2 to 22.5)	11.1 (4.2 to 22.6)	8 (2.2 to 19.2)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		

Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	287	104		
Units: Percentage of subjects				
number (confidence interval 95%)	14.3 (10.5 to 18.9)	9.6 (4.7 to 17)		

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[32]

End point description:

AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Safety population included all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

Within 30 Days after any 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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	44.8 (36.6 to 53.3)	43.6 (35.5 to 52)	49.1 (35.4 to 62.9)	29.4 (17.5 to 43.8)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	44.2 (38.5 to 50.1)	39.6 (30.3 to 49.6)		

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[33]

End point description:

AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Safety population included all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

From the Vaccination 1 up to 1 month after the Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	62.1 (53.6 to 70)	63.1 (54.8 to 70.8)	63.6 (49.6 to 76.2)	62.7 (48.1 to 75.9)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	62.6 (56.8 to 68.1)	63.2 (53.3 to 72.4)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With at Least 1 Immediate Adverse Event (AE) After Vaccination 1[34]

End point description:

Immediate AE was defined as AEs occurring within the first 30 minutes after investigational product

administration. Vaccination 1 safety population included all subjects who received the first dose of investigational products (rLP2086 or HAV vaccine) on Day 1 (Month 0).

End point type	Primary

End point timeframe:

Within 30 minutes after Vaccination 1

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 2.5)	0 (0 to 2.4)	0 (0 to 6.5)	0 (0 to 7)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 1.2)	0 (0 to 3.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Immediate Adverse Event (AE) After Vaccination 2

End point title	Percentage of Subjects With at Least 1 Immediate Adverse Event (AE) After Vaccination 2[35]

End point description:

Immediate AE was defined as AEs occurring within the first 30 minutes after investigational product administration. Vaccination 2 safety population included all subjects who received the second dose of investigational products (rLP2086 or saline) on Month 2 visit. Here "N" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 30 minutes after Vaccination 2

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	143	148	54	50
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 2.5)	0 (0 to 2.5)	0 (0 to 6.6)	0 (0 to 7.1)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	291	104		
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 1.3)	0 (0 to 3.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Immediate Adverse Event (AE) After Vaccination 3

End point title	Percentage of Subjects With at Least 1 Immediate Adverse Event (AE) After Vaccination 3[36]

End point description:

Immediate AE was defined as AEs occurring within the first 30 minutes after investigational product administration. Vaccination 3 safety population included all subjects who received the third dose of investigational product (rLP2086 or HAV vaccine) on Month 6 visit. Here "N" signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 30 minutes after Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	140	147	54	50
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 2.6)	0.7 (0 to 3.7)	0 (0 to 6.6)	0 (0 to 7.1)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	287	104		
Units: Percentage of subjects				
number (confidence interval 95%)	0.3 (0 to 1.9)	0 (0 to 3.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Days Subject's Missed School Due to Adverse Event (AE) During the Vaccination Phase

End point title	Number of Days Subject's Missed School Due to Adverse Event (AE) During the Vaccination Phase[37]

End point description:

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

End point type	Primary

End point timeframe:

From the Vaccination 1 up to 1 month after the Vaccination 3

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 analysed for this endpoint.

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	145	149	55	51
Units: Days				
arithmetic mean (standard deviation)	7 (± 3.7)	4 (± 2.6)	7.3 (± 2.3)	4.2 (± 2.5)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	294	106		
Units: Days				
arithmetic mean (standard deviation)	4.7 (± 3.1)	4.6 (± 2.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Aged >=24 Months to <10 Years With hSBA Titer >= LLOQ for Each of the 4 Primary MnB Test Strains 1 Month After Vaccination 3

End point title	Percentage of Subjects Aged >=24 Months to <10 Years With hSBA Titer >= LLOQ for Each of the 4 Primary MnB Test Strains 1 Month After Vaccination 3

End point description:

Percentage of subjects achieving hSBA titer >= LLOQ were computed along with corresponding 2-sided 95% CIs. LLOQ was 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24) and PMB2707 (B44). Evaluable immunogenicity population included all eligible subjects randomized to study, received scheduled investigational products, had pre and post vaccination blood drawn with valid and determinate assay results and had no important protocol deviation. Here, ''n'' signifies number of subjects evaluable for the specified test strain.

End point type	Secondary

End point timeframe:

1 Month after Vaccination 3

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	274	97		
Units: Percentage of subjects				
number (confidence interval 95%)				
PMB80 [A22] (n = 135, 45)	87.4 (80.6 to 92.5)	6.7 (1.4 to 18.3)		
PMB2001 [A56] (n = 139, 43)	100 (97.4 to 100)	20.9 (10 to 36)		
PMB2948 [B24] (n = 126, 46)	88.9 (82.1 to 93.8)	4.3 (0.5 to 14.8)		
PMB2707 [B44] (n = 134, 50)	79.1 (71.2 to 85.6)	0 (0 to 7.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titer >= LLOQ for Each of the 4 Primary MnB Test Strains 1 Month After Vaccination 2 and 6 Months After Vaccination 3

End point title	Percentage of Subjects With hSBA Titer >= LLOQ for Each of the 4 Primary MnB Test Strains 1 Month After Vaccination 2 and 6 Months After Vaccination 3

End point description:

Percentage of subjects achieving hSBA titer >= LLOQ were computed along with corresponding 2-sided 95% CIs. LLOQ was 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44). Evaluable immunogenicity population included all eligible subjects randomized to study, received scheduled investigational products, had pre and post vaccination blood drawn with valid and determinate assay results and had no important protocol deviation. Here, "n" signifies number of subjects evaluable for the specified categories.

End point type	Secondary

End point timeframe:

1 month (Mon) after Vaccination (Vac) 2 and 6 months after Vaccination 3

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	136	138	52	45
Units: Percentage of subjects				
number (confidence interval 95%)				
1 Mon after Vac2: PMB80[A22](n=64,66,24,21,130,45)	59.4 (46.4 to 71.5)	78.8 (67 to 87.9)	0 (0 to 14.2)	9.5 (1.2 to 30.4)
6 Mon after Vac3: PMB80[A22](n=63,63,26,21,126,47)	19 (10.2 to 30.9)	46 (33.4 to 59.1)	7.7 (0.9 to 25.1)	9.5 (1.2 to 30.4)
1Mon after Vac2:PMB2001[A56](n=66,67,21,22,13	100 (94.6 to 100)	100 (94.6 to 100)	9.5 (1.2 to 30.4)	22.7 (7.8 to 45.4)
6Mon after Vac3:PMB2001[A56](n=61,70,24,22,13	80.3 (68.2 to 89.4)	84.3 (73.6 to 91.9)	16.7 (4.7 to 37.4)	22.7 (7.8 to 45.4)
1Mon after Vac2:PMB2948[B24](n=65,63,24,21,12	49.2 (36.6 to 61.9)	65.1 (52 to 76.7)	8.3 (1 to 27)	9.5 (1.2 to 30.4)
6Mon after Vac3:PMB2948[B24](n=65,64,26,21,12	9.2 (3.5 to 19)	21.9 (12.5 to 34)	0 (0 to 13.2)	0 (0 to 16.1)
1Mon after Vac2:PMB2707[B44](n=63,67,26,24,13	57.1 (44 to 69.5)	40.3 (28.5 to 53)	0 (0 to 13.2)	0 (0 to 14.2)
6Mon after Vac3:PMB2707[B44](n=66,69,26,23,13	12.1 (5.4 to 22.5)	8.7 (3.3 to 18)	0 (0 to 13.2)	0 (0 to 14.8)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	274	97		
Units: Percentage of subjects				
number (confidence interval 95%)				
1 Mon after Vac2: PMB80[A22](n=64,66,24,21,130,45)	69.2 (60.5 to 77)	4.4 (0.5 to 15.1)		
6 Mon after Vac3: PMB80[A22](n=63,63,26,21,126,47)	32.5 (24.5 to 41.5)	8.5 (2.4 to 20.4)		

1Mon after Vac2:PMB2001[A56](n=66,67,21,22,13	100 (97.3 to 100)	16.3 (6.8 to 30.7)		
6Mon after Vac3:PMB2001[A56](n=61,70,24,22,13	82.4 (74.8 to 88.5)	19.6 (9.4 to 33.9)		
1Mon after Vac2:PMB2948[B24](n=65,63,24,21,12	57 (48 to 65.7)	8.9 (2.5 to 21.2)		
6Mon after Vac3:PMB2948[B24](n=65,64,26,21,12	15.5 (9.7 to 22.9)	0 (0 to 7.5)		
1Mon after Vac2:PMB2707[B44](n=63,67,26,24,13	48.5 (39.6 to 57.4)	0 (0 to 7.1)		
6Mon after Vac3:PMB2707[B44](n=66,69,26,23,13	10.4 (5.8 to 16.8)	0 (0 to 7.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Serum Bactericidal Assay Using hSBA Titers >=1:4, >=1:8, >=1:16, >=1:32, >=1:64 and >=1:128 for Each of the 4 Primary Test Strains

End point title	Percentage of Subjects With Serum Bactericidal Assay Using hSBA Titers >=1:4, >=1:8, >=1:16, >=1:32, >=1:64 and >=1:128 for Each of the 4 Primary Test Strains

End point description:

Evaluable immunogenicity population included all eligible subjects randomized to study, received scheduled investigational products, had pre and post vaccination blood drawn with valid and determinate assay results and had no important protocol deviation. Here, "n" signifies number of subjects evaluable for the specified categories.

End point type	Secondary

End point timeframe:

Before Vaccination 1 (T1), 1 month after Vaccination 2 (T2), 1 month after Vaccination 3 (T3) and 6 months after Vaccination 3 (T4)

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	136	138	52	45
Units: Percentage of subjects				
number (confidence interval 95%)				
T1: PMB80 [A22] - 1:4 (n=68,66,26,21,134,47)	5.9 (1.6 to 14.4)	19.7 (10.9 to 31.3)	3.8 (0.1 to 19.6)	9.5 (1.2 to 30.4)
T1: PMB80 [A22] - 1:8 (n=68,66,26,21,134,47)	5.9 (1.6 to 14.4)	18.2 (9.8 to 29.6)	3.8 (0.1 to 19.6)	9.5 (1.2 to 30.4)
T1: PMB80 [A22] - 1:16 (n=68,66,26,21,134,47)	4.4 (0.9 to 12.4)	13.6 (6.4 to 24.3)	3.8 (0.1 to 19.6)	9.5 (1.2 to 30.4)
T1: PMB80 [A22] - 1:32 (n=68,66,26,21,134,47)	1.5 (0 to 7.9)	4.5 (0.9 to 12.7)	0 (0 to 13.2)	9.5 (1.2 to 30.4)
T1: PMB80 [A22] - 1:64 (n=68,66,26,21,134,47)	0 (0 to 5.3)	0 (0 to 5.4)	0 (0 to 13.2)	4.8 (0.1 to 23.8)
T1: PMB80 [A22] - 1:128 (n=68,66,26,21,134,47)	0 (0 to 5.3)	0 (0 to 5.4)	0 (0 to 13.2)	4.8 (0.1 to 23.8)

T2: PMB80 [A22] - 1:4 (n=64,66,24,21,130,45)	65.6 (52.7 to 77.1)	83.3 (72.1 to 91.4)	8.3 (1 to 27)	14.3 (3 to 36.3)
T2: PMB80 [A22] - 1:8 (n=64,66,24,21,130,45)	62.5 (49.5 to 74.3)	81.8 (70.4 to 90.2)	8.3 (1 to 27)	9.5 (1.2 to 30.4)
T2: PMB80 [A22] - 1:32 (n=64,66,24,21,130,45)	35.9 (24.3 to 48.9)	47 (34.6 to 59.7)	0 (0 to 14.2)	9.5 (1.2 to 30.4)
T2: PMB80 [A22] - 1:64 (n=64,66,24,21,130,45)	14.1 (6.6 to 25)	19.7 (10.9 to 31.3)	0 (0 to 14.2)	4.8 (0.1 to 23.8)
T2: PMB80 [A22] - 1:128 (n=64,66,24,21,130,45)	1.6 (0 to 8.4)	7.6 (2.5 to 16.8)	0 (0 to 14.2)	0 (0 to 16.1)
T3: PMB80 [A22] - 1:4 (n=68,67,25,20,135,45)	86.8 (76.4 to 93.8)	98.5 (92 to 100)	8 (1 to 26)	15 (3.2 to 37.9)
T3: PMB80 [A22] - 1:8 (n=68,67,25,20,135,45)	86.8 (76.4 to 93.8)	98.5 (92 to 100)	8 (1 to 26)	15 (3.2 to 37.9)
T3: PMB80 [A22] - 1:32 (n=68,67,25,20,135,45)	63.2 (50.7 to 74.6)	71.6 (59.3 to 82)	4 (0.1 to 20.4)	5 (0.1 to 24.9)
T3: PMB80 [A22] - 1:64 (n=68,67,25,20,135,45)	38.2 (26.7 to 50.8)	40.3 (28.5 to 53)	4 (0.1 to 20.4)	0 (0 to 16.8)
T3:PMB80 [A22] - 1:128 (n=68,67,25,20,135,45)	14.7 (7.3 to 25.4)	16.4 (8.5 to 27.5)	0 (0 to 13.7)	0 (0 to 16.8)
T4: PMB80 [A22] - 1:4 (n=63,63,26,21,126,47)	25.4 (15.3 to 37.9)	55.6 (42.5 to 68.1)	11.5 (2.4 to 30.2)	9.5 (1.2 to 30.4)
T4: PMB80 [A22] - 1:8 (n=63,63,26,21,126,47)	22.2 (12.7 to 34.5)	55.6 (42.5 to 68.1)	7.7 (0.9 to 25.1)	9.5 (1.2 to 30.4)
T4: PMB80 [A22] - 1:32 (n=63,63,26,21,126,47)	14.3 (6.7 to 25.4)	25.4 (15.3 to 37.9)	0 (0 to 13.2)	4.8 (0.1 to 23.8)
T4: PMB80 [A22] - 1:64 (n=63,63,26,21,126,47)	4.8 (1 to 13.3)	11.1 (4.6 to 21.6)	0 (0 to 13.2)	4.8 (0.1 to 23.8)
T4: PMB80 [A22] - 1:128 (n=63,63,26,21,126,47)	4.8 (1 to 13.3)	0 (0 to 5.7)	0 (0 to 13.2)	0 (0 to 16.1)
T1: PMB2001 [A56] - 1:4 (n=67,65,24,23,132,47)	3 (0.4 to 10.4)	18.5 (9.9 to 30)	16.7 (4.7 to 37.4)	21.7 (7.5 to 43.7)
T1: PMB2001 [A56] - 1:8 (n=67,65,24,23,132,47)	1.5 (0 to 8)	15.4 (7.6 to 26.5)	8.3 (1 to 27)	21.7 (7.5 to 43.7)
T1: PMB2001 [A56] - 1:16 (n=67,65,24,23,132,47)	1.5 (0 to 8)	15.4 (7.6 to 26.5)	8.3 (1 to 27)	21.7 (7.5 to 43.7)
T1: PMB2001 [A56] - 1:32 (n=67,65,24,23,132,47)	0 (0 to 5.4)	13.8 (6.5 to 24.7)	8.3 (1 to 27)	17.4 (5 to 38.8)
T1: PMB2001 [A56] - 1:64 (n=67,65,24,23,132,47)	0 (0 to 5.4)	7.7 (2.5 to 17)	4.2 (0.1 to 21.1)	8.7 (1.1 to 28)
T1: PMB2001 [A56] -1:128 (n=67,65,24,23,132,47)	0 (0 to 5.4)	1.5 (0 to 8.3)	0 (0 to 14.2)	0 (0 to 14.8)
T2: PMB2001 [A56] - 1:4 (n=66,67,21,22,133,43)	100 (94.6 to 100)	100 (94.6 to 100)	9.5 (1.2 to 30.4)	22.7 (7.8 to 45.4)
T2: PMB2001 [A56] - 1:16 (n=66,67,21,22,133,43)	100 (94.6 to 100)	98.5 (92 to 100)	9.5 (1.2 to 30.4)	22.7 (7.8 to 45.4)
T2: PMB2001 [A56] - 1:32 (n=66,67,21,22,133,43)	97 (89.5 to 99.6)	92.5 (83.4 to 97.5)	9.5 (1.2 to 30.4)	13.6 (2.9 to 34.9)
T2: PMB2001 [A56] - 1:64 (n=66,67,21,22,133,43)	80.3 (68.7 to 89.1)	82.1 (70.8 to 90.4)	4.8 (0.1 to 23.8)	9.1 (1.1 to 29.2)
T2: PMB2001 [A56] - 1:128 (n=66,67,21,22,133,43)	62.1 (49.3 to 73.8)	46.3 (34 to 58.9)	0 (0 to 16.1)	4.5 (0.1 to 22.8)
T3: PMB2001 [A56] - 1:4 (n=68,71,24,19,139,43)	100 (94.7 to 100)	100 (94.9 to 100)	4.2 (0.1 to 21.1)	47.4 (24.4 to 71.1)
T3: PMB2001 [A56] - 1:16 (n=68,71,24,19,139,43)	100 (94.7 to 100)	100 (94.9 to 100)	4.2 (0.1 to 21.1)	42.1 (20.3 to 66.5)
T3: PMB2001 [A56] - 1:32 (n=68,71,24,19,139,43)	97.1 (89.8 to 99.6)	100 (94.9 to 100)	4.2 (0.1 to 21.1)	21.1 (6.1 to 45.6)
T3: PMB2001 [A56] - 1:64 (n=68,71,24,19,139,43)	92.6 (83.7 to 97.6)	94.4 (86.2 to 98.4)	4.2 (0.1 to 21.1)	5.3 (0.1 to 26)
T3: PMB2001 [A56] - 1:128 (n=68,71,24,19,139,43)	76.5 (64.6 to 85.9)	77.5 (66 to 86.5)	0 (0 to 14.2)	0 (0 to 17.6)

T4: PMB2001 [A56] - 1:4 (n=61,70,24,22,131,46)	82 (70 to 90.6)	85.7 (75.3 to 92.9)	20.8 (7.1 to 42.2)	22.7 (7.8 to 45.4)
T4: PMB2001 [A56] - 1:16 (n=61,70,24,22,131,46)	77 (64.5 to 86.8)	82.9 (72 to 90.8)	16.7 (4.7 to 37.4)	22.7 (7.8 to 45.4)
T4: PMB2001 [A56] - 1:32 (n=61,70,24,22,131,46)	59 (45.7 to 71.4)	71.4 (59.4 to 81.6)	16.7 (4.7 to 37.4)	9.1 (1.1 to 29.2)
T4: PMB2001 [A56] - 1:64 (n=61,70,24,22,131,46)	39.3 (27.1 to 52.7)	48.6 (36.4 to 60.8)	8.3 (1 to 27)	4.5 (0.1 to 22.8)
T4: PMB2001 (A56) - 1:128 (n=61,70,24,22,131,46)	16.4 (8.2 to 28.1)	21.4 (12.5 to 32.9)	0 (0 to 14.2)	0 (0 to 15.4)
T1: PMB2948 [B24] - 1:4 (n=67,67,26,21,134,47)	4.5 (0.9 to 12.5)	9 (3.4 to 18.5)	3.8 (0.1 to 19.6)	4.8 (0.1 to 23.8)
T1: PMB2948 [B24] - 1:8 (n=67,67,26,21,134,47)	3 (0.4 to 10.4)	7.5 (2.5 to 16.6)	3.8 (0.1 to 19.6)	4.8 (0.1 to 23.8)
T1: PMB2948 [B24] - 1:16 (n=67,67,26,21,134,47)	3 (0.4 to 10.4)	6 (1.7 to 14.6)	3.8 (0.1 to 19.6)	4.8 (0.1 to 23.8)
T1: PMB2948 [B24] - 1:32 (n=67,67,26,21,134,47)	1.5 (0 to 8)	4.5 (0.9 to 12.5)	3.8 (0.1 to 19.6)	4.8 (0.1 to 23.8)
T1: PMB2948 [B24] - 1:64 (n=67,67,26,21,134,47)	1.5 (0 to 8)	1.5 (0 to 8)	0 (0 to 13.2)	0 (0 to 16.1)
T1: PMB2948 [B24] - 1:128 (n=67,67,26,21,134,47)	1.5 (0 to 8)	0 (0 to 5.4)	0 (0 to 13.2)	0 (0 to 16.1)
T2: PMB2948 [B24] - 1:4 (n=65,63,24,21,128,45)	53.8 (41 to 66.3)	68.3 (55.3 to 79.4)	8.3 (1.1 to 27)	9.5 (1.2 to 30.4)
T2: PMB2948 [B24] - 1:16 (n=65,63,24,21,128,45)	43.1 (30.8 to 56)	58.7 (45.6 to 71)	8.3 (1 to 27)	9.5 (1.2 to 30.4)
T2: PMB2948 [B24] - 1:32 (n=65,63,24,21,128,45)	15.4 (7.6 to 26.5)	30.2 (19.2 to 43)	4.2 (0.1 to 21.1)	4.8 (0.1 to 23.8)
T2: PMB2948 [B24] - 1:64 (n=65,63,24,21,128,45)	3.1 (0.4 to 10.7)	15.9 (7.9 to 27.3)	4.2 (0.1 to 21.1)	4.8 (0.1 to 23.8)
T2: PMB2948 [B24] - 1:128 (n=65,63,24,21,128,45)	1.5 (0 to 8.3)	7.9 (2.6 to 17.6)	0 (0 to 14.2)	0 (0 to 16.1)
T3: PMB2948 [B24] - 1:4 (n=63,63,26,20,126,46)	90.5 (80.4 to 96.4)	95.2 (86.7 to 99)	11.5 (2.4 to 30.2)	0 (0 to 16.8)
T3: PMB2948 [B24] - 1:16 (n=63,63,26,20,126,46)	81 (69.1 to 89.8)	88.9 (78.4 to 95.4)	7.7 (0.9 to 25.1)	0 (0 to 16.8)
T3: PMB2948 [B24] - 1:32 (n=63,63,26,20,126,46)	38.1 (26.1 to 51.2)	55.6 (42.5 to 68.1)	3.8 (0.1 to 19.6)	0 (0 to 16.8)
T3: PMB2948 [B24] - 1:64 (n=63,63,26,20,126,46)	9.5 (3.6 to 19.6)	27 (16.6 to 39.7)	0 (0 to 13.2)	0 (0 to 16.8)
T3: PMB2948 [B24] - 1:128 (n=63,63,26,20,126,46)	4.8 (1 to 13.3)	9.5 (3.6 to 19.6)	0 (0 to 13.2)	0 (0 to 16.8)
T4: PMB2948 [B24] - 1:4 (n=65,64,26,21,129,47)	13.8 (6.5 to 24.7)	26.6 (16.3 to 39.1)	0 (0 to 13.2)	4.8 (0.1 to 23.8)
T4: PMB2948 [B24] - 1:16 (n=65,64,26,21,129,47)	9.2 (3.5 to 19)	20.3 (11.3 to 32.2)	0 (0 to 13.2)	0 (0 to 16.1)
T4: PMB2948 [B24] - 1:32 (n=65,64,26,21,129,47)	6.2 (1.7 to 15)	12.5 (5.6 to 23.2)	0 (0 to 13.2)	0 (0 to 16.1)
T4: PMB2948 [B24] - 1:64 (n=65,64,26,21,129,47)	4.6 (1 to 12.9)	4.7 (1 to 13.1)	0 (0 to 13.2)	0 (0 to 16.1)
T4: PMB2948 [B24] - 1:128 (n=65,64,26,21,129,47)	3.1 (0.4 to 10.7)	3.1 (0.4 to 10.8)	0 (0 to 13.2)	0 (0 to 16.1)
T1: PMB2707 [B44] - 1:4 (n=67,71,26,24,138,50)	0 (0 to 5.4)	1.4 (0 to 7.6)	0 (0 to 13.2)	0 (0 to 14.2)
T1: PMB2707 [B44] - 1:8 (n=67,71,26,24,138,50)	0 (0 to 5.4)	0 (0 to 5.1)	0 (0 to 13.2)	0 (0 to 14.2)
T1: PMB2707 [B44] - 1:16 (n=67,71,26,24,138,50)	0 (0 to 5.4)	0 (0 to 5.1)	0 (0 to 13.2)	0 (0 to 14.2)
T1: PMB2707 [B44] - 1:32 (n=67,71,26,24,138,50)	0 (0 to 5.4)	0 (0 to 5.1)	0 (0 to 13.2)	0 (0 to 14.2)
T1: PMB2707 [B44] - 1:64 (n=67,71,26,24,138,50)	0 (0 to 5.4)	0 (0 to 5.1)	0 (0 to 13.2)	0 (0 to 14.2)

T1: PMB2707 [B44] - 1:128 (n=67,71,26,24,138,50)	0 (0 to 5.4)	0 (0 to 5.1)	0 (0 to 13.2)	0 (0 to 14.2)
T2: PMB2707 [B44] - 1:4 (n=63,67,26,24,130,50)	66.7 (53.7 to 78)	49.3 (36.8 to 61.8)	0 (0 to 13.2)	0 (0 to 14.2)
T2: PMB2707 [B44] - 1:16 (n=63,67,26,24,130,50)	55.6 (42.5 to 68.1)	31.3 (20.6 to 43.8)	0 (0 to 13.2)	0 (0 to 14.2)
T2: PMB2707 [B44] - 1:32 (n=63,67,26,24,130,50)	46 (33.4 to 59.1)	14.9 (7.4 to 25.7)	0 (0 to 13.2)	0 (0 to 14.2)
T2: PMB2707 [B44] - 1:64(n=63,67,26,24,130,50)	27 (16.6 to 39.7)	9 (3.4 to 18.5)	0 (0 to 13.2)	0 (0 to 14.2)
T2: PMB2707 [B44] - 1:128 (n=63,67,26,24,130,50)	15.9 (7.9 to 27.3)	4.5 (0.9 to 12.5)	0 (0 to 13.2)	0 (0 to 14.2)
T3: PMB2707 [B44] - 1:4 (n=65,69,26,24,134,50)	81.5 (70 to 90.1)	82.6 (71.6 to 90.7)	0 (0 to 13.2)	0 (0 to 14.2)
T3: PMB2707 [B44] - 1:16 (n=65,69,26,24,134,50)	80 (68.2 to 88.9)	75.4 (63.5 to 84.9)	0 (0 to 13.2)	0 (0 to 14.2)
T3: PMB2707 [B44] - 1:32 (n=65,69,26,24,134,50)	67.7 (54.9 to 78.8)	63.8 (51.3 to 75)	0 (0 to 13.2)	0 (0 to 14.2)
T3: PMB2707 [B44] - 1:64 (n=65,69,26,24,134,50)	55.4 (42.5 to 67.7)	49.3 (37 to 61.6)	0 (0 to 13.2)	0 (0 to 14.2)
T3: PMB2707 [B44] - 1:128 (n=65,69,26,24,134,50)	36.9 (25.3 to 49.8)	30.4 (19.9 to 42.7)	0 (0 to 13.2)	0 (0 to 14.2)
T4: PMB2707 [B44] - 1:4 (n=66,69,26,23,135,49)	13.6 (6.4 to 24.3)	13 (6.1 to 23.3)	0 (0 to 13.2)	0 (0 to 14.8)
T4: PMB2707 [B44] - 1:16 (n=66,69,26,23,135,49)	9.1 (3.4 to 18.7)	7.2 (2.4 to 16.1)	0 (0 to 13.2)	0 (0 to 14.8)
T4: PMB2707 [B44] - 1:32 (n=66,69,26,23,135,49)	6.1 (1.7 to 14.8)	7.2 (2.4 to 16.1)	0 (0 to 13.2)	0 (0 to 14.8)
T4: PMB2707 [B44] - 1:64 (n=66,69,26,23,135,49)	6.1 (1.7 to 14.8)	4.3 (0.9 to 12.2)	0 (0 to 13.2)	0 (0 to 14.8)
T4: PMB2707 [B44] - 1:128 (n=66,69,26,23,135,49)	3 (0.4 to 10.5)	2.9 (0.4 to 10.1)	0 (0 to 13.2)	0 (0 to 14.8)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	274	97		
Units: Percentage of subjects				
number (confidence interval 95%)				
T1: PMB80 [A22] - 1:4 (n=68,66,26,21,134,47)	12.7 (7.6 to 19.5)	6.4 (1.3 to 17.5)		
T1: PMB80 [A22] - 1:8 (n=68,66,26,21,134,47)	11.9 (7 to 18.7)	6.4 (1.3 to 17.5)		
T1: PMB80 [A22] - 1:16 (n=68,66,26,21,134,47)	9 (4.7 to 15.1)	6.4 (1.3 to 17.5)		
T1: PMB80 [A22] - 1:32 (n=68,66,26,21,134,47)	3 (0.8 to 7.5)	4.3 (0.5 to 14.5)		
T1: PMB80 [A22] - 1:64 (n=68,66,26,21,134,47)	0 (0 to 2.7)	2.1 (0.1 to 11.3)		
T1: PMB80 [A22] - 1:128 (n=68,66,26,21,134,47)	0 (0 to 2.7)	2.1 (0.1 to 11.3)		
T2: PMB80 [A22] - 1:4 (n=64,66,24,21,130,45)	74.6 (66.2 to 81.8)	11.1 (3.7 to 24.1)		
T2: PMB80 [A22] - 1:8 (n=64,66,24,21,130,45)	72.3 (63.8 to 79.8)	8.9 (2.5 to 21.2)		

T2: PMB80 [A22] - 1:32 (n=64,66,24,21,130,45)	41.5 (33 to 50.5)	4.4 (0.5 to 15.1)		
T2: PMB80 [A22] - 1:64 (n=64,66,24,21,130,45)	16.9 (10.9 to 24.5)	2.2 (0.1 to 11.8)		
T2: PMB80 [A22] - 1:128 (n=64,66,24,21,130,45)	4.6 (1.7 to 9.8)	0 (0 to 7.9)		
T3: PMB80 [A22] - 1:4 (n=68,67,25,20,135,45)	92.6 (86.8 to 96.4)	11.1 (3.7 to 24.1)		
T3: PMB80 [A22] - 1:8 (n=68,67,25,20,135,45)	92.6 (86.8 to 96.4)	11.1 (3.7 to 24.1)		
T3: PMB80 [A22] - 1:32 (n=68,67,25,20,135,45)	67.4 (58.8 to 75.2)	4.4 (0.5 to 15.1)		
T3: PMB80 [A22] - 1:64 (n=68,67,25,20,135,45)	39.3 (31 to 48)	2.2 (0.1 to 11.8)		
T3:PMB80 [A22] - 1:128 (n=68,67,25,20,135,45)	15.6 (9.9 to 22.8)	0 (0 to 7.9)		
T4: PMB80 [A22] - 1:4 (n=63,63,26,21,126,47)	40.5 (31.8 to 49.6)	10.6 (3.5 to 23.1)		
T4: PMB80 [A22] - 1:8 (n=63,63,26,21,126,47)	38.9 (30.3 to 48)	8.5 (2.4 to 20.4)		
T4: PMB80 [A22] - 1:32 (n=63,63,26,21,126,47)	19.8 (13.3 to 27.9)	2.1 (0.1 to 11.3)		
T4: PMB80 [A22] - 1:64 (n=63,63,26,21,126,47)	7.9 (3.9 to 14.1)	2.1 (0.1 to 11.3)		
T4: PMB80 [A22] - 1:128 (n=63,63,26,21,126,47)	2.4 (0.5 to 6.8)	0 (0 to 7.5)		
T1: PMB2001 [A56] - 1:4 (n=67,65,24,23,132,47)	10.6 (5.9 to 17.2)	19.1 (9.1 to 33.3)		
T1: PMB2001 [A56] - 1:8 (n=67,65,24,23,132,47)	8.3 (4.2 to 14.4)	14.9 (6.2 to 28.3)		
T1: PMB2001 [A56] - 1:16 (n=67,65,24,23,132,47)	8.3 (4.2 to 14.4)	14.9 (6.2 to 28.3)		
T1: PMB2001 [A56] - 1:32 (n=67,65,24,23,132,47)	6.8 (3.2 to 12.5)	12.8 (4.8 to 25.7)		
T1: PMB2001 [A56] - 1:64 (n=67,65,24,23,132,47)	3.8 (1.2 to 8.6)	6.4 (1.3 to 17.5)		
T1: PMB2001 [A56] -1:128 (n=67,65,24,23,132,47)	0.8 (0 to 4.1)	0 (0 to 7.5)		
T2: PMB2001 [A56] - 1:4 (n=66,67,21,22,133,43)	100 (97.3 to 100)	16.3 (6.8 to 30.7)		
T2: PMB2001 [A56] - 1:16 (n=66,67,21,22,133,43)	99.2 (95.9 to 100)	16.3 (6.8 to 30.7)		
T2: PMB2001 [A56] - 1:32 (n=66,67,21,22,133,43)	94.7 (89.5 to 97.9)	11.6 (3.9 to 25.1)		
T2: PMB2001 [A56] - 1:64 (n=66,67,21,22,133,43)	81.2 (73.5 to 87.5)	7 (1.5 to 19.1)		
T2: PMB2001 [A56] - 1:128 (n=66,67,21,22,133,43)	54.1 (45.3 to 62.8)	2.3 (0.1 to 12.3)		
T3: PMB2001 [A56] - 1:4 (n=68,71,24,19,139,43)	100 (97.4 to 100)	23.3 (11.8 to 38.6)		
T3: PMB2001 [A56] - 1:16 (n=68,71,24,19,139,43)	100 (97.4 to 100)	20.9 (10 to 36)		
T3: PMB2001 [A56] - 1:32 (n=68,71,24,19,139,43)	98.6 (94.9 to 99.8)	11.6 (3.9 to 25.1)		
T3: PMB2001 [A56] - 1:64 (n=68,71,24,19,139,43)	93.5 (88.1 to 97)	4.7 (0.6 to 15.8)		
T3: PMB2001 [A56] - 1:128 (n=68,71,24,19,139,43)	77 (69.1 to 83.7)	0 (0 to 8.2)		
T4: PMB2001 [A56] - 1:4 (n=61,70,24,22,131,46)	84 (76.5 to 89.8)	21.7 (10.9 to 36.4)		
T4: PMB2001 [A56] - 1:16 (n=61,70,24,22,131,46)	80.2 (72.3 to 86.6)	19.6 (9.4 to 33.9)		

T4: PMB2001 [A56] - 1:32 (n=61,70,24,22,131,46)	65.6 (56.9 to 73.7)	13 (4.9 to 26.3)		
T4: PMB2001 [A56] - 1:64 (n=61,70,24,22,131,46)	44.3 (35.6 to 53.2)	6.5 (1.4 to 17.9)		
T4: PMB2001 (A56) - 1:128 (n=61,70,24,22,131,46)	19.1 (12.7 to 26.9)	0 (0 to 7.7)		
T1: PMB2948 [B24] - 1:4 (n=67,67,26,21,134,47)	6.7 (3.1 to 12.4)	4.3 (0.5 to 14.5)		
T1: PMB2948 [B24] - 1:8 (n=67,67,26,21,134,47)	5.2 (2.1 to 10.5)	4.3 (0.5 to 14.5)		
T1: PMB2948 [B24] - 1:16 (n=67,67,26,21,134,47)	4.5 (1.7 to 9.5)	4.3 (0.5 to 14.5)		
T1: PMB2948 [B24] - 1:32 (n=67,67,26,21,134,47)	3 (0.8 to 7.5)	4.3 (0.5 to 14.5)		
T1: PMB2948 [B24] - 1:64 (n=67,67,26,21,134,47)	1.5 (0.2 to 5.3)	0 (0 to 7.5)		
T1: PMB2948 [B24] - 1:128 (n=67,67,26,21,134,47)	0.7 (0 to 4.1)	0 (0 to 7.5)		
T2: PMB2948 [B24] - 1:4 (n=65,63,24,21,128,45)	60.9 (51.9 to 69.4)	8.9 (2.5 to 21.2)		
T2: PMB2948 [B24] - 1:16 (n=65,63,24,21,128,45)	50.8 (41.8 to 59.7)	8.9 (2.5 to 21.2)		
T2: PMB2948 [B24] - 1:32 (n=65,63,24,21,128,45)	22.7 (15.7 to 30.9)	4.4 (0.5 to 15.1)		
T2: PMB2948 [B24] - 1:64 (n=65,63,24,21,128,45)	9.4 (4.9 to 15.8)	4.4 (0.5 to 15.1)		
T2: PMB2948 [B24] - 1:128 (n=65,63,24,21,128,45)	4.7 (1.7 to 9.9)	0 (0 to 7.9)		
T3: PMB2948 [B24] - 1:4 (n=63,63,26,20,126,46)	92.9 (86.9 to 96.7)	6.5 (1.4 to 17.9)		
T3: PMB2948 [B24] - 1:16 (n=63,63,26,20,126,46)	84.9 (77.5 to 90.7)	4.3 (0.5 to 14.8)		
T3: PMB2948 [B24] - 1:32 (n=63,63,26,20,126,46)	46.8 (37.9 to 55.9)	2.2 (0.1 to 11.5)		
T3: PMB2948 [B24] - 1:64 (n=63,63,26,20,126,46)	18.3 (11.9 to 26.1)	0 (0 to 7.7)		
T3: PMB2948 [B24] - 1:128 (n=63,63,26,20,126,46)	7.1 (3.3 to 13.1)	0 (0 to 7.7)		
T4: PMB2948 [B24] - 1:4 (n=65,64,26,21,129,47)	20.2 (13.6 to 28.1)	2.1 (0.1 to 11.3)		
T4: PMB2948 [B24] - 1:16 (n=65,64,26,21,129,47)	14.7 (9.1 to 22)	0 (0 to 7.5)		
T4: PMB2948 [B24] - 1:32 (n=65,64,26,21,129,47)	9.3 (4.9 to 15.7)	0 (0 to 7.5)		
T4: PMB2948 [B24] - 1:64 (n=65,64,26,21,129,47)	4.7 (1.7 to 9.8)	0 (0 to 7.5)		
T4: PMB2948 [B24] - 1:128 (n=65,64,26,21,129,47)	3.1 (0.9 to 7.7)	0 (0 to 7.5)		
T1: PMB2707 [B44] - 1:4 (n=67,71,26,24,138,50)	0.7 (0 to 4)	0 (0 to 7.1)		
T1: PMB2707 [B44] - 1:8 (n=67,71,26,24,138,50)	0 (0 to 2.6)	0 (0 to 7.1)		
T1: PMB2707 [B44] - 1:16 (n=67,71,26,24,138,50)	0 (0 to 2.6)	0 (0 to 7.1)		
T1: PMB2707 [B44] - 1:32 (n=67,71,26,24,138,50)	0 (0 to 2.6)	0 (0 to 7.1)		
T1: PMB2707 [B44] - 1:64 (n=67,71,26,24,138,50)	0 (0 to 2.6)	0 (0 to 7.1)		
T1: PMB2707 [B44] - 1:128 (n=67,71,26,24,138,50)	0 (0 to 2.6)	0 (0 to 7.1)		
T2: PMB2707 [B44] - 1:4 (n=63,67,26,24,130,50)	57.7 (48.7 to 66.3)	0 (0 to 7.1)		

T2: PMB2707 [B44] - 1:16 (n=63,67,26,24,130,50)	43.1 (34.4 to 52)	0 (0 to 7.1)		
T2: PMB2707 [B44] - 1:32 (n=63,67,26,24,130,50)	30 (22.3 to 38.7)	0 (0 to 7.1)		
T2: PMB2707 [B44] - 1:64(n=63,67,26,24,130,50)	17.7 (11.6 to 25.4)	0 (0 to 7.1)		
T2: PMB2707 [B44] - 1:128 (n=63,67,26,24,130,50)	10 (5.4 to 16.5)	0 (0 to 7.1)		
T3: PMB2707 [B44] - 1:4 (n=65,69,26,24,134,50)	82.1 (74.5 to 88.2)	0 (0 to 7.1)		
T3: PMB2707 [B44] - 1:16 (n=65,69,26,24,134,50)	77.6 (69.6 to 84.4)	0 (0 to 7.1)		
T3: PMB2707 [B44] - 1:32 (n=65,69,26,24,134,50)	65.7 (57 to 73.7)	0 (0 to 7.1)		
T3: PMB2707 [B44] - 1:64 (n=65,69,26,24,134,50)	52.2 (43.4 to 60.9)	0 (0 to 7.1)		
T3: PMB2707 [B44] - 1:128 (n=65,69,26,24,134,50)	33.6 (25.7 to 42.2)	0 (0 to 7.1)		
T4: PMB2707 [B44] - 1:4 (n=66,69,26,23,135,49)	13.3 (8.1 to 20.3)	0 (0 to 7.3)		
T4: PMB2707 [B44] - 1:16 (n=66,69,26,23,135,49)	8.1 (4.1 to 14.1)	0 (0 to 7.3)		
T4: PMB2707 [B44] - 1:32 (n=66,69,26,23,135,49)	6.7 (3.1 to 12.3)	0 (0 to 7.3)		
T4: PMB2707 [B44] - 1:64 (n=66,69,26,23,135,49)	5.2 (2.1 to 10.4)	0 (0 to 7.3)		
T4: PMB2707 [B44] - 1:128 (n=66,69,26,23,135,49)	3 (0.8 to 7.4)	0 (0 to 7.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Bactericidal Assay Using Human Complement (hSBA) Geometric Mean Titers (GMTs) for Each of the 4 Primary Test Strains

End point title	Serum Bactericidal Assay Using Human Complement (hSBA) Geometric Mean Titers (GMTs) for Each of the 4 Primary Test Strains

End point description:

Evaluable immunogenicity population included all eligible subjects randomized to study, received scheduled investigational products, had pre and post vaccination blood drawn with valid and determinate assay results and had no important protocol deviation. Here, "n" signifies number of subjects evaluable for the specified categories and "99999" and "-99999" signifies "Not available" (NA) as CI was not estimable due to the lack of variability of geometric means.

End point type	Secondary

End point timeframe:

Before Vaccination 1 (T1), 1 month after Vaccination 2 (T2), 1 month after Vaccination 3 (T3) and 6 months after Vaccination 3 (T4)

End point values	Group 1 bivalent rLP2086 (>=24 months to <4 years)	Group 1 bivalent rLP2086 (>=4 years to <10 years)	Group 2 HAV/Saline (>=24 months to <4 years)	Group 2 HAV/Saline (>=4 years to <10 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	136	138	52	45
Units: titers				
geometric mean (confidence interval 95%)				
T1: PMB80 [A22] (n=68,66,26,21,134,47)	8.3 (7.9 to 8.8)	9.1 (8.3 to 9.9)	8.2 (7.8 to 8.7)	9.8 (7.2 to 13.2)
T2: PMB80 [A22](n=64,66,24,21,130,45)	17.4 (14.2 to 21.4)	23.1 (18.9 to 28.3)	8 (-99999 to 99999)	9.4 (7.4 to 12)
T3: PMB80 [A22](n=68,67,25,20,135,45)	33.7 (26.4 to 42.9)	38.2 (30.6 to 47.6)	8.7 (7.3 to 10.3)	8.9 (7.6 to 10.4)
T4: PMB80 [A22](n=63,63,26,21,126,47)	10.9 (9 to 13.1)	14.2 (11.8 to 17)	8.4 (7.8 to 9.1)	9.1 (7.4 to 11.3)
T1: PMB2001 [A56](n=67,65,24,23,132,47)	4.1 (3.9 to 4.3)	5.8 (4.6 to 7.3)	4.9 (3.7 to 6.6)	6.5 (4.3 to 9.8)
T2: PMB2001 [A56](n=66,67,21,22,133,43)	103.8 (84.2 to 127.9)	90 (71.9 to 112.7)	5 (3.6 to 7.1)	6.6 (4.2 to 10.5)
T3: PMB2001 [A56](n=68,71,24,19,139,43)	175.6 (139.1 to 221.6)	191 (153.9 to 237.1)	4.5 (3.5 to 5.7)	8.6 (5.4 to 13.8)
T4: PMB2001 [A56](n=61,70,24,22,131,46)	27 (19.7 to 36.9)	35.7 (26.6 to 47.8)	6 (4 to 8.9)	6 (4.2 to 8.7)
T1: PMB2948 [B24] (n=67,67,26,21,134,47)	4.3 (3.8 to 4.9)	4.6 (4 to 5.2)	4.3 (3.7 to 5.1)	4.4 (3.6 to 5.4)
T2: PMB2948 [B24](n=65,63,24,21,128,45)	9.1 (7 to 11.9)	13.7 (10.3 to 18.2)	4.8 (3.7 to 6.2)	4.9 (3.6 to 6.6)
T3: PMB2948 [B24](n=63,63,26,20,126,46)	19.1 (14.9 to 24.5)	26.8 (21.3 to 33.9)	4.6 (3.8 to 5.6)	4 (-99999 to 99999)
T4: PMB2948 [B24](n=65,64,26,21,129,47)	5.1 (4.1 to 6.3)	6.2 (4.9 to 7.7)	4 (-99999 to 99999)	4 (-99999 to 99999)
T1: PMB2707 [B44] (n=67,71,26,24,138,50)	4 (-99999 to 99999)	4 (-99999 to 99999)	4 (-99999 to 99999)	4 (-99999 to 99999)
T2: PMB2707 [B44](n=63,67,26,24,130,50)	17.1 (11.8 to 24.8)	8.2 (6.3 to 10.6)	4 (-99999 to 99999)	4 (-99999 to 99999)
T3: PMB2707 [B44](n=65,69,26,24,134,50)	43.6 (29.9 to 63.6)	36.5 (25.2 to 52.7)	4 (-99999 to 99999)	4 (-99999 to 99999)
T4: PMB2707 [B44](n=66,69,26,23,135,49)	5.2 (4.2 to 6.4)	5 (4.1 to 6.2)	4 (-99999 to 99999)	4 (-99999 to 99999)

End point values	Group 1 bivalent rLP2086 (>=24 months to <10 years)	Group 2 HAV/Saline (>=24 months to <10 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	274	97		
Units: titers				
geometric mean (confidence interval 95%)				
T1: PMB80 [A22] (n=68,66,26,21,134,47)	8.7 (8.3 to 9.1)	8.9 (7.8 to 10.1)		
T2: PMB80 [A22](n=64,66,24,21,130,45)	20.1 (17.4 to 23.2)	8.6 (7.7 to 9.7)		

T3: PMB80 [A22](n=68,67,25,20,135,45)	35.8 (30.5 to 42.2)	8.8 (7.8 to 9.8)		
T4: PMB80 [A22](n=63,63,26,21,126,47)	12.4 (10.9 to 14.2)	8.7 (7.9 to 9.7)		
T1: PMB2001 [A56](n=67,65,24,23,132,47)	4.9 (4.3 to 5.5)	5.6 (4.4 to 7.2)		
T2: PMB2001 [A56](n=66,67,21,22,133,43)	96.6 (83 to 112.5)	5.8 (4.4 to 7.6)		
T3: PMB2001 [A56](n=68,71,24,19,139,43)	183.3 (156.7 to 214.4)	6 (4.6 to 7.7)		
T4: PMB2001 [A56](n=61,70,24,22,131,46)	31.3 (25.3 to 38.7)	6 (4.6 to 7.8)		
T1: PMB2948 [B24] (n=67,67,26,21,134,47)	4.5 (4.1 to 4.9)	4.4 (3.9 to 4.9)		
T2: PMB2948 [B24](n=65,63,24,21,128,45)	11.1 (9.2 to 13.5)	4.8 (4 to 5.8)		
T3: PMB2948 [B24](n=63,63,26,20,126,46)	22.6 (19.1 to 26.8)	4.3 (3.9 to 4.8)		
T4: PMB2948 [B24](n=65,64,26,21,129,47)	5.6 (4.8 to 6.5)	4 (-99999 to 99999)		
T1: PMB2707 [B44] (n=67,71,26,24,138,50)	4 (-99999 to 99999)	4 (-99999 to 99999)		
T2: PMB2707 [B44](n=63,67,26,24,130,50)	11.7 (9.3 to 14.7)	4 (-99999 to 99999)		
T3: PMB2707 [B44](n=65,69,26,24,134,50)	39.8 (30.6 to 51.6)	4 (-99999 to 99999)		
T4: PMB2707 [B44](n=66,69,26,23,135,49)	5.1 (4.4 to 5.9)	4 (-99999 to 99999)		

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 local reactions and systemic events in e-diary within 7 days after first, second and third vaccination.

Adverse event reporting additional description:

SAEs and AEs were grouped by system organ class and preferred term. AEs included AEs collected in the e-diary (local and systemic reactions; systematic assessment) and AEs collected on the case report form at each visit (nonsystematic assessment).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Group 2 HAV/Saline (>=24 months to <10 years)

Reporting group description:

Subjects from >=24 months to <10 years of age, received intramuscular injection of saline on 2- month and HAV vaccine on a 0-, 6- month schedule.

Reporting group title	Group 1 bivalent rLP2086 (>=24 months to <10 years)

Reporting group description:

Subjects from >=24 months to <10 years of age, received intramuscular injection of rLP2086 vaccine on a 0-, 2-, 6- month schedule.

Serious adverse events	Group 2 HAV/Saline (>=24 months to <10 years)	Group 1 bivalent rLP2086 (>=24 months to <10 years)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 106 (0.94%)	5 / 294 (1.70%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Skin and subcutaneous tissue disorders			
Rash papular			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Synovitis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Bronchitis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group 2 HAV/Saline (>=24 months to <10 years)	Group 1 bivalent rLP2086 (>=24 months to <10 years)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 106 (82.08%)	281 / 294 (95.58%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Crying			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Fatigue (Systematic)			
alternative assessment type: Systematic			
subjects affected / exposed	41 / 106 (38.68%)	175 / 294 (59.52%)	
occurrences (all)	59	365	
Fatigue (Non Systematic)			
subjects affected / exposed	0 / 106 (0.00%)	3 / 294 (1.02%)	
occurrences (all)	0	3	
Injection site erythema (redness)			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 106 (16.98%)	177 / 294 (60.20%)	
occurrences (all)	26	328	
Injection site hypersensitivity			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Injection site pain (pain)			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 106 (33.02%)	248 / 294 (84.35%)	
occurrences (all)	53	595	
Injection site pain			
subjects affected / exposed	1 / 106 (0.94%)	4 / 294 (1.36%)	
occurrences (all)	1	4	
Injection site pruritus			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Injection site swelling (swelling)			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 106 (9.43%)	137 / 294 (46.60%)	
occurrences (all)	12	253	
Local swelling			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Pyrexia (fever)			

alternative assessment type: Systematic			
subjects affected / exposed	13 / 106 (12.26%)	72 / 294 (24.49%)	
occurrences (all)	16	102	
Pyrexia			
subjects affected / exposed	2 / 106 (1.89%)	16 / 294 (5.44%)	
occurrences (all)	2	18	
Vaccination site pain			
subjects affected / exposed	0 / 106 (0.00%)	2 / 294 (0.68%)	
occurrences (all)	0	2	
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Food allergy			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Seasonal allergy			
subjects affected / exposed	0 / 106 (0.00%)	3 / 294 (1.02%)	
occurrences (all)	0	3	
Reproductive system and breast disorders			
Balanoposthitis	Additional description: This event is a gender specific event.		
subjects affected / exposed[1]	1 / 44 (2.27%)	0 / 148 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Allergic cough			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Tonsillar hypertrophy			

subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 106 (0.00%)	4 / 294 (1.36%)	
occurrences (all)	0	4	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 106 (0.94%)	1 / 294 (0.34%)	
occurrences (all)	1	1	
Concussion			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	0 / 106 (0.00%)	2 / 294 (0.68%)	
occurrences (all)	0	2	
Corneal abrasion			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Foot fracture			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Laceration			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Foreign body in eye			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Head injury			
subjects affected / exposed	0 / 106 (0.00%)	2 / 294 (0.68%)	
occurrences (all)	0	2	
Nasal injury			

subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Radius fracture			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache (Systematic)			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 106 (20.75%)	98 / 294 (33.33%)	
occurrences (all)	31	147	
Headache (Non Systematic)			
subjects affected / exposed	0 / 106 (0.00%)	6 / 294 (2.04%)	
occurrences (all)	0	6	
Lethargy			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	0 / 106 (0.00%)	2 / 294 (0.68%)	
occurrences (all)	0	2	
Speech disorder			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Middle ear effusion			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Eye disorders			

Conjunctivitis allergic			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Aphthous ulcer			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Cheilitis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	2	
Dental caries			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Diarrhoea (diarrhea)			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 106 (12.26%)	51 / 294 (17.35%)	
occurrences (all)	16	69	
Diarrhoea			
subjects affected / exposed	0 / 106 (0.00%)	2 / 294 (0.68%)	
occurrences (all)	0	4	
Inguinal hernia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Lip swelling			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Teething			
subjects affected / exposed	2 / 106 (1.89%)	0 / 294 (0.00%)	
occurrences (all)	2	0	
Vomiting (Systematic)			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 106 (12.26%)	35 / 294 (11.90%)	
occurrences (all)	13	40	

Vomiting (Non Systematic)			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Rash generalised			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Rash macular			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Rash papular			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	3 / 106 (2.83%)	1 / 294 (0.34%)	
occurrences (all)	3	1	
Swelling face			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	2	
Urticaria			
subjects affected / exposed	0 / 106 (0.00%)	2 / 294 (0.68%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia (joint pain)			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 106 (6.60%)	43 / 294 (14.63%)	
occurrences (all)	12	61	
Arthritis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Myalgia (muscle pain)			
alternative assessment type: Systematic			

subjects affected / exposed	9 / 106 (8.49%)	83 / 294 (28.23%)	
occurrences (all)	13	121	
Joint swelling			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Scoliosis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Neck mass			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Synovitis			
subjects affected / exposed	0 / 106 (0.00%)	2 / 294 (0.68%)	
occurrences (all)	0	2	
Infections and infestations			
Bronchitis			
subjects affected / exposed	6 / 106 (5.66%)	19 / 294 (6.46%)	
occurrences (all)	7	25	
Chronic tonsillitis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	2 / 106 (1.89%)	9 / 294 (3.06%)	
occurrences (all)	2	9	
Enterobiasis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Exanthema subitum			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Foot and mouth disease			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	

Gastroenteritis viral			
subjects affected / exposed	0 / 106 (0.00%)	5 / 294 (1.70%)	
occurrences (all)	0	5	
Gastroenteritis			
subjects affected / exposed	10 / 106 (9.43%)	39 / 294 (13.27%)	
occurrences (all)	10	47	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 106 (0.94%)	1 / 294 (0.34%)	
occurrences (all)	1	1	
Gingivitis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	2	0	
Herpes dermatitis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Hordeolum			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Impetigo			
subjects affected / exposed	0 / 106 (0.00%)	5 / 294 (1.70%)	
occurrences (all)	0	5	
Infection parasitic			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Infectious mononucleosis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Laryngitis			
subjects affected / exposed	7 / 106 (6.60%)	6 / 294 (2.04%)	
occurrences (all)	7	7	
Meningitis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	

Nasopharyngitis			
subjects affected / exposed	2 / 106 (1.89%)	5 / 294 (1.70%)	
occurrences (all)	2	5	
Influenza			
subjects affected / exposed	2 / 106 (1.89%)	7 / 294 (2.38%)	
occurrences (all)	2	7	
Otitis media acute			
subjects affected / exposed	1 / 106 (0.94%)	1 / 294 (0.34%)	
occurrences (all)	1	1	
Otitis media viral			
subjects affected / exposed	0 / 106 (0.00%)	2 / 294 (0.68%)	
occurrences (all)	0	3	
Paronychia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	9 / 106 (8.49%)	33 / 294 (11.22%)	
occurrences (all)	11	50	
Pneumonia bacterial			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Pyelonephritis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	4 / 106 (3.77%)	3 / 294 (1.02%)	
occurrences (all)	5	3	
Respiratory tract infection			
subjects affected / exposed	4 / 106 (3.77%)	12 / 294 (4.08%)	
occurrences (all)	4	14	
Otitis media			
subjects affected / exposed	12 / 106 (11.32%)	44 / 294 (14.97%)	
occurrences (all)	14	54	
Rhinitis			
subjects affected / exposed	2 / 106 (1.89%)	4 / 294 (1.36%)	
occurrences (all)	2	4	

Scarlet fever			
subjects affected / exposed	1 / 106 (0.94%)	2 / 294 (0.68%)	
occurrences (all)	1	2	
Sinusitis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	3 / 106 (2.83%)	10 / 294 (3.40%)	
occurrences (all)	3	12	
Skin bacterial infection			
subjects affected / exposed	1 / 106 (0.94%)	0 / 294 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	16 / 106 (15.09%)	59 / 294 (20.07%)	
occurrences (all)	20	82	
Varicella zoster virus infection			
subjects affected / exposed	0 / 106 (0.00%)	1 / 294 (0.34%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 106 (0.94%)	5 / 294 (1.70%)	
occurrences (all)	1	5	
Varicella			
subjects affected / exposed	4 / 106 (3.77%)	7 / 294 (2.38%)	
occurrences (all)	4	7	
Viral upper respiratory tract infection			
subjects affected / exposed	8 / 106 (7.55%)	31 / 294 (10.54%)	
occurrences (all)	15	47	
Vulvitis	Additional description: This event is a gender specific event.		
subjects affected / exposed[2]	0 / 62 (0.00%)	1 / 146 (0.68%)	
occurrences (all)	0	1	

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: This event is a gender specific event.

[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: This event is a gender specific event.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported