Clinical trial results:
A Phase 3, Randomized, Active-controlled, Observer-blinded Trial To Assess The Safety And Tolerability Of A Meningococcal Serogroup B Bivalent Recombinant Lipoprotein (rLP2086) Vaccine Given In Healthy Subjects Aged Greater Than Or Equal To (>=) 10 To Less Than (<) 26 Years

Summary

EudraCT number	2009-015198-11
Trial protocol	SE CZ LT EE FI DK ES DE Outside EU/EEA
Global end of trial date	29 September 2014

Results information

Result version number	v1 (current)
This version publication date	29 June 2016
First version publication date	29 May 2015

Trial information

Trial identification

Sponsor protocol code	B1971014 (6108A1-3003)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01352793
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Clinical Trials.gov Call Centre, Pfizer Inc, 001 8007181021, ClinicalTrials.govCallCentre@pfizer.com
Scientific contact	Clinical Trials.gov Call Centre, Pfizer Inc, 001 8007181021, ClinicalTrials.govCallCentre@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001037-PIP02-11
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of bivalent rLP2086 vaccine compared to a control (hepatitis A virus [HAV] vaccine/saline), as assessed by serious adverse events (SAEs) and medically attended adverse events.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator:

HAV vaccine (at months 0 and 6) has been chosen as the control in this study because there is no proven safe, immunogenic, and effective vaccine against MnB that could serve as an active control. In comparison to other recommended vaccines for this age group, HAV vaccine has a well-established tolerability profile. In addition, HAV vaccine will confer a benefit to subjects who may become at increased risk for hepatitis A viral infection either during future travel or other exposures. The generally recommended regimen for HAV vaccine is 2 doses at 0 and 6 months. In this study, saline is given at month 2 to maintain the study blind.

Actual start date of recruitment	07 November 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 873
Country: Number of subjects enrolled	Spain: 150
Country: Number of subjects enrolled	Sweden: 72
Country: Number of subjects enrolled	Czech Republic: 309
Country: Number of subjects enrolled	Denmark: 255
Country: Number of subjects enrolled	Estonia: 250
Country: Number of subjects enrolled	Finland: 287
Country: Number of subjects enrolled	Germany: 195
Country: Number of subjects enrolled	Lithuania: 438
Country: Number of subjects enrolled	United States: 2344
Country: Number of subjects enrolled	Australia: 205
Country: Number of subjects enrolled	Chile: 334

Worldwide total number of subjects	5712
EEA total number of subjects	2829

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)	730
Adolescents (12-17 years)	2127
Adults (18-64 years)	2855
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 5712 subjects in 12 countries were enrolled in this study. Of these, 8 subjects were randomized but did not receive study vaccination.

Period 1

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

Arms

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

Arm description:

Randomized to receive Neisseria meningitidis serogroup B (MnB) bivalent recombinant lipoprotein 2086 (rLP2086) vaccine on a 0, 2-, 6-month schedule

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

Dosage and administration details:

Subjects received rLP2086 vaccine 120 microgram (mcg) intramuscularly in the deltoid muscle on a 0, 2-, 6- month schedule.

Arm title	Group 2: HAV/Saline/HAV

Arm description:

Randomized to receive hepatitis A virus (HAV) vaccine (Havrix) on a 0-, 6- month schedule and normal saline on 2-month

Arm type	Active comparator
Investigational medicinal product name	HAV vaccine
Investigational medicinal product code	
Other name	Havrix
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received HAV vaccine (Havrix) 0.5 milliliter (mL) pediatric dose containing 720 enzyme-linked immunosorbent assay (ELISA) units (EL.U.) or 1.0 mL adult dose containing 1440 EL.U based on subject’s age intramuscularly in the

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

Dosage and administration details:

Subjects received 0.5 mL of normal saline injection at Month 2.

Number of subjects in period 1	Group 1: rLP2086	Group 2: HAV/Saline/HAV
Started	3804	1908
Vaccination 1	3796	1908
Vaccination 2	3530	1806
Vaccination 3	3314	1710
Completed	3219	1663
Not completed	585	245
Physician decision	1	-
Adverse Event	44	10
No longer meets eligibility criteria	25	15
Death	1	-
Randomized but not vaccinated	8	-
Pregnancy	26	8
Medication error	2	2
Withdrawal by Subject	120	55
Protocol Violation	44	23
Unspecified	25	7
Lost to follow-up	289	125

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: rLP2086
Reporting group description:	
Randomized to receive Neisseria meningitidis serogroup B (MnB) bivalent recombinant lipoprotein 2086 (rLP2086) vaccine on a 0, 2-, 6-month schedule	
Reporting group title	Group 2: HAV/Saline/HAV
Reporting group description:	
Randomized to receive hepatitis A virus (HAV) vaccine (Havrix) on a 0-, 6- month schedule and normal saline on 2-month	

Reporting group values	Group 1: rLP2086	Group 2: HAV/Saline/HAV	Total
Number of subjects	3804	1908	5712
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	17.4	17.4	
standard deviation	± 4.6	± 4.6	-
Gender categorical			
Units: Subjects			
Female	1962	994	2956
Male	1842	914	2756

End points

End points reporting groups

Reporting group title	Group 1: rLP2086
Reporting group description:	
Randomized to receive Neisseria meningitidis serogroup B (MnB) bivalent recombinant lipoprotein 2086 (rLP2086) vaccine on a 0, 2-, 6-month schedule	
Reporting group title	Group 2: HAV/Saline/HAV
Reporting group description:	
Randomized to receive hepatitis A virus (HAV) vaccine (Havrix) on a 0-, 6- month schedule and normal saline on 2-month	

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

End point title	Percentage of Subjects With at Least One Serious Adverse Event (SAE) Throughout the Study[1]
End point description:	
An adverse event (AE) was any untoward medical occurrence in a subject who received study vaccine without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death, initial or prolonged inpatient hospitalization, life-threatening experience (immediate risk of dying), persistent or significant disability or incapacity, congenital anomaly. Safety population included all subjects who received at least 1 dose of study vaccine (bivalent rLP2086 or HAV vaccine or saline) and had safety information available.	
End point type	Primary
End point timeframe:	
Vaccination 1 up to 6 months 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 reported for this endpoint.

End point values	Group 1: rLP2086	Group 2: HAV/Saline/HAV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3796	1908		
Units: percentage of subjects				
number (confidence interval 95%)	1.55 (1.2 to 2)	2.52 (1.9 to 3.3)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With at Least One Medically Attended Adverse Event Within 30 Days After Vaccination 1[2]
End point description:	
A medically attended AE was defined as a non-serious AE that required medical attention. Vaccination 1	

safety population included all subjects who received the first dose of study vaccine (bivalent rLP2086 or HAV vaccine) and had safety information available from Vaccination 1 until prior to Vaccination 2.

End point type	Primary

End point timeframe:

Within 30 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 reported for this endpoint.

End point values	Group 1: rLP2086	Group 2: HAV/Saline/HAV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3796	1908		
Units: percentage of subjects				
number (confidence interval 95%)	7.03 (6.2 to 7.9)	6.13 (5.1 to 7.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least One Medically Attended Adverse Event Within 30 Days After Vaccination 2

End point title	Percentage of Subjects With at Least One Medically Attended Adverse Event Within 30 Days After Vaccination 2[3]

End point description:

A medically attended AE was defined as a non-serious AE that required medical attention. Vaccination 2 safety population included all subjects who received the second dose of study vaccine (bivalent rLP2086 or saline) and had safety information available from Vaccination 2 until prior to Vaccination 3.

End point type	Primary

End point timeframe:

Within 30 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 reported for this endpoint.

End point values	Group 1: rLP2086	Group 2: HAV/Saline/HAV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3529	1806		
Units: percentage of subjects				
number (confidence interval 95%)	5.5 (4.8 to 6.3)	6.09 (5 to 7.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least One Medically Attended Adverse Event Within 30 Days After Vaccination 3

End point title	Percentage of Subjects With at Least One Medically Attended Adverse Event Within 30 Days After Vaccination 3[4]

End point description:

A medically attended AE was defined as a non-serious AE that required medical attention. Vaccination 3 safety population included all subjects who received the third dose of study vaccine (bivalent rLP2086 or HAV vaccine or saline) and had safety information available from Vaccination 3 to post Vaccination 3 follow-up visit (1 month after Vaccination 3).

End point type	Primary

End point timeframe:

Within 30 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 reported for this endpoint.

End point values	Group 1: rLP2086	Group 2: HAV/Saline/HAV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3313	1710		
Units: percentage of subjects				
number (confidence interval 95%)	5.34 (4.6 to 6.2)	5.5 (4.5 to 6.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With at Least One Serious Adverse Event (SAE) During Pre- specified Time Periods

End point title	Percentage of Subjects With at Least One Serious Adverse Event (SAE) During Pre- specified Time Periods

End point description:

An AE was any untoward medical occurrence in a subject who received study vaccine without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death, initial or prolonged inpatient hospitalization, life-threatening experience (immediate risk of dying), persistent or significant disability or incapacity, congenital anomaly. Here, 'N' signifies those subjects who were evaluable for this measure during specified time period. Safety population included all subjects who received at least 1 dose of the study vaccine (bivalent rLP2086 or HAV vaccine or saline) and had safety information available.

End point type	Secondary

End point timeframe:

Within 30 days after Vaccination 1, 2, 3, any vaccination; vaccination phase (Vaccination 1 up to 1 month after Vaccination 3); follow-up phase (1 month up to 6 months after Vaccination 3)

End point values	Group 1: rLP2086	Group 2: HAV/Saline/HAV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3796	1908		
Units: percentage of subjects				
number (confidence interval 95%)				
30 days after Vaccination 1 (N=3796, 1908)	0.18 (0.1 to 0.4)	0.42 (0.2 to 0.8)		
30 days after Vaccination 2 (N=3529, 1806)	0.17 (0.1 to 0.4)	0.44 (0.2 to 0.9)		
30 days after Vaccination 3 (N=3313, 1710)	0.33 (0.2 to 0.6)	0.12 (0 to 0.4)		
30 days after any vaccination (N=3796, 1908)	0.61 (0.4 to 0.9)	0.94 (0.6 to 1.5)		
Vaccination phase (N=3796, 1908)	1.16 (0.8 to 1.6)	1.83 (1.3 to 2.5)		
Follow-up phase (N=3400, 1733)	0.44 (0.2 to 0.7)	0.87 (0.5 to 1.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With at Least One Medically Attended Adverse Event During Pre- specified Time Periods

End point title	Percentage of Subjects With at Least One Medically Attended Adverse Event During Pre- specified Time Periods

End point description:

A medically attended AE was defined as a non-serious AE that required medical attention. Safety population included all subjects who received at least 1 dose of the study vaccine (bivalent rLP2086 or HAV vaccine or saline) and had safety information available.

End point type	Secondary

End point timeframe:

Within 30 days after any vaccination; vaccination phase (Vaccination 1 up to 1 month after Vaccination 3); follow-up phase (1 month up to 6 months after Vaccination 3); throughout study (Vaccination 1 up to 6 months after Vaccination 3)

End point values	Group 1: rLP2086	Group 2: HAV/Saline/HAV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3796	1908		
Units: percentage of subjects				
number (confidence interval 95%)				
30 days after any vaccination (N=3796, 1908)	14.38 (13.3 to 15.5)	14.57 (13 to 16.2)		
Vaccination phase (N=3796, 1908)	24.6 (23.2 to 26)	24.53 (22.6 to 26.5)		
Follow-up phase (N=3400, 1733)	11.24 (10.2 to 12.3)	11.43 (10 to 13)		

Throughout study (N=3796, 1908)	29 (27.6 to 30.5)	29.04 (27 to 31.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With at Least One Newly Diagnosed Chronic Medical Condition During Pre-specified Time Periods

End point title	Percentage of Subjects With at Least One Newly Diagnosed Chronic Medical Condition During Pre-specified Time Periods

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. Newly diagnosed chronic medical condition did not include illnesses considered to be temporary conditions. Here, 'N' signifies those subjects who were evaluable for this measure during specified time period. Safety population included all subjects who received at least 1 dose of the study vaccine (bivalent rLP2086 or HAV vaccine or saline) and had safety information available.

End point type	Secondary

End point timeframe:

Within 30 days after Vaccination 1, 2, 3, any vaccination; vaccination phase(Vaccination 1 up to 1 month after Vaccination 3); follow-up phase(1 month up to 6 months after Vaccination 3); throughout study(Vaccination 1 up to 6 months after Vaccination

End point values	Group 1: rLP2086	Group 2: HAV/Saline/HAV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3796	1908		
Units: percentage of subjects				
number (confidence interval 95%)				
30 days after Vaccination 1 (N=3796, 1908)	0.21 (0.1 to 0.4)	0.1 (0 to 0.4)		
30 days after Vaccination 2 (N=3529, 1806)	0.17 (0.1 to 0.4)	0.33 (0.1 to 0.7)		
30 days after Vaccination 3 (N=3313, 1710)	0.09 (0 to 0.3)	0.12 (0 to 0.4)		
30 days after any vaccination (N=3796, 1908)	0.45 (0.3 to 0.7)	0.52 (0.3 to 1)		
Vaccination phase (N=3796, 1908)	1.03 (0.7 to 1.4)	1.05 (0.6 to 1.6)		
Follow-up phase (N=3400, 1733)	0.44 (0.2 to 0.7)	0.52 (0.2 to 1)		
Throughout study (N=3796, 1908)	1.4 (1 to 1.8)	1.52 (1 to 2.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With at Least One Adverse Event (AE) During Pre-specified Time Periods

End point title	Percentage of Subjects With at Least One Adverse Event (AE) During Pre-specified Time Periods

End point description:

An AE was any untoward medical occurrence in a subject who received study vaccine without regard to possibility of causal relationship. Here, 'N' signifies those subjects who were evaluable for this measure during specified time period. Safety population included all subjects who received at least 1 dose of the study vaccine (bivalent rLP2086 or HAV vaccine or saline) and had safety information available.

End point type	Secondary

End point timeframe:

Within 30 days after Vaccination 1, 2, 3, any vaccination; vaccination phase (Vaccination 1 up to 1 month after Vaccination 3)

End point values	Group 1: rLP2086	Group 2: HAV/Saline/HAV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3796	1908		
Units: percentage of subjects				
number (confidence interval 95%)				
30 days after Vaccination 1 (N=3796, 1908)	31.48 (30 to 33)	19.03 (17.3 to 20.9)		
30 days after Vaccination 2 (N=3529, 1806)	20.37 (19.1 to 21.7)	12.35 (10.9 to 14)		
30 days after Vaccination 3 (N=3313, 1710)	15 (13.8 to 16.3)	10.76 (9.3 to 12.3)		
30 days after any vaccination (N=3796, 1908)	43.02 (41.4 to 44.6)	31.45 (29.4 to 33.6)		
Vaccination phase (N=3796, 1908)	51.08 (49.5 to 52.7)	42.51 (40.3 to 44.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With at Least One Immediate Adverse Event (AE) After Each Study Vaccination

End point title	Percentage of Subjects With at Least One Immediate Adverse Event (AE) After Each Study Vaccination

End point description:

An AE was any untoward medical occurrence in a subject who received study vaccine without regard to possibility of causal relationship. Any AE that occurred within the first 30 minutes after the administration of study vaccine (bivalent rLP2086, HAV vaccine or saline) was classified as an immediate AE. Here, 'N' signifies those subjects who were evaluable for this measure during specified time period. Safety population included all subjects who received at least 1 dose of the study vaccine (bivalent rLP2086 or HAV vaccine or saline) and had safety information available.

End point type	Secondary

End point timeframe:

Within 30 minutes after Vaccination 1, 2, 3

End point values	Group 1: rLP2086	Group 2: HAV/Saline/HAV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3796	1908		
Units: percentage of subjects				
number (confidence interval 95%)				
Vaccination 1 (N=3796, 1908)	1.05 (0.8 to 1.4)	0.84 (0.5 to 1.4)		
Vaccination 2 (N=3529, 1806)	0.54 (0.3 to 0.8)	0.06 (0 to 0.3)		
Vaccination 3 (N=3313, 1710)	0.45 (0.3 to 0.7)	0.41 (0.2 to 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days Subject Missed School or Work Due to Adverse Events (AEs)

End point title	Number of Days Subject Missed School or Work Due to Adverse Events (AEs)

End point description:

Safety population included all subjects who received at least 1 dose of the study vaccine (bivalent rLP2086 or HAV vaccine or saline) and had safety information available.

End point type	Secondary

End point timeframe:

Vaccination 1 up to 1 month after Vaccination 3

End point values	Group 1: rLP2086	Group 2: HAV/Saline/HAV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3796	1908		
Units: days				
median (full range (min-max))	3 (1 to 110)	3 (1 to 136)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were recorded from Vaccination 1 to 1 month after the last vaccination. SAEs, newly diagnosed chronic medical conditions and medically attended adverse events were recorded from Vaccination 1 to 6 months after the last vaccination

Adverse event reporting additional description:

SAEs and AEs were grouped by system organ class and summarized. AEs collected on the case report form at each visit (non-systematic assessment).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Group 1: rLP2086

Reporting group description:

Randomized to receive Neisseria meningitidis serogroup B (MnB) bivalent recombinant lipoprotein 2086 (rLP2086) vaccine on a 0, 2-, 6-month schedule

Reporting group title	Group 2: HAV/Saline/HAV

Reporting group description:

Randomized to receive hepatitis A virus (HAV) vaccine (Havrix) on a 0-, 6- month schedule and normal saline on 2-month

Serious adverse events	Group 1: rLP2086	Group 2: HAV/Saline/HAV	
Total subjects affected by serious adverse events			
subjects affected / exposed	59 / 3796 (1.55%)	48 / 1908 (2.52%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
CNS germinoma			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	2 / 3796 (0.05%)	3 / 1908 (0.16%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion missed			

subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ectopic pregnancy			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 3796 (0.00%)	2 / 1908 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic reaction			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular torsion			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	3 / 3796 (0.08%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status asthmaticus			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	3 / 3796 (0.08%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 3796 (0.00%)	3 / 1908 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 3796 (0.03%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Substance abuse			
subjects affected / exposed	2 / 3796 (0.05%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Attention deficit or hyperactivity disorder			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			

subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizoaffective disorder			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 3796 (0.03%)	2 / 1908 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	2 / 3796 (0.05%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cartilage injury			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			

subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gun shot wound			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Head injury			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heat stroke			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Snake bite			

subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 3796 (0.03%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			
subjects affected / exposed	1 / 3796 (0.03%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Demyelination			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningism			

subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radicular syndrome			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3796 (0.00%)	2 / 1908 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer perforation			

subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary dyskinesia			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Ingrowing nail			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal tubular necrosis			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperprolactinaemia			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothalamo-pituitary disorder			

subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteochondrosis			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	3 / 3796 (0.08%)	4 / 1908 (0.21%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 3796 (0.00%)	3 / 1908 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	2 / 3796 (0.05%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	2 / 3796 (0.05%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pyelonephritis			
subjects affected / exposed	1 / 3796 (0.03%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal abscess			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute tonsillitis			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast abscess			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbuncle			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal viral infection			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis enterococcal			

subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis enteroviral			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pertussis			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal cyst			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingitis			
subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tick-borne viral encephalitis			

subjects affected / exposed	1 / 3796 (0.03%)	0 / 1908 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 3796 (0.00%)	1 / 1908 (0.05%)	
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: 1 %

Non-serious adverse events	Group 1: rLP2086	Group 2: HAV/Saline/HAV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1671 / 3796 (44.02%)	640 / 1908 (33.54%)	
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	60 / 3796 (1.58%)	30 / 1908 (1.57%)	
occurrences (all)	64	32	
Contusion			
subjects affected / exposed	50 / 3796 (1.32%)	23 / 1908 (1.21%)	
occurrences (all)	54	24	
Fall			
subjects affected / exposed	38 / 3796 (1.00%)	24 / 1908 (1.26%)	
occurrences (all)	39	26	
Nervous system disorders			
Headache			
subjects affected / exposed	249 / 3796 (6.56%)	102 / 1908 (5.35%)	
occurrences (all)	296	122	
General disorders and administration site conditions			

Injection site pain			
subjects affected / exposed	722 / 3796 (19.02%)	149 / 1908 (7.81%)	
occurrences (all)	1007	172	
Pyrexia			
subjects affected / exposed	237 / 3796 (6.24%)	44 / 1908 (2.31%)	
occurrences (all)	264	44	
Injection site erythema			
subjects affected / exposed	142 / 3796 (3.74%)	6 / 1908 (0.31%)	
occurrences (all)	173	6	
Vaccination site pain			
subjects affected / exposed	126 / 3796 (3.32%)	9 / 1908 (0.47%)	
occurrences (all)	173	9	
Fatigue			
subjects affected / exposed	82 / 3796 (2.16%)	19 / 1908 (1.00%)	
occurrences (all)	89	20	
Injection site swelling			
subjects affected / exposed	84 / 3796 (2.21%)	6 / 1908 (0.31%)	
occurrences (all)	100	6	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	89 / 3796 (2.34%)	33 / 1908 (1.73%)	
occurrences (all)	100	39	
Vomiting			
subjects affected / exposed	60 / 3796 (1.58%)	27 / 1908 (1.42%)	
occurrences (all)	65	31	
Abdominal pain			
subjects affected / exposed	47 / 3796 (1.24%)	32 / 1908 (1.68%)	
occurrences (all)	49	33	
Diarrhoea			
subjects affected / exposed	42 / 3796 (1.11%)	17 / 1908 (0.89%)	
occurrences (all)	43	18	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	83 / 3796 (2.19%)	41 / 1908 (2.15%)	
occurrences (all)	104	47	
Cough			

subjects affected / exposed	73 / 3796 (1.92%)	34 / 1908 (1.78%)	
occurrences (all)	77	35	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	76 / 3796 (2.00%)	26 / 1908 (1.36%)	
occurrences (all)	84	27	
Back pain			
subjects affected / exposed	49 / 3796 (1.29%)	26 / 1908 (1.36%)	
occurrences (all)	52	26	
Arthralgia			
subjects affected / exposed	40 / 3796 (1.05%)	27 / 1908 (1.42%)	
occurrences (all)	47	28	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	157 / 3796 (4.14%)	87 / 1908 (4.56%)	
occurrences (all)	188	97	
Nasopharyngitis			
subjects affected / exposed	149 / 3796 (3.93%)	84 / 1908 (4.40%)	
occurrences (all)	170	101	
Pharyngitis			
subjects affected / exposed	75 / 3796 (1.98%)	47 / 1908 (2.46%)	
occurrences (all)	80	49	
Gastroenteritis			
subjects affected / exposed	64 / 3796 (1.69%)	38 / 1908 (1.99%)	
occurrences (all)	68	42	
Bronchitis			
subjects affected / exposed	65 / 3796 (1.71%)	36 / 1908 (1.89%)	
occurrences (all)	66	39	
Sinusitis			
subjects affected / exposed	54 / 3796 (1.42%)	33 / 1908 (1.73%)	
occurrences (all)	58	34	
Urinary tract infection			
subjects affected / exposed	50 / 3796 (1.32%)	24 / 1908 (1.26%)	
occurrences (all)	55	34	
Pharyngitis streptococcal			

subjects affected / exposed	45 / 3796 (1.19%)	22 / 1908 (1.15%)	
occurrences (all)	50	25	
Tonsillitis			
subjects affected / exposed	38 / 3796 (1.00%)	21 / 1908 (1.10%)	
occurrences (all)	41	22	
Viral pharyngitis			
subjects affected / exposed	41 / 3796 (1.08%)	13 / 1908 (0.68%)	
occurrences (all)	59	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 July 2012	Age range was changed to included subjects of 10 years; Subject withdrawal guidelines were clarified; AE reporting section was updated; Primary and secondary objectives and endpoints were revised to describe specific safety-related outcome measures; An exclusion criterion regarding subjects who were scheduled to receive human papilloma virus (HPV) vaccination as part of a series was added; Permitted treatment was revised to make non study vaccine prohibition consistent with other protocols; Definition of medically attended AE and newly diagnosed chronic medical condition were added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported