



Clinical trial results:

A phase III, observer-blind, randomized, multi-country study to assess the reactogenicity and safety of the Porcine circovirus (PCV) free liquid formulation of GSK's oral live attenuated human rotavirus (HRV) vaccine as compared to the lyophilized formulation of the GSK's HRV vaccine, when administered as a 2-dose vaccination in infants starting at age 6-12 weeks.

Summary

EudraCT number	2018-001986-18
Trial protocol	Outside EU/EEA
Global end of trial date	30 November 2020

Results information

Result version number	v1
This version publication date	10 June 2021
First version publication date	10 June 2021

Trial information

Trial identification

Sponsor protocol code	208236
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03954743
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline, 044 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2020
Global end of trial reached?	Yes
Global end of trial date	30 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the reactogenicity of the liquid HRV vaccine and lyophilized HRV vaccine in terms of solicited adverse events (AEs) during the 8-day (Day 1-Day 8) follow-up period after each vaccination.
- To assess the safety of the liquid HRV vaccine and lyophilized HRV vaccine in terms of unsolicited AEs during the 31-day (Day 1-Day 31) follow-up period after each vaccination and serious adverse events (SAEs) during the entire study period.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of the vaccines, with appropriate medical treatment readily available in case of anaphylaxis and syncope.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 July 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 239
Country: Number of subjects enrolled	Hong Kong: 364
Country: Number of subjects enrolled	Taiwan: 215
Country: Number of subjects enrolled	Turkey: 275
Country: Number of subjects enrolled	United States: 258
Worldwide total number of subjects	1351
EEA total number of subjects	0

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)	1351
Children (2-11 years)	0

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:

The study was conducted in 5 countries/regions (Canada, Hong Kong, Taiwan, Turkey and United States).

Pre-assignment

Screening details:

All 1351 participants enrolled in the study, received a study vaccination and were included in the Exposed Set.

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

Blinding implementation details:

Data were collected in an observer-blind manner. By observer-blind, it is meant that during the study period, the vaccine(s) recipient and those responsible for the evaluation of any study endpoint (e.g. safety and reactogenicity) were all unaware of which vaccine was administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	HRV PCV-free Liq Group

Arm description:

Subjects aged 6 to 12 weeks at the time of first vaccination, who received two doses of oral live-attenuated human rotavirus (HRV) porcine circovirus (PCV)-free vaccine in liquid formulation, one at Day 1 and one at Month 1 or Month 2, according to the immunization schedule for rotavirus (RV) vaccine administration in participating countries. PCV-free implies no detection of PCV-1 and PCV-2 according to the limit of detection of the tests used.

Arm type	Experimental
Investigational medicinal product name	PCV-free liquid formulation of GSK Biologicals' oral live attenuated HRV vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

2 doses administered orally at Day 1 and at Month 1 or Month 2, according to the immunization schedule for RV vaccine administration in participating countries.

Arm title	HRV Lyo Group
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Arm description:

Subjects aged 6 to 12 weeks at the time of first vaccination, who received two doses of oral live-attenuated human rotavirus (HRV) vaccine in lyophilized formulation, one at Day 1 and one at Month 1 or Month 2, according to the immunization schedule for rotavirus (RV) vaccine administration in participating countries.

Arm type	Active comparator
Investigational medicinal product name	Lyophilized formulation of GSK's oral live attenuated HRV vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

2 doses administered orally at Day 1 and at Month 1 or Month 2, according to the immunization schedule for RV vaccine administration in participating countries.

Number of subjects in period 1	HRV PCV-free Liq Group	HRV Lyo Group
Started	677	674
Completed	653	657
Not completed	24	17
Adverse event, non-fatal	1	-
MIGRATED / MOVED FROM THE STUDY AREA	3	1
Lost to follow-up	6	4
Protocol deviation	1	-
CONSENT WITHDRAWAL NOT DUE TO ADV. EVENT	13	12

Baseline characteristics

Reporting groups

Reporting group title	HRV PCV-free Liq Group
Reporting group description:	
Subjects aged 6 to 12 weeks at the time of first vaccination, who received two doses of oral live-attenuated human rotavirus (HRV) porcine circovirus (PCV)-free vaccine in liquid formulation, one at Day 1 and one at Month 1 or Month 2, according to the immunization schedule for rotavirus (RV) vaccine administration in participating countries. PCV-free implies no detection of PCV-1 and PCV-2 according to the limit of detection of the tests used.	
Reporting group title	HRV Lyo Group
Reporting group description:	
Subjects aged 6 to 12 weeks at the time of first vaccination, who received two doses of oral live-attenuated human rotavirus (HRV) vaccine in lyophilized formulation, one at Day 1 and one at Month 1 or Month 2, according to the immunization schedule for rotavirus (RV) vaccine administration in participating countries.	

Reporting group values	HRV PCV-free Liq Group	HRV Lyo Group	Total
Number of subjects	677	674	1351
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)	677	674	1351
Children (2-11 years)	0	0	0
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: weeks			
arithmetic mean	9.0	9.0	
standard deviation	± 1.5	± 1.5	-
Sex: Female, Male			
Units: Subjects			
Female	336	357	693
Male	341	317	658
Race/Ethnicity, Customized			
Units: Subjects			
American Indian Or Alaska Native	2	1	3
Asian	302	301	603
Black Or African American	14	10	24
Native Hawaiian Or Other Pacific Islander	0	2	2
Other, Not specified	20	14	34
White	339	346	685

End points

End points reporting groups

Reporting group title	HRV PCV-free Liq Group
Reporting group description:	
Subjects aged 6 to 12 weeks at the time of first vaccination, who received two doses of oral live-attenuated human rotavirus (HRV) porcine circovirus (PCV)-free vaccine in liquid formulation, one at Day 1 and one at Month 1 or Month 2, according to the immunization schedule for rotavirus (RV) vaccine administration in participating countries. PCV-free implies no detection of PCV-1 and PCV-2 according to the limit of detection of the tests used.	
Reporting group title	HRV Lyo Group
Reporting group description:	
Subjects aged 6 to 12 weeks at the time of first vaccination, who received two doses of oral live-attenuated human rotavirus (HRV) vaccine in lyophilized formulation, one at Day 1 and one at Month 1 or Month 2, according to the immunization schedule for rotavirus (RV) vaccine administration in participating countries.	

Primary: Number of subjects with any solicited general adverse events (AEs) after the first vaccination

End point title	Number of subjects with any solicited general adverse events (AEs) after the first vaccination ^[1]
End point description:	
Assessed solicited general AEs were fever (defined as temperature $\geq 38.0^{\circ}\text{C}/100.4^{\circ}\text{F}$, the preferred location for measuring temperature in this study being the oral cavity, the axilla and the rectum), irritability/fussiness, diarrhea (defined as passage of three or more looser than normal stools within a day), vomiting (defined as one or more episodes of forceful emptying of partially digested stomach contents ≥ 1 hour after feeding within a day), loss of appetite and cough/runny nose. Any = occurrence of AE regardless of intensity grade or relation to study vaccination.	
End point type	Primary
End point timeframe:	
During the 8-day follow-up period after the first vaccination (vaccines administered at Day 1)	

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HRV PCV-free Liq Group	HRV Lyo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	677	674		
Units: Subjects				
Cough / Runny Nose, Any	139	166		
Diarrhea, Any	41	47		
Fever, $\geq 38.0^{\circ}\text{C}$	27	21		
Irritability / Fussiness, Any	431	428		
Loss of appetite, Any	201	186		
Vomiting, Any	113	122		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any solicited general adverse events (AEs) after the second vaccination

End point title	Number of subjects with any solicited general adverse events (AEs) after the second vaccination ^[2]
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End point description:

Assessed solicited general AEs were fever (defined as temperature $\geq 38.0^{\circ}\text{C}/100.4^{\circ}\text{F}$, the preferred location for measuring temperature in this study being the oral cavity, the axilla and the rectum), irritability/fussiness, diarrhea (defined as passage of three or more looser than normal stools within a day), vomiting (defined as one or more episodes of forceful emptying of partially digested stomach contents ≥ 1 hour after feeding within a day), loss of appetite and cough/runny nose. Any = occurrence of AE regardless of intensity grade or relation to study vaccination.

End point type	Primary
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End point timeframe:

During the 8-day follow-up period after the second vaccination (vaccines administered at Month 1 or Month 2)

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HRV PCV-free Liq Group	HRV Lyo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	663	657		
Units: Subjects				
Cough / Runny Nose, Any	147	145		
Diarrhea, Any	28	36		
Fever, $\geq 38.0^{\circ}\text{C}$	46	40		
Irritability / Fussiness, Any	368	362		
Loss of appetite, Any	170	168		
Vomiting, Any	82	88		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any unsolicited AEs

End point title	Number of subjects with any unsolicited AEs ^[3]
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End point description:

An unsolicited AE is defined as any untoward medical occurrence in a clinical study subject, temporally associated with the use of a study treatment, whether or not considered related to the study treatment, and reported in addition to those solicited during the clinical study and any 'solicited' AE with onset outside the specified period of follow-up for solicited symptoms. Any = occurrence of AE regardless of intensity grade or relation to study vaccination.

End point type	Primary
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End point timeframe:

During the 31-day follow-up period across doses (vaccines administered at Day 1 and at Month 1 or Month 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HRV PCV-free Liq Group	HRV Lyo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	677	674		
Units: Subjects	201	206		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any serious adverse events (SAEs)

End point title	Number of subjects with any serious adverse events (SAEs) ^[4]
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End point description:

An SAE is defined as any untoward medical occurrence that results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization and/or results in disability/incapacity. Any = occurrence of SAE regardless of intensity grade or relation to study vaccination.

End point type	Primary
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End point timeframe:

Throughout the study period (from Day 1 up to Month 7 or Month 8)

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HRV PCV-free Liq Group	HRV Lyo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	677	674		
Units: Subjects	39	38		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: During the 8-day (Day 1 to Day 8) follow-up period after each vaccination. Unsolicited AEs: During the 31-day (Day 1 to Day 31) follow-up period after any vaccination. SAEs: Throughout the study period (from Day 1 up to Month 7 or Month 8).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	HRV Lyo Group
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Reporting group description:

Subjects aged 6 to 12 weeks at the time of first vaccination, who received two doses of oral live-attenuated human rotavirus (HRV) vaccine in lyophilized formulation, one at Day 1 and one at Month 1 or Month 2, according to the immunization schedule for rotavirus (RV) vaccine administration in participating countries.

Reporting group title	HRV PCV-free Liq Group
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Reporting group description:

Subjects aged 6 to 12 weeks at the time of first vaccination, who received two doses of oral live-attenuated human rotavirus (HRV) porcine circovirus (PCV)-free vaccine in liquid formulation, one at Day 1 and one at Month 1 or Month 2, according to the immunization schedule for rotavirus (RV) vaccine administration in participating countries. PCV-free implies no detection of PCV-1 and PCV-2 according to the limit of detection of the tests used.

Serious adverse events	HRV Lyo Group	HRV PCV-free Liq Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 674 (5.64%)	39 / 677 (5.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear canal abrasion			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			

subjects affected / exposed	1 / 674 (0.15%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Osteogenesis imperfecta			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scaphocephaly			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Kawasaki's disease			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 674 (0.45%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			

subjects affected / exposed	1 / 674 (0.15%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
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			
Acute respiratory failure			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (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			
Eczema			
subjects affected / exposed	1 / 674 (0.15%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	1 / 674 (0.15%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	2 / 674 (0.30%)	3 / 677 (0.44%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Citrobacter infection			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovirus infection			
subjects affected / exposed	1 / 674 (0.15%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 674 (0.15%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema subitum			
subjects affected / exposed	3 / 674 (0.45%)	3 / 677 (0.44%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	4 / 674 (0.59%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis enteroviral			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			

subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 674 (0.00%)	3 / 677 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Human bocavirus infection			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 674 (0.30%)	3 / 677 (0.44%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis streptococcal			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus infection			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			

subjects affected / exposed	2 / 674 (0.30%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Picornavirus infection			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (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	3 / 674 (0.45%)	3 / 677 (0.44%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	2 / 674 (0.30%)	5 / 677 (0.74%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			
subjects affected / exposed	2 / 674 (0.30%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Roseola			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			

subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	6 / 674 (0.89%)	5 / 677 (0.74%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	4 / 674 (0.59%)	6 / 677 (0.89%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 674 (0.15%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral rash			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (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			
Lactose intolerance			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
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	HRV Lyo Group	HRV PCV-free Liq Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	571 / 674 (84.72%)	591 / 677 (87.30%)	
Pregnancy, puerperium and perinatal conditions			
Weight decrease neonatal			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
Face oedema			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	3 / 674 (0.45%)	1 / 677 (0.15%)	
occurrences (all)	3	1	
Ill-defined disorder			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Injection site pain			
subjects affected / exposed	2 / 674 (0.30%)	2 / 677 (0.30%)	
occurrences (all)	2	2	
Irritability postvaccinal			
subjects affected / exposed	0 / 674 (0.00%)	2 / 677 (0.30%)	
occurrences (all)	0	2	
Pain			
subjects affected / exposed	1 / 674 (0.15%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	70 / 674 (10.39%)	92 / 677 (13.59%)	
occurrences (all)	79	103	
Swelling			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Swelling face			

subjects affected / exposed occurrences (all)	0 / 674 (0.00%) 0	1 / 677 (0.15%) 1	
Vaccination site pain subjects affected / exposed occurrences (all)	4 / 674 (0.59%) 5	5 / 677 (0.74%) 6	
Immune system disorders Milk allergy subjects affected / exposed occurrences (all)	3 / 674 (0.45%) 3	0 / 677 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all)	0 / 674 (0.00%) 0	2 / 677 (0.30%) 2	
Cough subjects affected / exposed occurrences (all)	239 / 674 (35.46%) 323	241 / 677 (35.60%) 295	
Nasal congestion subjects affected / exposed occurrences (all)	4 / 674 (0.59%) 4	5 / 677 (0.74%) 5	
Rhinorrhoea subjects affected / exposed occurrences (all)	10 / 674 (1.48%) 12	2 / 677 (0.30%) 2	
Productive cough subjects affected / exposed occurrences (all)	0 / 674 (0.00%) 0	1 / 677 (0.15%) 1	
Sneezing subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	0 / 677 (0.00%) 0	
Stridor subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	0 / 677 (0.00%) 0	
Wheezing subjects affected / exposed occurrences (all)	0 / 674 (0.00%) 0	1 / 677 (0.15%) 1	
Psychiatric disorders			

Irritability subjects affected / exposed occurrences (all)	487 / 674 (72.26%) 796	512 / 677 (75.63%) 812	
Investigations			
Body temperature increased subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	2 / 677 (0.30%) 2	
Cardiac murmur subjects affected / exposed occurrences (all)	0 / 674 (0.00%) 0	1 / 677 (0.15%) 1	
Weight decreased subjects affected / exposed occurrences (all)	0 / 674 (0.00%) 0	1 / 677 (0.15%) 1	
Injury, poisoning and procedural complications			
Arthropod bite subjects affected / exposed occurrences (all)	0 / 674 (0.00%) 0	1 / 677 (0.15%) 1	
Vaccination complication subjects affected / exposed occurrences (all)	9 / 674 (1.34%) 9	7 / 677 (1.03%) 7	
Congenital, familial and genetic disorders			
Ankyloglossia congenital subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	2 / 677 (0.30%) 2	
Buried penis syndrome subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	0 / 677 (0.00%) 0	
Developmental hip dysplasia subjects affected / exposed occurrences (all)	0 / 674 (0.00%) 0	1 / 677 (0.15%) 1	
Hydrocele subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	0 / 677 (0.00%) 0	
Nervous system disorders			
Lethargy			

subjects affected / exposed occurrences (all)	2 / 674 (0.30%) 3	1 / 677 (0.15%) 1	
Somnolence subjects affected / exposed occurrences (all)	5 / 674 (0.74%) 6	2 / 677 (0.30%) 3	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	1 / 677 (0.15%) 1	
Eye disorders Blepharitis subjects affected / exposed occurrences (all)	0 / 674 (0.00%) 0	1 / 677 (0.15%) 1	
Dacryostenosis acquired subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	0 / 677 (0.00%) 0	
Eye discharge subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	1 / 677 (0.15%) 1	
Keratitis subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	0 / 677 (0.00%) 0	
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	0 / 677 (0.00%) 0	
Abdominal distension subjects affected / exposed occurrences (all)	1 / 674 (0.15%) 1	0 / 677 (0.00%) 0	
Abdominal pain subjects affected / exposed occurrences (all)	3 / 674 (0.45%) 3	1 / 677 (0.15%) 1	
Abnormal faeces subjects affected / exposed occurrences (all)	0 / 674 (0.00%) 0	2 / 677 (0.30%) 2	
Anal fissure			

subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
Aphthous ulcer		
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)
occurrences (all)	1	0
Change of bowel habit		
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)
occurrences (all)	1	0
Constipation		
subjects affected / exposed	3 / 674 (0.45%)	10 / 677 (1.48%)
occurrences (all)	3	10
Diarrhoea		
subjects affected / exposed	81 / 674 (12.02%)	61 / 677 (9.01%)
occurrences (all)	100	76
Eructation		
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)
occurrences (all)	1	0
Faeces discoloured		
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
Flatulence		
subjects affected / exposed	7 / 674 (1.04%)	2 / 677 (0.30%)
occurrences (all)	7	2
Gastrointestinal pain		
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)
occurrences (all)	2	0
Gastrooesophageal reflux disease		
subjects affected / exposed	3 / 674 (0.45%)	5 / 677 (0.74%)
occurrences (all)	3	5
Haematochezia		
subjects affected / exposed	4 / 674 (0.59%)	2 / 677 (0.30%)
occurrences (all)	4	3
Infantile colic		
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
Infantile spitting up		

subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Infrequent bowel movements			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Mucous stools			
subjects affected / exposed	1 / 674 (0.15%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
Salivary hypersecretion			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Teething			
subjects affected / exposed	7 / 674 (1.04%)	7 / 677 (1.03%)	
occurrences (all)	8	9	
Vomiting			
subjects affected / exposed	170 / 674 (25.22%)	153 / 677 (22.60%)	
occurrences (all)	219	198	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	4 / 674 (0.59%)	2 / 677 (0.30%)	
occurrences (all)	4	2	
Dermatitis allergic			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Dermatitis atopic			
subjects affected / exposed	2 / 674 (0.30%)	6 / 677 (0.89%)	
occurrences (all)	2	6	
Dermatitis contact			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Dermatitis diaper			
subjects affected / exposed	5 / 674 (0.74%)	6 / 677 (0.89%)	
occurrences (all)	6	6	
Dry skin			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	

Eczema			
subjects affected / exposed	8 / 674 (1.19%)	16 / 677 (2.36%)	
occurrences (all)	8	17	
Eczema infantile			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	1 / 674 (0.15%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
Petechiae			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	9 / 674 (1.34%)	10 / 677 (1.48%)	
occurrences (all)	9	11	
Rash erythematous			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
Rash macular			
subjects affected / exposed	4 / 674 (0.59%)	0 / 677 (0.00%)	
occurrences (all)	4	0	
Seborrhoeic dermatitis			
subjects affected / exposed	3 / 674 (0.45%)	3 / 677 (0.44%)	
occurrences (all)	3	3	
Musculoskeletal and connective tissue disorders			
Acquired plagiocephaly			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	9 / 674 (1.34%)	8 / 677 (1.18%)	
occurrences (all)	9	8	
Bronchitis			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
Candida nappy rash			

subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)
occurrences (all)	1	0
Conjunctivitis viral		
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)
occurrences (all)	1	0
Conjunctivitis		
subjects affected / exposed	7 / 674 (1.04%)	3 / 677 (0.44%)
occurrences (all)	7	3
Croup infectious		
subjects affected / exposed	3 / 674 (0.45%)	2 / 677 (0.30%)
occurrences (all)	3	2
Ear infection		
subjects affected / exposed	1 / 674 (0.15%)	1 / 677 (0.15%)
occurrences (all)	1	1
Enterovirus infection		
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)
occurrences (all)	1	0
Fungal skin infection		
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)
occurrences (all)	1	0
Gastroenteritis		
subjects affected / exposed	3 / 674 (0.45%)	1 / 677 (0.15%)
occurrences (all)	3	1
Gastroenteritis viral		
subjects affected / exposed	2 / 674 (0.30%)	0 / 677 (0.00%)
occurrences (all)	2	0
Hand-foot-and-mouth disease		
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)
occurrences (all)	1	0
Hordeolum		
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)
occurrences (all)	1	0
Influenza		
subjects affected / exposed	1 / 674 (0.15%)	2 / 677 (0.30%)
occurrences (all)	1	2
Nasopharyngitis		

subjects affected / exposed	22 / 674 (3.26%)	30 / 677 (4.43%)
occurrences (all)	24	31
Omphalitis		
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
Oral candidiasis		
subjects affected / exposed	2 / 674 (0.30%)	3 / 677 (0.44%)
occurrences (all)	2	4
Otitis externa		
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
Otitis media		
subjects affected / exposed	3 / 674 (0.45%)	8 / 677 (1.18%)
occurrences (all)	3	9
Otitis media acute		
subjects affected / exposed	3 / 674 (0.45%)	1 / 677 (0.15%)
occurrences (all)	3	1
Paronychia		
subjects affected / exposed	3 / 674 (0.45%)	0 / 677 (0.00%)
occurrences (all)	3	0
Pharyngitis		
subjects affected / exposed	2 / 674 (0.30%)	6 / 677 (0.89%)
occurrences (all)	2	7
Pneumonia viral		
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
Pustule		
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
Respiratory syncytial virus infection		
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)
occurrences (all)	1	0
Respiratory tract infection		
subjects affected / exposed	46 / 674 (6.82%)	47 / 677 (6.94%)
occurrences (all)	53	52
Rhinovirus infection		

subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
Skin infection			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Tinea barbae			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Tinea capitis			
subjects affected / exposed	0 / 674 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	34 / 674 (5.04%)	26 / 677 (3.84%)	
occurrences (all)	35	31	
Urinary tract infection			
subjects affected / exposed	2 / 674 (0.30%)	0 / 677 (0.00%)	
occurrences (all)	2	0	
Viral rash			
subjects affected / exposed	2 / 674 (0.30%)	0 / 677 (0.00%)	
occurrences (all)	2	0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 674 (0.15%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	261 / 674 (38.72%)	290 / 677 (42.84%)	
occurrences (all)	361	371	
Increased appetite			
subjects affected / exposed	1 / 674 (0.15%)	0 / 677 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 September 2019	The protocol was amended primarily to include the possibility of home visit at Visit 3 (Month 2-4) safety assessments for authorized Canadian sites only. In addition, other administrative and editorial changes required in the protocol were also updated.
30 March 2020	This protocol amendment outlines measures that may be applicable during special circumstances (e.g., COVID-19 pandemic). The purpose of the amendment is to protect participant's welfare and safety, and as far as possible ensure the potential benefit to the participant and promote data integrity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported