Clinical trial results:
A phase III, randomized, open study to assess the immunogenicity, reactogenicity and safety of two different formulations of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix, when given as a two-dose primary vaccination, in healthy infants with no previous history of rotavirus illness or vaccination

Summary

EudraCT number	2012-001875-35
Trial protocol	Outside EU/EEA
Global end of trial date	28 December 2019

Results information

Result version number	v1 (current)
This version publication date	30 November 2020
First version publication date	30 November 2020

Trial information

Trial identification

Sponsor protocol code	116566

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02141204
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	GSK Response Center, GlaxoSmithKline, 044 208-990-4466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 044 208-990-4466, 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	14 September 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 December 2019
Global end of trial reached?	Yes
Global end of trial date	28 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate non-inferiority of GSK Biologicals' HRV liquid vaccine compared to GSK Biologicals' HRV lyophilized vaccine in terms of geometric mean concentrations (GMCs) for anti-RV antibodies, one month post dose 2 of HRV liquid vaccine and HRV lyophilized vaccine.
Criterion: Non-inferiority will be stated if the lower limit of the two-sided 95% confidence interval (CI) for the ratio of anti RV IgA antibody GMCs between HRV liquid vaccine over the HRV lyophilized vaccine, one month after dose 2 is greater than or equal to 0.5.

Protection of trial subjects:

All subjects were observed closely for 30 min following the administration of the vaccine, with appropriate medical treatment readily available in case of anaphylaxis. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up for 30 days after the last vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	India: 451
Worldwide total number of subjects	451
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)	451
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 at 8 centers in India.

Pre-assignment

Screening details:

Out of 451 subjects enrolled in the study, 1 subject did not receive any study treatment and 1 vaccinated subject was eliminated from all analysis due to incorrect impartial witness.
449 subjects were vaccinated and included in the Exposed Set, 419 subjects completed the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	HRV Liq Group

Arm description:

Subjects aged 6 to 10 weeks at the time of first vaccination, who received two oral doses of Liquid Human Rotavirus Vaccine (HRV) according to a two-dose schedule, at Day 1 and Month 1.

Arm type	Experimental
Investigational medicinal product name	Liquid Human Rotavirus Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Two doses administered orally according to a 0, 1-month schedule.

Arm title	HRV Lyo Group

Arm description:

Subjects aged 6 to 10 weeks at the time of first vaccination who received two oral doses of Lyophilized Human Rotavirus Vaccine (HRV) according to a two-dose schedule, at Day 1 and Month 1.

Arm type	Active comparator
Investigational medicinal product name	Lyophilized Human Rotavirus Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Two doses administered orally according to a 0, 1-month schedule.

Number of subjects in period 1[1]	HRV Liq Group	HRV Lyo Group
Started	224	225
Completed	209	210
Not completed	15	15
CONSENT WITHDRAWAL NOT DUE TO AE	1	2
NOT WILLING TO PARTICIPATE THIS VISIT	9	7
MIGRATED / MOVED FROM THE STUDY AREA	3	5
Lost to follow-up	2	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of 451 subjects enrolled in the study, 1 subject did not receive any study treatment and 1 vaccinated subject was eliminated from all analysis due to incorrect impartial witness.
449 subjects were vaccinated and included in the Exposed Set, 419 subjects completed the study.

Baseline characteristics

Reporting groups	
Reporting group title	HRV Liq Group
Reporting group description:	
Subjects aged 6 to 10 weeks at the time of first vaccination, who received two oral doses of Liquid Human Rotavirus Vaccine (HRV) according to a two-dose schedule, at Day 1 and Month 1.	
Reporting group title	HRV Lyo Group
Reporting group description:	
Subjects aged 6 to 10 weeks at the time of first vaccination who received two oral doses of Lyophilized Human Rotavirus Vaccine (HRV) according to a two-dose schedule, at Day 1 and Month 1.	

Reporting group values	HRV Liq Group	HRV Lyo Group	Total
Number of subjects	224	225	449
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)	224	225	449
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	6.8	6.8	
standard deviation	± 1.0	± 1.1	-
Sex: Female, Male Units: Subjects			
Female	100	120	220
Male	124	105	229
Race/Ethnicity, Customized Units: Subjects			
Asian	224	225	449

End points

End points reporting groups

Reporting group title	HRV Liq Group
Reporting group description:	
Subjects aged 6 to 10 weeks at the time of first vaccination, who received two oral doses of Liquid Human Rotavirus Vaccine (HRV) according to a two-dose schedule, at Day 1 and Month 1.	
Reporting group title	HRV Lyo Group
Reporting group description:	
Subjects aged 6 to 10 weeks at the time of first vaccination who received two oral doses of Lyophilized Human Rotavirus Vaccine (HRV) according to a two-dose schedule, at Day 1 and Month 1.	

Primary: Anti-rotavirus (Anti-RV) immunoglobulin A (IgA) antibody concentrations

End point title	Anti-rotavirus (Anti-RV) immunoglobulin A (IgA) antibody concentrations
End point description:	
Serum anti-RV IgA antibody concentrations were expressed as geometric mean concentrations (GMCs). Analysis was performed on Per Protocol Set (PPS) for immunogenicity, which included all eligible subjects who received both doses of HRV vaccine, complied with vaccination schedule and for whom immunogenicity data were available at the specified time point.	
End point type	Primary
End point timeframe:	
At Month 2	

End point values	HRV Liq Group	HRV Lyo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	192		
Units: U/mL				
geometric mean (confidence interval 95%)				
Anti-RV IgA	90.25 (67.28 to 121.06)	94.16 (70.29 to 126.13)		

Statistical analyses

Statistical analysis title	Anti-RV IgA GMCs (non-inferiority)
Statistical analysis description:	
Non-inferiority comparison between GSK Biologicals' HRV liquid vaccine (HRV Liq Group) and GSK Biologicals' HRV lyophilized vaccine (HRV Lyo Group) in terms of geometric mean concentrations (GMCs) for anti-RV antibodies, one month after the administration of the second dose of study vaccine.	
Comparison groups	HRV Liq Group v HRV Lyo Group

Number of subjects included in analysis	381
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	ANCOVA
Parameter estimate	GMC ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.34

Notes:

[1] - Lower limit (LL) of the two-sided 95% confidence interval (CI) for the ratio of anti-RV IgA antibody GMCs between HRV Liq Group over the HRV Lyo Group should be greater than or equal to (≥) 0.5.

Secondary: Percentage of seroconverted subjects for anti-RV IgA antibodies

End point title	Percentage of seroconverted subjects for anti-RV IgA antibodies

End point description:

Seroconversion is defined as: - for subjects with a pre-vaccination anti-RV IgA antibody concentration lower than (<) 20 U/mL, seroconversion is achieved when the post-vaccination concentration is greater than or equal to (≥) 20 U/mL and
- for subjects with a pre-vaccination anti-RV IgA antibody concentration ≥ 20 U/mL, seroconversion is achieved when the post-vaccination concentration is ≥ 2 times the pre-vaccination concentration.
Analysis was performed on PPS for immunogenicity, which included all eligible subjects who received both doses of HRV vaccine, complied with vaccination schedule and for whom immunogenicity data were available at the specified time point.

End point type	Secondary

End point timeframe:

At Month 2

End point values	HRV Liq Group	HRV Lyo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	192		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-RV IgA	54.5 (47.1 to 61.7)	50.0 (42.7 to 57.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general adverse events (AEs)

End point title	Number of subjects with any solicited general adverse events (AEs)

End point description:

Solicited general AEs assessed were fever (defined as temperature ≥ 38.0°C/100.4°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.
Analysis was performed on the Exposed Set (ES), which included all subjects with at least one study vaccine administration documented and with the diary card completed.

End point type	Secondary

End point timeframe:

During the 8-day follow-up period after each vaccination (vaccines administered at Day 1 and Month 1)

End point values	HRV Liq Group	HRV Lyo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	225		
Units: Subjects				
Cough/Runny Nose (Dose 1), Any (N=224;225)	22	24		
Cough/Runny Nose (Dose 2), Any (N=214;213)	17	23		
Diarrhea (Dose 1), Any (N=224;225)	4	2		
Diarrhea (Dose 2), Any (N=214;213)	3	3		
Fever (Dose 1), ≥ 38.0°C (N=224;225)	57	48		
Fever (Dose 2), ≥ 38.0°C (N=214;213)	50	53		
Irritability/Fussiness (Dose 1), Any (N=224;225)	71	83		
Irritability/Fussiness (Dose 2), Any (N=214;213)	56	61		
Loss of appetite (Dose 1), Any (N=224;225)	33	42		
Loss of appetite (Dose 2), Any (N=214;213)	28	25		
Vomiting (Dose 1), Any (N=224;225)	22	22		
Vomiting (Dose 2), Any (N=214;213)	15	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited AEs

End point title	Number of subjects with any unsolicited AEs

End point description:

An unsolicited AE is defined as any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product, 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 AE. Any = occurrence of AE regardless of intensity grade or relation to study vaccination.
Analysis was performed on the ES, which included all subjects with at least one study vaccine administration documented.

End point type	Secondary

End point timeframe:

During the 31-day follow-up period across doses (vaccines administered at Day 1 and Month 1)

End point values	HRV Liq Group	HRV Lyo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	225		
Units: Subjects				
Any AE(s)	54	58		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any serious adverse events (SAEs)

End point description:

SAEs assessed included any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization and/or resulted in disability/incapacity.
Any = occurrence of SAE regardless of intensity grade or relation to study vaccination.
Analysis was performed on the ES, which included all subjects with at least one study vaccine administration documented.

End point type	Secondary

End point timeframe:

Throughout the study period (from Day 1 up to Month 2)

End point values	HRV Liq Group	HRV Lyo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	225		
Units: Subjects				
Any SAE(s)	7	2		

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 HRV vaccination. Unsolicited AEs: During the 31-day (Day 1 to Day 31) follow-up period after any HRV vaccination. SAEs: Throughout the study period (Day 1 to Month 2).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	HRV Liq Group

Reporting group description:

Subjects aged 6 to 10 weeks at the time of first vaccination, who received two oral doses of Liquid Human Rotavirus Vaccine (HRV) according to a two-dose schedule, at Day 1 and Month 1.

Reporting group title	HRV Lyo Group

Reporting group description:

Subjects aged 6 to 10 weeks at the time of first vaccination who received two oral doses of Lyophilized Human Rotavirus Vaccine (HRV) according to a two-dose schedule, at Day 1 and Month 1.

Serious adverse events	HRV Liq Group	HRV Lyo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 224 (3.13%)	2 / 225 (0.89%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal			

disorders			
Respiratory distress			
subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	3 / 224 (1.34%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 224 (0.89%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	HRV Liq Group	HRV Lyo Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	146 / 224 (65.18%)	162 / 225 (72.00%)	
Injury, poisoning and procedural complications			

Arthropod bite			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Crying			
subjects affected / exposed	1 / 224 (0.45%)	2 / 225 (0.89%)	
occurrences (all)	1	2	
Injection site pain			
subjects affected / exposed	10 / 224 (4.46%)	7 / 225 (3.11%)	
occurrences (all)	12	9	
Injection site swelling			
subjects affected / exposed	13 / 224 (5.80%)	12 / 225 (5.33%)	
occurrences (all)	17	17	
Pain			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	87 / 224 (38.84%)	91 / 225 (40.44%)	
occurrences (all)	119	116	
Ear and labyrinth disorders			
Otorrhoea			
subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Abnormal faeces			

subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	6 / 224 (2.68%)	6 / 225 (2.67%)	
occurrences (all)	8	8	
Faeces discoloured			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	2 / 224 (0.89%)	0 / 225 (0.00%)	
occurrences (all)	2	0	
Oral disorder			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Regurgitation			
subjects affected / exposed	1 / 224 (0.45%)	1 / 225 (0.44%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	33 / 224 (14.73%)	31 / 225 (13.78%)	
occurrences (all)	38	38	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	37 / 224 (16.52%)	47 / 225 (20.89%)	
occurrences (all)	44	58	
Nasal congestion			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	1 / 224 (0.45%)	4 / 225 (1.78%)	
occurrences (all)	1	4	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	2 / 224 (0.89%)	0 / 225 (0.00%)	
occurrences (all)	2	0	
Intertrigo			

subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Rash papular			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Psychiatric disorders			
Irritability			
subjects affected / exposed	87 / 224 (38.84%)	102 / 225 (45.33%)	
occurrences (all)	128	144	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Fungal skin infection			
subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	0 / 224 (0.00%)	1 / 225 (0.44%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	2 / 224 (0.89%)	5 / 225 (2.22%)	
occurrences (all)	2	6	
Respiratory tract infection			
subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences (all)	1	0	
Rhinitis			

subjects affected / exposed	1 / 224 (0.45%)	1 / 225 (0.44%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	7 / 224 (3.13%)	5 / 225 (2.22%)	
occurrences (all)	8	5	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	44 / 224 (19.64%)	53 / 225 (23.56%)	
occurrences (all)	61	68	
Dehydration			
subjects affected / exposed	1 / 224 (0.45%)	0 / 225 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2013	NDAC- Vaccines (New Drug Advisory Committee on Vaccines) of Drugs Controller General of India (DCGI) recommended to conduct this study as a Phase IV study instead of phase III as initially planned because Rotarix liquid file application is considered as a line extension of Rotarix Lyophilized formulation. The protocol was amended to adapt the change recommended by NDAC-Vaccines of DCGI.
31 October 2017	- The phase of this clinical trial is revised from Phase IV to Phase III. - The study objectives have been updated to include a confirmatory primary objective and the study has been powered accordingly. - The statistical considerations have been revised to define the success criteria for the primary objective. - Collection and testing of stool samples from subjects who develop gastroenteritis (GE) during the study period is removed. - The study procedures, list of assays and section on biological samples evaluation have been updated accordingly.
30 October 2019	- The PPS was modified to include subjects seroposi-tive at baseline. - The statistical method to derive the 95% CI for the GMC group ratio was revised to be an ANCOVA. - The seroconversion threshold was redefined to account for seropositive subjects at pre-vaccination.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported