



Clinical trial results:

A phase 3 open-label study to evaluate the immunogenicity and safety of a mixed (HEXA/PENTA/HEXA) primary series schedule that includes V419 (PR5I) at 2 and 6 months of age and Pediacel at 4 months of age.

Summary

EudraCT number	2012-004221-25
Trial protocol	ES
Global end of trial date	19 March 2014

Results information

Result version number	v2 (current)
This version publication date	01 June 2019
First version publication date	27 May 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	V419-010
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01839188
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol Number: V419-010, MCMVaccBV Protocol ID: PRI02C

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	19 March 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	19 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immune response and the safety of a primary series schedule that includes V419 (PR5I) at 2 and 6 months of age and Pediacel at 4 months of age. Primary objectives of this study were 1) to demonstrate that the mixed schedule induces acceptable responses for Hepatitis B (HB) one month after completion of the mixed schedule; and 2) to demonstrate that the mixed schedule induces acceptable responses for Haemophilus influenza type b (Hib) one month after completion of the mixed schedule. Secondary objectives of this study were: 1) to describe the antibody response to all PR5I antigens one month after completion of the mixed schedule; 2) to describe the antibody response to meningococcal serogroup C (MCC) conjugate vaccine one month after the second dose of MenC vaccine; and 3) to describe the safety profile after each dose of study vaccines administered.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research. The following additional measures defined for this individual study were in place for the protection of trial subjects:

Subjects in the study received the study vaccines (PR5I and Pediacel®) in line with the recommended infant immunisation schedule in Spain, and the immunisation schedule was consistent with other paediatric vaccines routinely given at the same age. NeisVac-C®, Prevenar 13®, and RotaTeq® were administered in accordance with their respective Summary of Product Characteristics. Subjects with allergy to any of the vaccine components or history of a life-threatening reaction to a vaccine containing the same substances as the study vaccines (including concomitants) were not vaccinated. Vaccines were administered by qualified study personnel. After each vaccination, subjects were kept under observation for 30 minutes to ensure their safety. Adequate treatment provisions, including epinephrine, were available for immediate use, should an anaphylactic or anaphylactoid reaction occur.

Background therapy:

Infants were previously vaccinated with only 1 dose of monovalent Hepatitis B vaccine, within the 3 days after birth, outside of the study context.

Evidence for comparator: -

Actual start date of recruitment	01 May 2013
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	Spain: 385
Worldwide total number of subjects	385
EEA total number of subjects	385

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)	385
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 enrolled N=385 infant participants previously vaccinated with only 1 dose of monovalent Hepatitis B vaccine, within 3 days after birth, outside of study context.

Pre-assignment

Screening details:

Participants progressed through the study as a single group, with all participants receiving the same mixed-schedule vaccination series. Vaccination (V1) was administered on Study Day 0 (2 months of age), with V2 (4 months of age) and V3 (6 months of age) administered at Study Months 2 and 4, respectively.

Period 1

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

Arms

Arm title	PR5I (V1); Pediacel® (V2); PR5I (V3)
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Arm description:

[Vaccination 1]: Single doses of PR5I (V419) + NeisVac-C® + Prevenar 13® by intramuscular (IM) injection + oral RotaTeq®, given at 2 months of age. [Vaccination 2]: Single doses of Pediacel® + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 4 months of age. [Vaccination 3]: Single dose of PR5I (V419) by IM injection + oral RotaTeq®, given at 6 months of age.

Arm type	Experimental
Investigational medicinal product name	PR5I
Investigational medicinal product code	
Other name	V419; Vaxelis®; DTaP-HBIPV-Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Hexavalent PR5I vaccine (DTaPHB-IPV-Hib = Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed [DTaP], Hepatitis B [HB; Recombinant DNA], Inactivated Poliovirus [IPV], and Haemophilus influenzae type b [Hib] conjugate vaccine [adsorbed]) at 0.5 mL for IM injection (left upper thigh) at 2 and 6 months of age.

Investigational medicinal product name	Pediacel®
Investigational medicinal product code	
Other name	DTaP-IPV-Hib
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Pentavalent Pediacel® vaccine (DTaPIPv-Hib = Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed [DTaP], Inactivated Poliovirus [IPV], and Haemophilus influenzae type b [Hib] conjugate vaccine [adsorbed]) at 0.5 mL for IM injection (left upper thigh) at 4 months of age.

Investigational medicinal product name	RotaTeq®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution in single-dose container
Routes of administration	Intramuscular use, Oral use

Dosage and administration details:

Human-bovine rotavirus reassortants (live) vaccine 2 mL oral administration at 2, 4 and 6 months of age. RotaTeq® administered prior to any other vaccine administration to avoid having the infant participants spit up the RotaTeq® when crying.

Investigational medicinal product name	NeisVac-C®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Meningococcal group C (MCC) polysaccharide conjugate vaccine (adsorbed) at 0.5 mL for IM injection (right upper thigh) at 2 and 4 months of age.

Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Pneumococcal polysaccharide conjugate vaccine [PCV; 13-valent, adsorbed]) at 0.5 mL for IM injection (right upper thigh) at 2 and 4 months of age.

Number of subjects in period 1	PR5I (V1); PediaceI® (V2); PR5I (V3)
Started	385
Treated	385
Completed	384
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups

Reporting group title	PR5I (V1); Pediacel® (V2); PR5I (V3)
Reporting group description:	
[Vaccination 1]: Single doses of PR5I (V419) + NeisVac-C® + Prevenar 13® by intramuscular (IM) injection + oral RotaTeq®, given at 2 months of age. [Vaccination 2]: Single doses of Pediacel® + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 4 months of age. [Vaccination 3]: Single dose of PR5I (V419) by IM injection + oral RotaTeq®, given at 6 months of age.	

Reporting group values	PR5I (V1); Pediacel® (V2); PR5I (V3)	Total	
Number of subjects	385	385	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	385	385	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: Days			
arithmetic mean	60.72		
standard deviation	± 7.75	-	
Sex: Female, Male			
Units: Subjects			
Female	199	199	
Male	186	186	
Body Weight			
Units: kg			
arithmetic mean	5.14		
standard deviation	± 0.59	-	

Subject analysis sets

Subject analysis set title	PR5I (V1)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
[Vaccination 1]: Single doses of PR5I (V419) + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 2 months of age.	
Subject analysis set title	Pediacel® (V2)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
[Vaccination 2]: Single doses of Pediacel® + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 4 months of age.	

Subject analysis set title	PR5I (V3)
Subject analysis set type	Sub-group analysis
Subject analysis set description: [Vaccination 3]: Single dose of PR5I (V419) by IM injection + oral RotaTeq®, given at 6 months of age.	
Subject analysis set title	PR5I (V1)
Subject analysis set type	Per protocol
Subject analysis set description: [Vaccination 1]: Single doses of PR5I (V419) + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 2 months of age.	
Subject analysis set title	Pediacel® (V2)
Subject analysis set type	Per protocol
Subject analysis set description: [Vaccination 2]: Single doses of Pediacel® + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 4 months of age.	
Subject analysis set title	PR5I (V3)
Subject analysis set type	Per protocol
Subject analysis set description: [Vaccination 3]: Single dose of PR5I (V419) by IM injection + oral RotaTeq®, given at 6 months of age.	
Subject analysis set title	PR5I (V1); Pediacel® (V2)
Subject analysis set type	Per protocol
Subject analysis set description: [Vaccination 1]: Single doses of PR5I (V419) + NeisVac-C® + Prevenar 13® by intramuscular (IM) injection + oral RotaTeq®, given at 2 months of age. [Vaccination 2]: Single doses of Pediacel® + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 4 months of age.	

Reporting group values	PR5I (V1)	Pediacel® (V2)	PR5I (V3)
Number of subjects	384	383	383
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Days arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female Male			
Body Weight Units: kg arithmetic mean standard deviation	±	±	±

Reporting group values	PR5I (V1)	Pediacel® (V2)	PR5I (V3)
Number of subjects	385	385	384
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Days arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Subjects			
Female Male			
Body Weight Units: kg arithmetic mean standard deviation	±	±	±

Reporting group values	PR5I (V1); Pediacel® (V2)		
Number of subjects	385		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Days arithmetic mean standard deviation	±		
Sex: Female, Male Units: Subjects			
Female Male			

Body Weight			
Units: kg			
arithmetic mean			
standard deviation	±		

End points

End points reporting groups

Reporting group title	PR5I (V1); Pediacel® (V2); PR5I (V3)
Reporting group description: [Vaccination 1]: Single doses of PR5I (V419) + NeisVac-C® + Prevenar 13® by intramuscular (IM) injection + oral RotaTeq®, given at 2 months of age. [Vaccination 2]: Single doses of Pediacel® + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 4 months of age. [Vaccination 3]: Single dose of PR5I (V419) by IM injection + oral RotaTeq®, given at 6 months of age.	
Subject analysis set title	PR5I (V1)
Subject analysis set type	Sub-group analysis
Subject analysis set description: [Vaccination 1]: Single doses of PR5I (V419) + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 2 months of age.	
Subject analysis set title	Pediacel® (V2)
Subject analysis set type	Sub-group analysis
Subject analysis set description: [Vaccination 2]: Single doses of Pediacel® + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 4 months of age.	
Subject analysis set title	PR5I (V3)
Subject analysis set type	Sub-group analysis
Subject analysis set description: [Vaccination 3]: Single dose of PR5I (V419) by IM injection + oral RotaTeq®, given at 6 months of age.	
Subject analysis set title	PR5I (V1)
Subject analysis set type	Per protocol
Subject analysis set description: [Vaccination 1]: Single doses of PR5I (V419) + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 2 months of age.	
Subject analysis set title	Pediacel® (V2)
Subject analysis set type	Per protocol
Subject analysis set description: [Vaccination 2]: Single doses of Pediacel® + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 4 months of age.	
Subject analysis set title	PR5I (V3)
Subject analysis set type	Per protocol
Subject analysis set description: [Vaccination 3]: Single dose of PR5I (V419) by IM injection + oral RotaTeq®, given at 6 months of age.	
Subject analysis set title	PR5I (V1); Pediacel® (V2)
Subject analysis set type	Per protocol
Subject analysis set description: [Vaccination 1]: Single doses of PR5I (V419) + NeisVac-C® + Prevenar 13® by intramuscular (IM) injection + oral RotaTeq®, given at 2 months of age. [Vaccination 2]: Single doses of Pediacel® + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 4 months of age.	

Primary: Percentage of Participants with an Anti-Hepatitis B Surface Antigen (HBsAg) Antibody Titer ≥ 10 mIU/mL

End point title	Percentage of Participants with an Anti-Hepatitis B Surface Antigen (HBsAg) Antibody Titer ≥ 10 mIU/mL ^[1]
End point description: The percentage of participants with an anti-HBsAg antibody titer ≥ 10 mill-International Units/mL (mIU/mL) was assessed. Participant serum samples were collected for analysis with an enhanced chemiluminescence assay to determine the concentration of antibodies to HBsAg. Analysis Population: all participants receiving ≥ 1 dose of study vaccination without protocol deviation, having post-vaccination immunogenicity data available for the evaluation of the respective analysis endpoint.	
End point type	Primary

End point timeframe:

Month 5 (one month after receiving 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: This is a single arm study, subjects were all enrolled in the same treatment group. The success of the study required that the primary objective was achieved for both Hepatitis B and PRP. For Hepatitis B, the immune response to PR5I vaccine was considered as acceptable if the lower bound of the 2-sided 95% CI of the % of subjects with anti-HBs titre ≥ 10 mIU/mL one month after the third dose of the mixed schedule was greater than 90%.

End point values	PR5I (V1); Pediace® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	369			
Units: Percentage of Participants				
number (confidence interval 95%)	98.9 (97.2 to 99.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with an Anti-Polyribosylribitol Phosphate (PRP) Antibody Titer ≥ 0.15 $\mu\text{g/mL}$

End point title	Percentage of Participants with an Anti-Polyribosylribitol Phosphate (PRP) Antibody Titer ≥ 0.15 $\mu\text{g/mL}$ ^[2]
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End point description:

The percentage of participants with an anti-Polyribosylribitol Phosphate (PRP) antibody titer ≥ 0.15 $\mu\text{g/mL}$ was assessed. Participant serum samples were collected for analysis by radioimmunoassay to determine the concentration of antibodies to PRP, a Haemophilus influenzae type b (Hib) capsular polysaccharide. Analysis Population: all participants receiving ≥ 1 dose of study vaccination without protocol deviation, having post-vaccination immunogenicity data available for the evaluation of the respective analysis endpoint.

End point type	Primary
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End point timeframe:

Month 5 (one month after receiving Vaccination 3)

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: This is a single arm study, subjects were all enrolled in the same treatment group. The success of the study required that the primary objective was achieved for both Hepatitis B and PRP. For Hib (PRP), the immune response to PR5I vaccine was considered as acceptable if the lower bound of the 2-sided 95% CI of the % of subjects with anti-PRP titre ≥ 0.15 $\mu\text{g/mL}$ one month after the third dose of the mixed schedule was greater than 80%.

End point values	PR5I (V1); Pediace® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	365			
Units: Percentage of Participants				
number (confidence interval 95%)	100.0 (99.0 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of Antibodies to Hepatitis B Surface Antigen (HBsAg)

End point title	Geometric Mean Concentration of Antibodies to Hepatitis B Surface Antigen (HBsAg)
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End point description:

Participant serum samples were collected for analysis with an enhanced chemiluminescence assay to determine the geometric mean concentration of antibodies to Hepatitis B Surface Antigen (HBsAg). The unit of measure is milli International Units/mL (mIU/mL). Analysis Population: all participants receiving ≥ 1 dose of study vaccination without protocol deviation, having post-vaccination immunogenicity data available for the evaluation of the respective analysis endpoint.

End point type	Secondary
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End point timeframe:

Month 5 (one month after receiving Vaccination 3)

End point values	PR5I (V1); Pediace® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	369			
Units: mIU/mL				
geometric mean (confidence interval 95%)	1054.97 (911.49 to 1221.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of Antibodies to Polyribosylribitol Phosphate (PRP) Antigen

End point title	Geometric Mean Concentration of Antibodies to Polyribosylribitol Phosphate (PRP) Antigen
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End point description:

Participant serum samples were collected for analysis by radioimmunoassay (RIA) to determine the geometric mean concentration of antibodies to polyribosylribitol phosphate (PRP), a Haemophilus influenzae type b (Hib) capsular polysaccharide. Analysis Population: all participants receiving ≥ 1 dose of study vaccination without protocol deviation, having post-vaccination immunogenicity data available for the evaluation of the respective analysis endpoint.

End point type	Secondary
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End point timeframe:

Month 5 (one month after receiving Vaccination 3)

End point values	PR5I (V1); Pediace® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	365			
Units: µg/mL				
geometric mean (confidence interval 95%)	8.00 (7.17 to 8.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of Antibodies to Diphtheria Toxin

End point title	Geometric Mean Concentration of Antibodies to Diphtheria Toxin
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End point description:

Participant serum samples were collected for analysis with a Micrometabolic Inhibition Test (MIT) to determine the geometric mean concentration of neutralizing antibodies to diphtheria toxin. The unit of measure is International Units/mL (IU/mL). Analysis Population: all participants receiving ≥1 dose of study vaccination without protocol deviation, having post-vaccination immunogenicity data available for the evaluation of the respective analysis endpoint.

End point type	Secondary
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End point timeframe:

Month 5 (one month after receiving Vaccination 3)

End point values	PR5I (V1); Pediace® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	359			
Units: IU/mL				
geometric mean (confidence interval 95%)	0.47 (0.42 to 0.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of Antibodies to Tetanus Toxin

End point title	Geometric Mean Concentration of Antibodies to Tetanus Toxin
End point description:	
Participant serum samples were collected for analysis by Enzyme-linked Immunosorbent Assay (ELISA) to determine the geometric mean concentration of antibodies to tetanus toxin. The unit of measure is International Units/mL (IU/mL). Analysis Population: all participants receiving ≥ 1 dose of study vaccination without protocol deviation, having post-vaccination immunogenicity data available for the evaluation of the respective analysis endpoint.	
End point type	Secondary
End point timeframe:	
Month 5 (one month after receiving Vaccination 3)	

End point values	PR5I (V1); Pediace® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	350			
Units: IU/mL				
geometric mean (confidence interval 95%)	2.44 (2.31 to 2.59)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentrations of Antibodies to Pertussis Antigens

End point title	Geometric Mean Concentrations of Antibodies to Pertussis Antigens
End point description:	
Participant serum samples were collected for analysis by ELISA to determine the geometric mean concentration of antibodies (Abs) to the following Pertussis antigens: pertussis toxoid (PT), filamentous hemagglutinin (FHA), pertactin (PRN) and fimbriae types (FIM) 2&3. The unit of measure is ELISA Units/mL (EU/mL). Analysis Population: all participants receiving ≥ 1 dose of study vaccination without protocol deviation, having post-vaccination immunogenicity data available for the evaluation of the respective analysis endpoint.	
End point type	Secondary
End point timeframe:	
Month 5 (one month after receiving Vaccination 3)	

End point values	PR5I (V1); Pediace® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	349			
Units: EU/mL				
geometric mean (confidence interval 95%)				

Anti-PT Abs	107.46 (101.55 to 113.71)			
Anti-FHA Abs	67.09 (62.38 to 72.15)			
Anti-PRN Abs	56.46 (51.60 to 61.78)			
Anti-FIM 2&3 Abs	360.99 (332.58 to 391.82)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers for Antibodies to Inactivated Poliovirus 1-3 (IPV1-3)

End point title	Geometric Mean Titers for Antibodies to Inactivated Poliovirus 1-3 (IPV1-3)
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End point description:

Participant serum samples were collected for analysis with a Micrometabolic Inhibition Test (MIT) to determine the geometric mean titer of neutralizing antibodies (Abs) to Inactivated Poliovirus 1, 2, & 3 (IPV1, IPV2, & IPV3). The unit of measure is titer, expressed as the reciprocal dilution of the highest dilution that neutralizes 50% of the challenge virus. Analysis Population: all participants receiving ≥ 1 dose of study vaccination without protocol deviation, having post-vaccination immunogenicity data available for the evaluation of the respective analysis endpoint.

End point type	Secondary
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End point timeframe:

Month 5 (one month after receiving Vaccination 3)

End point values	PR5I (V1); Pediace® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	356			
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-IPV1 Abs	663.97 (588.10 to 749.62)			
Anti-IPV2 Abs	1198.93 (1051.90 to 1366.51)			
Anti-IPV3 Abs	764.64 (664.70 to 879.61)			

Statistical analyses

Secondary: Percentage of Participants Responding to Polyribosylribitol Phosphate (PRP) Antigen, Diphtheria Toxin (D), Tetanus Toxin (T), and Inactivated Poliovirus 1, 2, & 3 (IPV1, IPV2, & IPV3)

End point title	Percentage of Participants Responding to Polyribosylribitol Phosphate (PRP) Antigen, Diphtheria Toxin (D), Tetanus Toxin (T), and Inactivated Poliovirus 1, 2, & 3 (IPV1, IPV2, & IPV3)
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End point description:

Participants were considered as responding if the observed concentration or titer for antibodies (Abs) to specific antigens exceeded the following thresholds:

- 1) For anti-PRP Abs (Hib capsular polysaccharide) – Response defined as a concentration ≥ 1 $\mu\text{g/mL}$ (measured by RIA);
- 2) For anti-D Abs – Response defined at 2 concentrations: ≥ 0.01 IU/mL and ≥ 0.10 IU/mL (measured by MIT);
- 3) For anti-T Abs – Response defined at 2 concentrations: ≥ 0.01 IU/mL and ≥ 0.10 IU/mL (measured by ELISA);
- 4) For anti-IPV1, anti-IPV2, and anti-IPV3 Abs – Response defined as a titer ≥ 8 (measured by MIT).

The percentage of participants considered as responding to the individual antigen (per the response threshold[s]) were assessed. Analysis Population: All participants receiving ≥ 1 dose of study vaccination without protocol deviation, having post-vaccination immunogenicity data available for the evaluation of the respective analysis endpoint.

End point type	Secondary
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End point timeframe:

Month 5 (one month after receiving Vaccination 3)

End point values	PR5I (V1); Pediace® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	370			
Units: Percentage of Participants				
number (confidence interval 95%)				
Anti-PRP Ab ≥ 1 $\mu\text{g/mL}$	95.3 (92.6 to 97.3)			
Anti-Diphtheria Ab ≥ 0.01 IU/mL	100.0 (99.0 to 100.0)			
Anti-Diphtheria Ab ≥ 0.10 IU/mL	92.2 (88.9 to 94.8)			
Anti-Tetanus ≥ 0.01 IU/mL	100.0 (99.0 to 100.0)			
Anti-Tetanus Ab ≥ 0.10 IU/mL	100.0 (99.0 to 100.0)			
Anti-IPV1 Ab Titer ≥ 8	100.0 (99.0 to 100.0)			
Anti-IPV2 Ab Titer ≥ 8	100.0 (99.0 to 100.0)			
Anti-IPV3 Ab Titer ≥ 8	100.0 (99.0 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titer of Anti-Meningococcal Group C Polysaccharide Conjugate (MCC) Antibodies

End point title	Geometric Mean Titer of Anti-Meningococcal Group C Polysaccharide Conjugate (MCC) Antibodies
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End point description:

Participant serum samples were collected to determine the geometric mean titer of anti-MCC antibodies, measured by the Serum Bactericidal Antibody assay using rabbit complement (rSBA). The unit of measure is titer, expressed as the reciprocal of the final serum dilution giving $\geq 50\%$ killing of the challenge bacterial strain. Analysis Population: all participants receiving ≥ 1 dose of study vaccination without protocol deviation, having post-vaccination immunogenicity data available for the evaluation of the respective analysis endpoint.

End point type	Secondary
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End point timeframe:

Month 3 (one month after receiving Vaccination 2)

End point values	PR5I (V1); Pediace® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	375			
Units: Titer				
geometric mean (confidence interval 95%)	739.63 (659.94 to 828.96)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an Anti-Meningococcal Group C Polysaccharide Conjugate (MCC) Antibody Titer ≥ 8

End point title	Percentage of Participants with an Anti-Meningococcal Group C Polysaccharide Conjugate (MCC) Antibody Titer ≥ 8
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End point description:

The percentage of participants with an anti-MCC antibody titer ≥ 8 was assessed. Participant serum samples were collected and analyzed for anti-MCC antibodies with the Serum Bactericidal Antibody assay using rabbit complement (rSBA). Analysis Population: all participants receiving ≥ 1 dose of study vaccination without protocol deviation, having post-vaccination immunogenicity data available for the evaluation of the respective analysis endpoint.

End point type	Secondary
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End point timeframe:

Month 3 (one month after receiving Vaccination 2)

End point values	PR5I (V1); PediaceI® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	375			
Units: Percentage of Participants				
number (confidence interval 95%)	99.2 (97.7 to 99.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Body Temperature $\geq 38^{\circ}\text{C}$ after Each Vaccination

End point title	Percentage of Participants with a Body Temperature $\geq 38^{\circ}\text{C}$ after Each Vaccination
End point description: The percentage of participants with a body temperature $\geq 38.0^{\circ}\text{C}$ from Day 1 to Day 5 after each vaccination was assessed. Per protocol, the participant's parent(s)/legal representative recorded daily body temperature measurements each evening by the axillary route (N=3 collected via rectal route; N=1 collected via oral route) and recorded these observations on the Vaccine Report Card (VRC). Temperatures were based on actual temperatures recorded with no adjustments for the route of assessment. Analysis Population: all participants receiving ≥ 1 dose of any vaccination with corresponding safety follow-up data, having available body temperature data.	
End point type	Secondary
End point timeframe: Up to Day 5 following each vaccination	

End point values	PR5I (V1)	PediaceI® (V2)	PR5I (V3)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	384	383	383	
Units: Percentage of Participants				
number (not applicable)	4.9	6.3	4.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing a Solicited Injection Site Reaction (ISR) Related to the PR5I/PediaceI® Vaccination

End point title	Number of Participants Experiencing a Solicited Injection Site Reaction (ISR) Related to the PR5I/PediaceI® Vaccination
End point description: The number of participants experiencing solicited ISRs related to the PR5I or PediaceI® vaccination was assessed. Solicited ISRs (erythema, pain and swelling) occurring at the PR5I or PediaceI® injection site were always considered related to the PR5I or PediaceI® vaccine, respectively. All AEs/ISRs were	

recorded on the VRC by the participant's parent(s)/legal representative. Data are presented for the number of participants experiencing solicited ISRs up to Day 5 after each vaccination and after any vaccination. Analysis Population: All participants receiving ≥ 1 dose of PR5I/Pediacel® vaccination with corresponding safety follow-up data after each vaccination (for V1, V2, and V3 arms) and after any vaccination (for overall V1; V2; V3 arm) with PR5I/Pediacel®.

End point type	Secondary
End point timeframe:	
Up to Day 5 following each vaccination	

End point values	PR5I (V1); Pediacel® (V2); PR5I (V3)	PR5I (V1)	Pediacel® (V2)	PR5I (V3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	385	385	385	384
Units: Participants				
Injection-site erythema	136	81	65	69
Injection-site pain	200	152	97	93
Injection-site swelling	121	68	52	65

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing a Solicited Injection Site Reaction (ISR) Related to the NeisVac-C® (MCC) Vaccination

End point title	Number of Participants Experiencing a Solicited Injection Site Reaction (ISR) Related to the NeisVac-C® (MCC) Vaccination
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End point description:

The number of participants experiencing solicited ISRs related to the NeisVac-C® (MCC) vaccination was assessed. Solicited ISRs (erythema, pain and swelling) occurring at the NeisVac-C® (MCC) injection site were always considered related to the NeisVac-C® (MCC) vaccine. All AEs/ISRs were recorded on the VRC by the participant's parent(s)/legal representative. Data are presented for the number of participants experiencing solicited ISRs up to Day 5 after each NeisVac-C® vaccination and after any NeisVac-C® vaccination. Analysis Population: all participants receiving ≥ 1 dose of NeisVac-C® vaccination with corresponding safety follow-up data after each vaccination (for V1 and V2 arms) and after any vaccination (for V1; V2 arm) with NeisVac-C®.

End point type	Secondary
End point timeframe:	
Up to Day 5 following each vaccination	

End point values	PR5I (V1)	Pediacel® (V2)	PR5I (V1); Pediacel® (V2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	385	385	385	
Units: Participants				
Injection-site erythema	41	59	85	
Injection-site pain	113	89	151	

Injection-site swelling	34	42	66	
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing an Unsolicited Injection Site Reaction (ISR) Related to the PR5I/Pediacel® Vaccination

End point title	Number of Participants Experiencing an Unsolicited Injection Site Reaction (ISR) Related to the PR5I/Pediacel® Vaccination
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End point description:

The number of participants experiencing unsolicited ISRs related to the PR5I or Pediacel® vaccination was assessed. Unsolicited ISRs occurring at the PR5I or Pediacel® injection site were always considered related to the PR5I or Pediacel® vaccine, respectively. All AEs/ISRs were recorded on the VRC by the participant's parent(s)/legal representative. Data are presented for the number of participants experiencing unsolicited ISRs up to Day 15 after each vaccination and after any vaccination. Analysis Population: all participants receiving ≥1 dose of PR5I/Pediacel® vaccination with corresponding safety follow-up data after each vaccination (for V1, V2, and V3 arms) and after any vaccination (for overall V1; V2; V3 arm) with PR5I/Pediacel®.

End point type	Secondary
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End point timeframe:

Up to Day 15 following each vaccination

End point values	PR5I (V1); Pediacel® (V2); PR5I (V3)	PR5I (V1)	Pediacel® (V2)	PR5I (V3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	385	385	385	384
Units: Participants				
Injection-site bruising	1	1	0	0
Injection-site discomfort	1	0	1	0
Injection-site haematoma	3	1	1	1
Injection-site haemorrhage	1	0	1	0
Injection-site induration	16	5	4	8
Injection-site warmth	1	1	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing an Unsolicited Injection Site Reaction (ISR) Related to the NeisVac-C® (MCC) Vaccination

End point title	Number of Participants Experiencing an Unsolicited Injection Site Reaction (ISR) Related to the NeisVac-C® (MCC) Vaccination
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End point description:

The number of participants experiencing unsolicited ISRs related to the NeisVac-C® (MCC) vaccination was assessed. Unsolicited ISRs occurring at the NeisVac-C® (MCC) injection site were always considered related to the NeisVac-C® (MCC) vaccine. All AEs/ISRs were recorded on the VRC by the participant's parent(s)/legal representative. Data are presented for the number of participants experiencing unsolicited ISRs up to Day 15 after each NeisVac-C® vaccination and after any NeisVac-C® vaccination. Analysis Population: all participants receiving ≥ 1 dose of NeisVac-C® vaccination with corresponding safety follow-up data after each vaccination (for V1 and V2 arms) and after any vaccination (for V1; V2 arm) with NeisVac-C®.

End point type	Secondary
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End point timeframe:

Up to Day 15 following each vaccination

End point values	PR5I (V1)	Pediacel® (V2)	PR5I (V1); Pediacel® (V2)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	385	385	385	
Units: Participants				
Injection-site discolouration	1	0	1	
Injection-site haematoma	0	2	2	
Injection-site induration	2	2	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing a Solicited Systemic Adverse Event (AE)

End point title	Number of Participants Experiencing a Solicited Systemic Adverse Event (AE)
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End point description:

The number of participants experiencing solicited systemic AEs (crying, decreased appetite, irritability, somnolence, pyrexia, and vomiting) was assessed. Each day from Day 1 to Day 5 following each vaccination, the participant's parent(s)/legal representative recorded all solicited AEs on the VRC. Data are presented for the number of participants experiencing solicited AEs up to Day 5 after each vaccination and after any vaccination. Analysis Population: all participants receiving ≥ 1 dose of any vaccination with corresponding safety follow-up data after each vaccination (for V1, V2, and V3 arms) and after any vaccination (for overall V1; V2; V3 arm).

End point type	Secondary
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End point timeframe:

Up to Day 5 following each vaccination

End point values	PR5I (V1); Pediactal® (V2); PR5I (V3)	PR5I (V1)	Pediactal® (V2)	PR5I (V3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	385	385	385	384
Units: Participants				
Crying	255	188	131	102
Decreased appetite	195	141	88	76
Irritability	268	196	154	119
Pyrexia	52	19	24	18
Somnolence	229	184	126	84
Vomiting	88	56	35	27

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing an Unsolicited Systemic Adverse Event (AE)

End point title	Number of Participants Experiencing an Unsolicited Systemic Adverse Event (AE)
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End point description:

The number of participants experiencing unsolicited systemic AEs was assessed. Data are presented for the number of participants experiencing unsolicited AEs up to Day 15 after each vaccination and after any vaccination. Analysis Population: all participants receiving ≥ 1 dose of any vaccination with corresponding safety follow-up data after each vaccination (for V1, V2, and V3 arms) and after any vaccination (for overall V1; V2; V3 arm).

End point type	Secondary
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End point timeframe:

Up to Day 15 following each vaccination

End point values	PR5I (V1); Pediactal® (V2); PR5I (V3)	PR5I (V1)	Pediactal® (V2)	PR5I (V3)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	385	385	385	384
Units: Participants	163	58	53	89

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing a Serious Adverse Event (SAE)

End point title	Number of Participants Experiencing a Serious Adverse Event (SAE)
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End point description:

An SAE is an adverse event (AE) that: results in death; is life threatening; results in persistent or significant disability or incapacity; results in or prolongs a hospitalization; is a congenital anomaly or birth defect; is a cancer; or may jeopardize the participant, potentially require medical or surgical intervention. Analysis Population: all participants receiving ≥ 1 dose of study vaccination.

End point type	Secondary
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End point timeframe:

Up to ~6 months (at any time during the study)

End point values	PR5I (V1); Pediace® (V2); PR5I (V3)			
Subject group type	Reporting group			
Number of subjects analysed	385			
Units: Participants	12			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to ~6 months (Serious adverse events and deaths were collected for the duration of the study. Solicited ISRs / AEs were collected up to 5 days following each vaccination; unsolicited ISRs / AEs were collected up to 15 days following each vaccination.)

Adverse event reporting additional description:

Analysis population includes all participants receiving ≥ 1 dose of study vaccination.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	PR5I (V1); Pediacel® (V2); PR5I (V3)
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Reporting group description:

[Vaccination 1]: Single doses of PR5I (V419) + NeisVac-C® + Prevenar 13® by intramuscular (IM) injection + oral RotaTeq®, given at 2 months of age. [Vaccination 2]: Single doses of Pediacel® + NeisVac-C® + Prevenar 13® by IM injection + oral RotaTeq®, given at 4 months of age. [Vaccination 3]: Single dose of PR5I (V419) by IM injection + oral RotaTeq®, given at 6 months of age.

Serious adverse events	PR5I (V1); Pediacel® (V2); PR5I (V3)		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 385 (3.12%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 385 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	1 / 385 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			

subjects affected / exposed	1 / 385 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Choking			
subjects affected / exposed	1 / 385 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	5 / 385 (1.30%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Periorbital cellulitis			
subjects affected / exposed	1 / 385 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 385 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 385 (0.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	PR5I (V1); PediaceI® (V2); PR5I (V3)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	360 / 385 (93.51%)		
Nervous system disorders			
Somnolence			

subjects affected / exposed	229 / 385 (59.48%)		
occurrences (all)	414		
General disorders and administration site conditions			
Crying			
subjects affected / exposed	255 / 385 (66.23%)		
occurrences (all)	452		
Injection site erythema			
subjects affected / exposed	152 / 385 (39.48%)		
occurrences (all)	316		
Injection site induration			
subjects affected / exposed	19 / 385 (4.94%)		
occurrences (all)	21		
Injection site pain			
subjects affected / exposed	208 / 385 (54.03%)		
occurrences (all)	544		
Injection site swelling			
subjects affected / exposed	130 / 385 (33.77%)		
occurrences (all)	261		
Pyrexia			
subjects affected / exposed	56 / 385 (14.55%)		
occurrences (all)	69		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	11 / 385 (2.86%)		
occurrences (all)	12		
Diarrhoea			
subjects affected / exposed	15 / 385 (3.90%)		
occurrences (all)	17		
Vomiting			
subjects affected / exposed	93 / 385 (24.16%)		
occurrences (all)	136		
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	9 / 385 (2.34%)		
occurrences (all)	12		
Psychiatric disorders			

Irritability subjects affected / exposed occurrences (all)	268 / 385 (69.61%) 499		
Infections and infestations			
Bronchiolitis subjects affected / exposed occurrences (all)	16 / 385 (4.16%) 16		
Conjunctivitis subjects affected / exposed occurrences (all)	11 / 385 (2.86%) 11		
Nasopharyngitis subjects affected / exposed occurrences (all)	21 / 385 (5.45%) 23		
Respiratory tract infection subjects affected / exposed occurrences (all)	12 / 385 (3.12%) 13		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	8 / 385 (2.08%) 9		
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	196 / 385 (50.91%) 319		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported