Clinical trial results:
A Phase 4, Open-label, Multicenter Study to Evaluate the Safety, Tolerability, and Immunogenicity of Vaxelis™ in Healthy Children Previously Vaccinated With a 2-Dose Primary Infant Series of Either Vaxelis™ or Hexyon™

Summary

EudraCT number	2021-004053-23
Trial protocol	ES DE IT
Global end of trial date	17 January 2023

Results information

Result version number	v1 (current)
This version publication date	08 July 2023
First version publication date	08 July 2023

Trial information

Trial identification

Sponsor protocol code	V419-016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05289271
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, Rahway, NJ, United States, P.O. Box 2000
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, 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	17 January 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 August 2022
Global end of trial reached?	Yes
Global end of trial date	17 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the safety, tolerability, and immunogenicity of a booster dose of Vaxelis™ (V419) given at ~11 to 13 months of age in healthy participants who were previously vaccinated with a 2-dose primary infant series of either Vaxelis™ or Hexyon™

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 March 2022
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	Germany: 53
Country: Number of subjects enrolled	Spain: 104
Country: Number of subjects enrolled	Italy: 11
Worldwide total number of subjects	168
EEA total number of subjects	168

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)	168
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: -

Pre-assignment

Screening details:

Healthy participants approximately 11 to 13 months of age, (≥327 days to ≤396 days inclusive).were enrolled in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: V, V, V

Arm description:

Participants who received a 2-dose regimen of Vaxelis™ as infants prior to enrollment received a Vaxelis™ booster at ~11 months of age.

Arm type	Experimental
Investigational medicinal product name	Vaxelis™
Investigational medicinal product code	
Other name	V419
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL sterile suspension in prefilled syringe for intramuscular administration.

Arm title	Group 2: H, H, V

Arm description:

Participants who received a 2-dose regimen of Hexyon™ as infants prior to enrollment received a Vaxelis™ booster at ~11 months of age.

Arm type	Experimental
Investigational medicinal product name	Vaxelis™
Investigational medicinal product code	
Other name	V419
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL sterile suspension in prefilled syringe for intramuscular administration.

Number of subjects in period 1	Group 1: V, V, V	Group 2: H, H, V
Started	86	82
Treated	85	82
Completed	85	82
Not completed	1	0

Mistakenly allocated, untreated	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: V, V, V
Reporting group description:	
Participants who received a 2-dose regimen of Vaxelis™ as infants prior to enrollment received a Vaxelis™ booster at ~11 months of age.	
Reporting group title	Group 2: H, H, V
Reporting group description:	
Participants who received a 2-dose regimen of Hexyon™ as infants prior to enrollment received a Vaxelis™ booster at ~11 months of age.	

Reporting group values	Group 1: V, V, V	Group 2: H, H, V	Total
Number of subjects	86	82	168
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)	86	82	168
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: Days			
arithmetic mean	348.8	344.7	
standard deviation	± 18.8	± 16.4	-
Sex: Female, Male Units:			
Female	44	33	77
Male	42	49	91
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	85	82	167
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	45	60	105
Not Hispanic or Latino	34	21	55
Unknown or Not Reported	7	1	8

End points

End points reporting groups

Reporting group title	Group 1: V, V, V
Reporting group description:	
Participants who received a 2-dose regimen of Vaxelis™ as infants prior to enrollment received a Vaxelis™ booster at ~11 months of age.	
Reporting group title	Group 2: H, H, V
Reporting group description:	
Participants who received a 2-dose regimen of Hexyon™ as infants prior to enrollment received a Vaxelis™ booster at ~11 months of age.	

Primary: Percentage of participants with a solicited injection-site adverse event (AE)

End point title	Percentage of participants with a solicited injection-site adverse event (AE)[1]
End point description:	
Solicited injection-site AEs are predefined local (at the injection/administration site) events for which the participant's legally authorized representative was specifically questioned. Participant's legally acceptable representative used a Vaccination Report Card (VRC) to report the following solicited injection-site AEs : swelling, redness (erythema), and pain/tenderness. 95% confidence intervals (CIs) were calculated based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all participants who received study vaccination.	
End point type	Primary
End point timeframe:	
Up to 5 days postvaccination	

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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	82		
Units: Percentage of participants				
number (confidence interval 95%)				
Injection site erythema	52.9 (41.8 to 63.9)	50.0 (38.7 to 61.3)		
Injection site pain	74.1 (63.5 to 83.0)	56.1 (44.7 to 67.0)		
Injection site swelling	52.9 (41.8 to 63.9)	40.2 (29.6 to 51.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with a solicited systemic AE

End point title	Percentage of participants with a solicited systemic AE[2]

End point description:

Solicited systemic AE are predefined systemic events for which the participant's legally authorized representative was specifically questioned. Participant's legally acceptable representative used a VRC to report the following solicited systemic AEs: vomiting, drowsiness (somnolence), loss of appetite, and irritability. 95% CIs were calculated based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all participants who received study vaccination.

End point type	Primary

End point timeframe:

Up to 5 days postvaccination

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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	82		
Units: Percentage of participants				
number (confidence interval 95%)				
Decreased appetite	43.5 (32.8 to 54.7)	36.6 (26.2 to 48.0)		
Irritability	77.6 (67.3 to 86.0)	58.5 (47.1 to 69.3)		
Somnolence	64.7 (53.6 to 74.8)	47.6 (36.4 to 58.9)		
Vomiting	3.5 (0.7 to 10.0)	8.5 (3.5 to 16.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with unsolicited AEs

End point title	Percentage of participants with unsolicited AEs[3]

End point description:

An unsolicited AE is an AE that was not solicited using a VRC and that is communicated by a participant's legally authorized representative who has signed the informed consent. An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. 95% CIs were calculated based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all participants who received study vaccination.

End point type	Primary

End point timeframe:

Up to 15 days postvaccination

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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	82		
Units: Percentage of participants				
number (confidence interval 95%)	97.6 (91.8 to 99.7)	92.7 (84.8 to 97.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with a serious AE (SAE)

End point title	Percentage of participants with a serious AE (SAE)[4]

End point description:

An SAE is any untoward medical occurrence that results in death, is life-threatening, requires hospitalization or prolongs existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an other important medical event. 95% CIs were calculated based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all participants who received study vaccination.

End point type	Primary

End point timeframe:

Up to 40 days postvaccination

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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	82		
Units: Percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 4.2)	1.2 (0.0 to 6.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with diphtheria toxoid antibodies ≥0.1 IU/mL

End point title	Percentage of participants with diphtheria toxoid antibodies ≥0.1 IU/mL[5]

End point description:

Human antibodies to diphtheria toxoid were quantified using the Meso Scale Discovery Electrochemiluminescence serological assay based on an established reference standard sample curve with the lower limit of quantitation (LLOQ) for diphtheria antibody of 0.005 IU/mL. The percentage of participants with diphtheria toxoid antibodies ≥0.1 international units per milliliter (IU/mL) one month after Vaxelis™ as the 3rd dose of a vaccination series is presented. The 95% CIs are based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all enrolled participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

30 days postvaccination (at ~12 months of age)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	74		
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (94.8 to 100.0)	98.6 (92.7 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with tetanus toxoid antibodies ≥0.1 IU/mL

End point title	Percentage of participants with tetanus toxoid antibodies ≥0.1 IU/mL[6]

End point description:

Human antibodies to tetanus toxoid were quantified using the Meso Scale Discovery Electrochemiluminescence serological assay based on an established reference standard sample curve with a LLOQ for tetanus antibody of 0.01 IU/mL. The percentage of participants with tetanus toxoid antibodies ≥0.1 IU/mL one month after Vaxelis™ as the 3rd dose of a vaccination series is presented. The 95% CIs are based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all enrolled participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

30 days postvaccination (at ~12 months of age)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	74		
Units: Percentage of participants				
number (confidence interval 95%)	98.6 (92.2 to 100.0)	98.6 (92.7 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with pertussis toxoid (PT) vaccine response

End point title	Percentage of participants with pertussis toxoid (PT) vaccine response[7]

End point description:

Human antibodies to pertussis toxoid were quantified using the Meso Scale Discovery Electrochemiluminescence serological assay based on an established reference standard sample curve with a LLOQ for pertussis antibody of 2.00 EU/mL. The percentage of participants meeting response criteria for PT is based on pre-vaccination level of PT is presented. The 95% CIs are based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all enrolled participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

30 days postvaccination (at ~12 months of age)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	71		
Units: Percentage of participants				
number (confidence interval 95%)	98.4 (91.6 to 100.0)	94.4 (86.2 to 98.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with filamentous hemagglutinin (FHA) vaccine response

End point title	Percentage of participants with filamentous hemagglutinin (FHA) vaccine response[8]

End point description:

Human antibodies to FHA were quantified using the Meso Scale Discovery Electrochemiluminescence serological assay based on an established reference standard sample curve with a LLOQ for FHA antibody of 2.00 EU/mL. The percentage of participants meeting response criteria for FHA response will be based on pre-vaccination level of FHA. The 95% CIs are based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all enrolled participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

30 days postvaccination (at ~12 months of age)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	71		
Units: Percentage of participants				
number (confidence interval 95%)	98.4 (91.6 to 100.0)	90.1 (80.7 to 95.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with Haemophilus influenzae type b polyribosylribitol phosphate (Hib-PRP) antibodies ≥1.0 µg/mL

End point title	Percentage of participants with Haemophilus influenzae type b polyribosylribitol phosphate (Hib-PRP) antibodies ≥1.0 µg/mL[9]

End point description:

Human antibodies to Hib-PRP were quantified using the Vacczyme™ Human Anti-Haemophilus influenzae Type b Enzyme Immunoassay Kit. Levels of anti-Hib IgG were quantified by interpolation from a standard curve that has been calibrated to the FDA lot 1983 reference serum. The percentage of participants with Hib-PRP antibodies ≥0.1 IU/mL one month after Vaxelis™ as the 3rd dose of a vaccination series is presented. The 95% CIs are based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all enrolled participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

30 days postvaccination (at ~12 months of age)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	76		
Units: Percentage of participants				
number (confidence interval 95%)	89.0 (79.5 to 95.1)	90.8 (81.9 to 96.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with hepatitis B surface antigen (HBsAg) antibodies ≥10 mIU/mL

End point title	Percentage of participants with hepatitis B surface antigen (HBsAg) antibodies ≥10 mIU/mL[10]

End point description:

Human antibodies to HBsAg were quantified using an Enhanced Chemiluminescence (ECi) assay, with the hepatitis B WHO International reference standard at 10 mIU/mL as a control in every assay, and the

LLOQ of the assay is 5 mIU/mL. The percentage of participants with HBsAg antibodies ≥10 milli-international per liter (mIU/mL) one month after Vaxelis™ as the 3rd dose of a vaccination series is presented. The 95% CIs are based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all enrolled participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

30 days postvaccination (at ~12 months of age)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	69		
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (93.6 to 100.0)	94.2 (85.8 to 98.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with poliovirus serotype 1 neutralizing antibodies (Nab) ≥1:8 dilution

End point title	Percentage of participants with poliovirus serotype 1 neutralizing antibodies (Nab) ≥1:8 dilution[11]

End point description:

Human antibodies to poliovirus serotype 1 were quantified with a neutralization assay by utilizing Vero cells and wild type poliovirus strain 1 as the challenge virus. The Karber method was used to determine the serum dilution that neutralized 50% of the challenge virus, with results expressed as titers (1:dilution), and the LLOQ was 1:4. dilution. The percentage of participants with poliovirus serotype 1 Nab ≥1:8 dilution one month after Vaxelis™ as the 3rd dose of a vaccination series is presented. The 95% CIs are based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all enrolled participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

30 days postvaccination (at ~12 months of age)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	69		
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (94.6 to 100.0)	95.7 (87.8 to 99.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with poliovirus serotype 2 neutralizing antibodies (Nab) ≥1:8 dilution

End point title	Percentage of participants with poliovirus serotype 2 neutralizing antibodies (Nab) ≥1:8 dilution[12]

End point description:

Human antibodies to poliovirus serotype 2 were quantified with a neutralization assay by utilizing Vero cells and wild type poliovirus strain 2 as the challenge virus. The Karber method was used to determine the serum dilution that neutralized 50% of the challenge virus, with results expressed as titers (1:dilution), and the LLOQ was 1:4. dilution. The percentage of participants with poliovirus serotype 2 Nab ≥1:8 dilution one month after Vaxelis™ as the 3rd dose of a vaccination series is presented. The 95% CIs are based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all enrolled participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

30 days postvaccination (at ~12 months of age)

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	69		
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (94.6 to 100.0)	100.0 (94.8 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with poliovirus serotype 3 neutralizing antibodies (Nab) ≥1:8 dilution

End point title	Percentage of participants with poliovirus serotype 3 neutralizing antibodies (Nab) ≥1:8 dilution[13]

End point description:

Human antibodies to poliovirus serotype 3 were quantified with a neutralization assay by utilizing Vero cells and wild type poliovirus strain 3 as the challenge virus. The Karber method was used to determine the serum dilution that neutralized 50% of the challenge virus, with results expressed as titers (1:dilution), and the LLOQ was 1:4. dilution. The percentage of participants with poliovirus serotype 3 Nab ≥1:8 dilution one month after Vaxelis™ as the 3rd dose of a vaccination series is presented. The

CIs are based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all enrolled participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

30 days postvaccination (at ~12 months of age)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	69		
Units: Percentage of participants				
number (confidence interval 95%)	97.0 (89.5 to 99.6)	100.0 (94.8 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with pertactin (PRN) vaccine response

End point title	Percentage of participants with pertactin (PRN) vaccine response

End point description:

Human antibodies to PRN were quantified using the Meso Scale Discovery Electrochemiluminescence serological assay based on an established reference standard sample curve with a LLOQ for PRN of 2.00 EU/mL.The percentage of participants meeting response criteria for PRN was based on pre-vaccination level of PRN. The 95% CIs are based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all enrolled participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Secondary

End point timeframe:

30 days postvaccination (at ~12 months of age)

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	71		
Units: Percentage of participants				
number (confidence interval 95%)	92.2 (82.7 to 97.4)	22.5 (13.5 to 34.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with fimbriae 2/3 (FIM 2/3) vaccine response

End point title	Percentage of participants with fimbriae 2/3 (FIM 2/3) vaccine response

End point description:

Human antibodies to FIM 2/3 were quantified using the Meso Scale Discovery Electrochemiluminescence serological assay based on an established reference standard sample curve with a LLOQ for pertussis antibody of 2.00 EU/mL. The percentage of participants meeting response criteria for FIM 2/3 was based on pre-vaccination level of FIM 2/3. The 95% CIs are based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all enrolled participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Secondary

End point timeframe:

30 days postvaccination (at ~12 months of age)

End point values	Group 1: V, V, V	Group 2: H, H, V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	71		
Units: Percentage of participants				
number (confidence interval 95%)	95.3 (86.9 to 99.0)	69.0 (56.9 to 79.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events (AEs): from vaccination up to 40 days post-vaccination; All-cause mortality (ACM): From allocation up to 40 days post-vaccination	
Adverse event reporting additional description:	
AE population: All participants who received study vaccination. ACM population: all allocated participants.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	Group 2: H, H, V
Reporting group description:	
Participants who received a 2-dose regimen of Hexyon™ as infants prior to enrollment received a Vaxelis™ booster at ~11 months of age.	
Reporting group title	Group 1: V, V, V
Reporting group description:	
Participants who received a 2-dose regimen of Vaxelis™ as infants prior to enrollment received a Vaxelis™ booster at ~11 months of age.	

Serious adverse events	Group 2: H, H, V	Group 1: V, V, V	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 82 (1.22%)	0 / 85 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Gastroenteritis adenovirus			
subjects affected / exposed	1 / 82 (1.22%)	0 / 85 (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: 5 %

Non-serious adverse events	Group 2: H, H, V	Group 1: V, V, V	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	75 / 82 (91.46%)	83 / 85 (97.65%)	
Nervous system disorders			

Somnolence			
subjects affected / exposed	39 / 82 (47.56%)	55 / 85 (64.71%)	
occurrences (all)	42	55	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	41 / 82 (50.00%)	45 / 85 (52.94%)	
occurrences (all)	41	45	
Injection site induration			
subjects affected / exposed	6 / 82 (7.32%)	0 / 85 (0.00%)	
occurrences (all)	6	0	
Injection site swelling			
subjects affected / exposed	33 / 82 (40.24%)	45 / 85 (52.94%)	
occurrences (all)	33	45	
Pyrexia			
subjects affected / exposed	40 / 82 (48.78%)	34 / 85 (40.00%)	
occurrences (all)	47	35	
Injection site pain			
subjects affected / exposed	46 / 82 (56.10%)	63 / 85 (74.12%)	
occurrences (all)	46	63	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 82 (7.32%)	1 / 85 (1.18%)	
occurrences (all)	6	1	
Vomiting			
subjects affected / exposed	8 / 82 (9.76%)	5 / 85 (5.88%)	
occurrences (all)	8	5	
Psychiatric disorders			
Irritability			
subjects affected / exposed	48 / 82 (58.54%)	66 / 85 (77.65%)	
occurrences (all)	49	66	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	30 / 82 (36.59%)	37 / 85 (43.53%)	
occurrences (all)	31	38	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 August 2022	Amendment 01: The sponsor Merck Sharp & Dohme Corp. underwent an entity name and address change to Merck Sharp & Dohme LLC, Rahway, NJ, USA.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported