



Clinical trial results:

Long-Term Persistence of Hepatitis B and Pertussis Antibody

Responses in Healthy

4 To 5 Year-Old Children Previously Vaccinated With a 2-Dose Or 3-Dose Infants

Series and Toddler Dose With Vaxelis® or INFANRIX® hexa

Summary

EudraCT number	2016-000274-37
Trial protocol	FI
Global end of trial date	01 August 2016

Results information

Result version number	v1 (current)
This version publication date	09 June 2019
First version publication date	09 June 2019

Trial information

Trial identification

Sponsor protocol code	V419-012
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02759354
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol Number: V419-012

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, 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	01 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 July 2016
Global end of trial reached?	Yes
Global end of trial date	01 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to assess the long-term persistence of hepatitis B surface antigen (HBsAg) and pertussis antibodies after vaccination with Vaxelis®. The present study was therefore an extended follow-up of the 4 to 5 year-old participants who participated in two previous clinical studies (V419-007 and V419-008), without any vaccine administration, and a blood sample as the main procedure. Its design was driven by both initial studies design and timing.

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:

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Evidence for comparator:

-

Actual start date of recruitment	26 April 2016
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	Finland: 754
Worldwide total number of subjects	754
EEA total number of subjects	754

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	754
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:

This multicenter extension study was conducted in Finland at approximately 10 sites from studies V419-007 and V419-008, which had eligible participants (i.e. participants who completed the full 3+1 or 2+1 vaccination schedule in the original studies).

Pre-assignment

Screening details:

Of the 760 screened participants, 754 were enrolled and completed the study. A total of 752 participants were included in the Persistence Analysis Set, 752 with blood samples available for hepatitis B surface antigen (HBsAg) analyses, and 751 for pertussis analyses.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group Vaxelis (3+1)

Arm description:

Participants previously vaccinated with a 3-dose primary series of Vaxelis® at 2, 3 and 4 months of age, and a toddler dose at 12 months of age (study V419-007). On Day 1 of this extension study (approximately [~] 4 years after completion of the 3+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.

Arm type	Experimental
Investigational medicinal product name	Blood Sample
Investigational medicinal product code	
Other name	Vaxelis®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Blood sample at ~4 years of age

Arm title	Group Infanrix hexa (3+1)
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Arm description:

Participants previously vaccinated with a 3-dose primary series of INFANRIX® hexa at 2, 3 and 4 months of age, and a toddler dose at 12 months of age (study V419-007). On Day 1 of this extension study (~4 years after completion of the 3+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.

Arm type	Active comparator
Investigational medicinal product name	Blood sample
Investigational medicinal product code	
Other name	INFANRIX® hexa
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Blood sample at ~4 years of age

Arm title	Group Vaxelis (2+1)
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Arm description:

Participants previously vaccinated with a 2-dose primary series of Vaxelis® at 2 and 4 months of age, and a toddler dose at 11-12 months of age (study V419-008). On Day 1 of this extension study (~4 years after completion of the 2+1 schedule), a 4 mL blood sample was obtained to assay for long-term

antibody persistence.

Arm type	Experimental
Investigational medicinal product name	Blood sample
Investigational medicinal product code	
Other name	Vaxelis®
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Blood sample at ~4 years of age	
Arm title	Group Infanrix hexa (2+1)

Arm description:

Participants previously vaccinated with a 2-dose primary series of INFANRIX® hexa at 2 and 4 months of age, and a toddler dose at 11-12 months of age (study V419-008). On Day 1 of this extension study (~4 years after completion of the 2+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.

Arm type	Active comparator
Investigational medicinal product name	Blood sample
Investigational medicinal product code	
Other name	INFANRIX® hexa
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Blood sample at ~4 years of age

Number of subjects in period 1	Group Vaxelis (3+1)	Group Infanrix hexa (3+1)	Group Vaxelis (2+1)
Started	192	190	181
Completed	192	190	181

Number of subjects in period 1	Group Infanrix hexa (2+1)
Started	191
Completed	191

Baseline characteristics

Reporting groups

Reporting group title	Group Vaxelis (3+1)
Reporting group description: Participants previously vaccinated with a 3-dose primary series of Vaxelis® at 2, 3 and 4 months of age, and a toddler dose at 12 months of age (study V419-007). On Day 1 of this extension study (approximately [~] 4 years after completion of the 3+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.	
Reporting group title	Group Infanrix hexa (3+1)
Reporting group description: Participants previously vaccinated with a 3-dose primary series of INFANRIX® hexa at 2, 3 and 4 months of age, and a toddler dose at 12 months of age (study V419-007). On Day 1 of this extension study (~4 years after completion of the 3+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.	
Reporting group title	Group Vaxelis (2+1)
Reporting group description: Participants previously vaccinated with a 2-dose primary series of Vaxelis® at 2 and 4 months of age, and a toddler dose at 11-12 months of age (study V419-008). On Day 1 of this extension study (~4 years after completion of the 2+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.	
Reporting group title	Group Infanrix hexa (2+1)
Reporting group description: Participants previously vaccinated with a 2-dose primary series of INFANRIX® hexa at 2 and 4 months of age, and a toddler dose at 11-12 months of age (study V419-008). On Day 1 of this extension study (~4 years after completion of the 2+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.	

Reporting group values	Group Vaxelis (3+1)	Group Infanrix hexa (3+1)	Group Vaxelis (2+1)
Number of subjects	192	190	181
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)	0	0	0
Children (2-11 years)	192	190	181
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: Years			
arithmetic mean	4.8	4.8	3.9
standard deviation	± 0.2	± 0.2	± 0.1
Sex: Female, Male Units: Subjects			
Female	99	86	84
Male	93	104	97

Reporting group values	Group Infanrix hexa	Total	
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Number of subjects	191	754	
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)	0	0	
Children (2-11 years)	191	754	
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: Years			
arithmetic mean	3.9		
standard deviation	± 0.1	-	
Sex: Female, Male			
Units: Subjects			
Female	94	363	
Male	97	391	

End points

End points reporting groups

Reporting group title	Group Vaxelis (3+1)
Reporting group description: Participants previously vaccinated with a 3-dose primary series of Vaxelis® at 2, 3 and 4 months of age, and a toddler dose at 12 months of age (study V419-007). On Day 1 of this extension study (approximately [~] 4 years after completion of the 3+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.	
Reporting group title	Group Infanrix hexa (3+1)
Reporting group description: Participants previously vaccinated with a 3-dose primary series of INFANRIX® hexa at 2, 3 and 4 months of age, and a toddler dose at 12 months of age (study V419-007). On Day 1 of this extension study (~4 years after completion of the 3+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.	
Reporting group title	Group Vaxelis (2+1)
Reporting group description: Participants previously vaccinated with a 2-dose primary series of Vaxelis® at 2 and 4 months of age, and a toddler dose at 11-12 months of age (study V419-008). On Day 1 of this extension study (~4 years after completion of the 2+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.	
Reporting group title	Group Infanrix hexa (2+1)
Reporting group description: Participants previously vaccinated with a 2-dose primary series of INFANRIX® hexa at 2 and 4 months of age, and a toddler dose at 11-12 months of age (study V419-008). On Day 1 of this extension study (~4 years after completion of the 2+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.	

Primary: Percentage of Participants Responding to Hepatitis B Surface Antigen (HBsAg)

End point title	Percentage of Participants Responding to Hepatitis B Surface Antigen (HBsAg) ^[1]
End point description: Participant serum samples were collected for testing with an enhanced chemiluminescence assay for antibodies to HBsAg. Response was defined as a titer ≥ 10 milli International units (mIU)/mL. Confidence Intervals were calculated based on the exact binomial method of D. Collett. All analyses were performed on the Persistence Analysis Set, defined as all participants previously vaccinated with a complete 3+1 or 2+1 schedule, as part of studies V419 007 or V419-008 respectively, for whom immunogenicity results were available.	
End point type	Primary
End point timeframe: Day 1 (approximately 4 years after completion of the 3+1/2+1 schedule)	
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: No statistical analyses were reported for this end point.	

End point values	Group Vaxelis (3+1)	Group Infanrix hexa (3+1)	Group Vaxelis (2+1)	Group Infanrix hexa (2+1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	191	189	181	190
Units: Percentage of Participants				
number (confidence interval 95%)	70.16 (63.13 to 76.55)	82.01 (75.78 to 87.21)	65.75 (58.34 to 72.63)	83.68 (77.65 to 88.64)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Responding to Pertussis Toxin

End point title	Percentage of Participants Responding to Pertussis Toxin ^{[2][3]}
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End point description:

Participant serum samples were collected for testing with an Enzyme-linked Immunosorbent Assay (ELISA) for antibodies to pertussis toxin. The unit of measure is ELISA units/mL. LLOQ=4 EU/mL. Confidence Intervals were calculated based on the exact binomial method of D. Collett. All analyses were performed on the Persistence Analysis Set, defined as all participants previously vaccinated with a complete 2+1 schedule, as part of study V419-008 respectively, for whom immunogenicity results were available.

End point type	Primary
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End point timeframe:

Day 1 (approximately 4 years after completion of the 2+1 schedule)

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 endpoint does not exist for the two groups in V419-007 and accordingly there are no statistics to report.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to the enrollment dynamics in the initial studies and country specificities regarding administration of pre-school booster (children in the 007 study had already received a school-age booster at 4 years of age in Finland, before V419-012 study started), the assessment of pertussis antibody persistence was not possible for subjects from study V419-007 (3+1 schedule).

End point values	Group Vaxelis (2+1)	Group Infanrix hexa (2+1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	178	188		
Units: Percentage of participants				
number (confidence interval 95%)				
Concentration \geq LLOQ	58.43 (50.82 to 65.75)	41.49 (34.37 to 48.89)		
Concentration $\geq 2 \times$ LLOQ	40.45 (33.17 to 48.05)	21.81 (16.13 to 28.40)		
Concentration $\geq 4 \times$ LLOQ	14.61 (9.77 to 20.67)	3.72 (1.51 to 7.52)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Responding to Pertussis Filamentous Hemagglutinin

End point title	Percentage of Participants Responding to Pertussis Filamentous
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End point description:

Participant serum samples were collected for testing with an ELISA for antibodies to pertussis filamentous hemagglutinin. LLOQ=3 EU/mL. Confidence Intervals were calculated based on the exact binomial method of D. Collett. All analyses were performed on the Persistence Analysis Set, defined as all participants previously vaccinated with a complete 2+1 schedule, as part of study V419-008 respectively, for whom immunogenicity results were available.

End point type

Primary

End point timeframe:

Day 1 (approximately 4 years after completion of the 2+1 schedule)

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: This endpoint does not exist for the two groups in V419-007 and accordingly there are no statistics to report.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to the enrollment dynamics in the initial studies and country specificities regarding administration of pre-school booster (children in the 007 study had already received a school-age booster at 4 years of age in Finland, before V419-012 study started), the assessment of pertussis antibody persistence was not possible for subjects from study V419-007 (3+1 schedule).

End point values	Group Vaxelis (2+1)	Group Infanrix hexa (2+1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	188		
Units: Percentage of participants				
number (confidence interval 95%)				
Concentration \geq LLOQ	80.92 (74.27 to 86.49)	88.30 (82.82 to 92.52)		
Concentration $\geq 2 \times$ LLOQ	46.82 (39.21 to 54.54)	70.74 (63.68 to 77.14)		
Concentration $\geq 4 \times$ LLOQ	26.01 (19.65 to 33.22)	45.21 (37.96 to 52.62)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Responding to Pertussis Pertactin

End point title

Percentage of Participants Responding to Pertussis

End point description:

Participant serum samples were collected for testing with an ELISA for antibodies to pertussis pertactin. LLOQ=4 EU/mL. Confidence Intervals were calculated based on the exact binomial method of D. Collett. All analyses were performed on the Persistence Analysis Set, defined as all participants previously vaccinated with a complete 2+1 schedule, as part of study V419-008 respectively, for whom immunogenicity results were available.

End point type

Primary

End point timeframe:

Day 1 (approximately 4 years after completion of the 2+1 schedule)

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: This endpoint does not exist for the two groups in V419-007 and accordingly there are no statistics to report.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to the enrollment dynamics in the initial studies and country specificities regarding administration of pre-school booster (children in the 007 study had already received a school-age booster at 4 years of age in Finland, before V419-012 study started), the assessment of pertussis antibody persistence was not possible for subjects from study V419-007 (3+1 schedule).

End point values	Group Vaxelis (2+1)	Group Infanrix hexa (2+1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	190		
Units: Percentage of participants				
number (confidence interval 95%)				
Concentration \geq LLOQ	66.11 (58.70 to 72.99)	72.63 (65.71 to 78.84)		
Concentration $\geq 2 \times$ LLOQ	43.89 (36.52 to 51.47)	51.05 (43.71 to 58.36)		
Concentration $\geq 4 \times$ LLOQ	15.56 (10.59 to 21.69)	18.42 (13.18 to 24.68)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Responding to Pertussis Fimbriae

End point title	Percentage of Participants Responding to Pertussis Fimbriae ^[8] ^[9]
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End point description:

Participant serum samples were collected for testing with an ELISA for antibodies to pertussis fimbriae. LLOQ=4 EU/mL. Confidence Intervals were calculated based on the exact binomial method of D. Collett. All analyses were performed on the Persistence Analysis Set, defined as all participants previously vaccinated with a complete 2+1 schedule, as part of study V419-008 respectively, for whom immunogenicity results were available.

End point type	Primary
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End point timeframe:

Day 1 (approximately 4 years after completion of the 2+1 schedule)

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: This endpoint does not exist for the two groups in V419-007 and accordingly there are no statistics to report.

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to the enrollment dynamics in the initial studies and country specificities regarding administration of pre-school booster (children in the 007 study had already received a school-age booster at 4 years of age in Finland, before V419-012 study started), the assessment of pertussis antibody persistence was not possible for subjects from study V419-007 (3+1 schedule).

End point values	Group Vaxelis (2+1)	Group Infanrix hexa (2+1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	183		
Units: Percentage of participants				
number (confidence interval 95%)				
Concentration \geq LLOQ	94.35 (89.86 to 97.26)	3.28 (1.21 to 7.00)		

Concentration $\geq 2 \times \text{LLOQ}$	88.14 (82.44 to 92.50)	2.19 (0.60 to 5.50)		
Concentration $\geq 4 \times \text{LLOQ}$	69.49 (62.14 to 76.18)	1.09 (0.13 to 3.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of Antibodies to HBsAg

End point title	Geometric Mean Concentration of Antibodies to HBsAg
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End point description:

Participant serum samples were collected for testing with an enhanced chemiluminescence assay for antibodies to HBsAg. The unit of measure is milli International Units/mL (mIU/mL). Confidence Intervals were calculated based on the t-distribution of the log-transformed antibody concentration. All analyses were performed on the Persistence Analysis Set, defined as all participants previously vaccinated with a complete 3+1 or 2+1 schedule, as part of studies V419 007 or V419-008 respectively, for whom immunogenicity results were available.

End point type	Secondary
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End point timeframe:

Day 1 (approximately 4 years after completion of the 3+1 or 2+1 schedule)

End point values	Group Vaxelis (3+1)	Group Infanrix hexa (3+1)	Group Vaxelis (2+1)	Group Infanrix hexa (2+1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	191	189	181	190
Units: mIU/mL				
geometric mean (confidence interval 95%)	24.43 (19.52 to 30.59)	51.30 (40.19 to 65.46)	19.44 (15.48 to 24.40)	71.00 (54.94 to 91.77)

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of Antibodies to Pertussis Toxin

End point title	Geometric Mean Concentration of Antibodies to Pertussis
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End point description:

Participant serum samples were collected for testing with an ELISA for antibodies to pertussis toxin. The unit of measure is ELISA units/mL (EU/mL). Confidence Intervals were calculated based on the t-distribution of the log-transformed antibody concentration. All analyses were performed on the Persistence Analysis Set, defined as all participants previously vaccinated with a complete 2+1 schedule, as part of study V419-008 respectively, for whom immunogenicity results were available.

End point type	Secondary
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End point timeframe:

Day 1 (approximately 4 years after completion of the 2+1 schedule)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to the enrollment dynamics in the initial studies and country specificities regarding administration of pre-school booster (children in the 007 study had already received a school-age booster at 4 years of age in Finland, before V419-012 study started), the assessment of pertussis antibody persistence was not possible for subjects from study V419-007 (3+1 schedule).

End point values	Group Vaxelis (2+1)	Group Infanrix hexa (2+1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	178	188		
Units: EU/mL				
geometric mean (confidence interval 95%)	5.31 (4.61 to 6.12)	3.64 (3.24 to 4.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of Antibodies to Pertussis Filamentous Hemagglutinin

End point title	Geometric Mean Concentration of Antibodies to Pertussis Filamentous Hemagglutinin ^[11]
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End point description:

Participant serum samples were collected for testing with an ELISA for antibodies to pertussis filamentous hemagglutinin. Confidence Intervals were calculated based on the t-distribution of the log-transformed antibody concentration. All analyses were performed on the Persistence Analysis Set, defined as all participants previously vaccinated with a complete 2+1 schedule, as part of study V419-008 respectively, for whom immunogenicity results were available.

End point type	Secondary
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End point timeframe:

Day 1 (approximately 4 years after completion of the 2+1 schedule)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to the enrollment dynamics in the initial studies and country specificities regarding administration of pre-school booster (children in the 007 study had already received a school-age booster at 4 years of age in Finland, before V419-012 study started), the assessment of pertussis antibody persistence was not possible for subjects from study V419-007 (3+1 schedule).

End point values	Group Vaxelis (2+1)	Group Infanrix hexa (2+1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	188		
Units: EU/mL				
geometric mean (confidence interval 95%)	6.62 (5.54 to 7.91)	11.05 (9.13 to 13.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of Antibodies to Pertussis Pertactin

End point title	Geometric Mean Concentration of Antibodies to Pertussis Pertactin ^[12]
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End point description:

Participant serum samples were collected for testing with an ELISA for antibodies to pertussis pertactin. Confidence Intervals were calculated based on the t-distribution of the log-transformed antibody concentration. All analyses were performed on the Persistence Analysis Set, defined as all participants previously vaccinated with a complete 2+1 schedule, as part of study V419-008 respectively, for whom immunogenicity results were available.

End point type	Secondary
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End point timeframe:

Day 1 (approximately 4 years after completion of the 2+1 schedule)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to the enrollment dynamics in the initial studies and country specificities regarding administration of pre-school booster (children in the 007 study had already received a school-age booster at 4 years of age in Finland, before V419-012 study started), the assessment of pertussis antibody persistence was not possible for subjects from study V419-007 (3+1 schedule).

End point values	Group Vaxelis (2+1)	Group Infanrix hexa (2+1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	190		
Units: EU/mL				
geometric mean (confidence interval 95%)	5.94 (5.14 to 6.86)	7.19 (6.20 to 8.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of Antibodies to Pertussis Fimbriae

End point title	Geometric Mean Concentration of Antibodies to Pertussis Fimbriae ^[13]
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End point description:

Participant serum samples were collected for testing with an ELISA for antibodies to pertussis fimbriae. Confidence Intervals were calculated based on the t-distribution of the log-transformed antibody concentration. All analyses were performed on the Persistence Analysis Set, defined as all participants previously vaccinated with a complete 2+1 schedule, as part of study V419-008 respectively, for whom immunogenicity results were available.

End point type	Secondary
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End point timeframe:

Day 1 (approximately 4 years after completion of the 2+1 schedule)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Due to the enrollment dynamics in the initial studies and country specificities regarding administration of pre-school booster (children in the 007 study had already received a school-age booster at 4 years of age in Finland, before V419-012 study started), the assessment of pertussis antibody persistence was not possible for subjects from study V419-007 (3+1 schedule).

End point values	Group Vaxelis (2+1)	Group Infanrix hexa (2+1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	183		
Units: EU/mL				
geometric mean (confidence interval 95%)	25.99 (21.90 to 30.85)	2.13 (2.01 to 2.25)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants with One or More Serious Adverse Events Related to Study Procedure

End point title	Percentage of Participants with One or More Serious Adverse Events Related to Study Procedure
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End point description:

A serious adverse event (SAE) is any untoward medical occurrence or effect that at any dose results in death or is life-threatening. Life-threatening in this context refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it was more severe. All analyses were performed on the Persistence Analysis Set, defined as all participants previously vaccinated with a complete 3+1 or 2+1 schedule, as part of studies V419 007 or V419-008 respectively, for whom immunogenicity results were available.

End point type	Other pre-specified
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End point timeframe:

Up to 4 days following blood sample on Day 1 (approximately 4 years after completion of the 3+1 or 2+1 schedule)

End point values	Group Vaxelis (3+1)	Group Infanrix hexa (3+1)	Group Vaxelis (2+1)	Group Infanrix hexa (2+1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	191	189	181	191
Units: Percentage of Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Up to 4 days after Day 1

Adverse event reporting additional description:

Adverse Events (AEs) are reported for the Persistence Analysis Set which included all participants previously vaccinated in studies V419-007 or V419-008 with immunogenicity results available. Vaccine safety was not assessed in this study.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Group Vaxelis (3+1)
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Reporting group description:

Participants previously vaccinated with a 3-dose primary series of Vaxelis® at 2, 3 and 4 months of age, and a toddler dose at 12 months of age (study V419-007). On Day 1 of this extension study (approximately [~] 4 years after completion of the 3+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.

Reporting group title	Group Infanrix hexa (3+1)
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Reporting group description:

Participants previously vaccinated with a 3-dose primary series of INFANRIX® hexa at 2, 3 and 4 months of age, and a toddler dose at 12 months of age (study V419-007). On Day 1 of this extension study (~4 years after completion of the 3+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.

Reporting group title	Group Vaxelis (2+1)
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Reporting group description:

Participants previously vaccinated with a 2-dose primary series of Vaxelis® at 2 and 4 months of age, and a toddler dose at 11-12 months of age (study V419-008). On Day 1 of this extension study (~4 years after completion of the 2+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.

Reporting group title	Group Infanrix hexa (2+1)
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Reporting group description:

Participants previously vaccinated with a 2-dose primary series of INFANRIX® hexa at 2 and 4 months of age, and a toddler dose at 11-12 months of age (study V419-008). On Day 1 of this extension study (~4 years after completion of the 2+1 schedule), a 4 mL blood sample was obtained to assay for long-term antibody persistence.

Serious adverse events	Group Vaxelis (3+1)	Group Infanrix hexa (3+1)	Group Vaxelis (2+1)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 191 (0.00%)	0 / 189 (0.00%)	0 / 181 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Group Infanrix hexa (2+1)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 191 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Group Vaxelis (3+1)	Group Infanrix hexa (3+1)	Group Vaxelis (2+1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 191 (0.00%)	0 / 189 (0.00%)	0 / 181 (0.00%)

Non-serious adverse events	Group Infanrix hexa (2+1)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 191 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No vaccine was administered in this study; therefore, vaccine safety was not assessed in this study.

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Vaccine safety was not assessed in the present study.

Notes: