Clinical trial results:
Immunogenicity and Safety of DTaP-IPV-HB-PRP~T Combined Vaccine Given at 3, 5, and 12 Months of Age Concomitantly or Sequentially with 4CMenB Vaccine in Italian and Finnish Infants

Summary

EudraCT number	2019-002585-12
Trial protocol	IT FI
Global end of trial date	13 December 2023

Results information

Result version number	v1 (current)
This version publication date	01 May 2025
First version publication date	01 May 2025

Trial information

Trial identification

Sponsor protocol code	A3L00057

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1239-0365

Notes:

Sponsors

Sponsor organisation name	Sanofi Winthrop Industrie
Sponsor organisation address	82 Avenue Raspail, Gentilly, France, 94250
Public contact	Trial Transparency team, Sanofi Winthrop Industrie, Contact-US@sanofi.com
Scientific contact	Trial Transparency team, Sanofi Winthrop Industrie, Contact-US@sanofi.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	04 October 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of the co-administration of diphtheria (D), tetanus (T), pertussis (acellular, component), hepatitis B (recombinant deoxyribonucleic acid [rDNA]), poliomyelitis (inactivated) and Haemophilus influenzae type b conjugate vaccine (adsorbed) (DTaP-IPV-HB-PRP~T combined vaccine) with 4-component meningococcal B (4CMenB) vaccine in terms of seroprotection rates for anti-hepatitis B surface antigen (HBsAg) and anti-haemophilus influenzae type b polyribosyl ribitol phosphate (Hib PRP) antibodies (Ab) compared to the sequential administration of the same vaccines.

Protection of trial subjects:

Vaccinations were performed by qualified and trained study personnel. Participants with allergy to any of the vaccine components were not vaccinated. After vaccination, participants were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment were also available on site in case of any immediate allergic reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 January 2021
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: 98
Country: Number of subjects enrolled	Italy: 299
Worldwide total number of subjects	397
EEA total number of subjects	397

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)	397
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 11 sites in Italy and Finland.

Pre-assignment

Screening details:

A total of 397 participants were randomized in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Co-administration

Arm description:

Participants received 0.5 milliliter (mL) intramuscular (IM) injection of hexavalent DTaP-IPV-HB-PRP~T combined vaccine administered concomitantly with 0.5 mL IM injection each of pneumococcal polysaccharide conjugate (13-valent, adsorbed) (PCV13) vaccine and 4CMenB vaccine at 3, 5, and 12 months of age.

Arm type	Experimental
Investigational medicinal product name	DTaP-IPV-HB-PRP~T combined vaccine
Investigational medicinal product code	
Other name	Hexyon®, Hexaxim®, Hexacima®
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received 0.5 mL IM injection of hexavalent DTaP-IPV-HB-PRP~T combined vaccine at 3, 5 and 12 months of age.

Investigational medicinal product name	4CMenB vaccine
Investigational medicinal product code	
Other name	Bexsero®
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received 0.5 mL IM injection of 4CMenB vaccine at 3, 5, and 12 months of age.

Investigational medicinal product name	PCV13 vaccine
Investigational medicinal product code	
Other name	Prevenar® 13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received 0.5 mL IM injection of PCV13 vaccine at 3, 5, and 12 months of age.

Arm title	Group 2: Sequential administration

Arm description:

Participants received 0.5 mL IM injection of hexavalent DTaP-IPV-HB-PRP~T combined vaccine administered concomitantly with 0.5 mL IM injection of PCV13 vaccine at 3, 5, and 12 months of age and a sequential administration of 0.5 mL IM injection of 4CMenB vaccine at 4, 6, and 13 months of age.

Arm type	Experimental

Investigational medicinal product name	DTaP-IPV-HB-PRP~T combined vaccine
Investigational medicinal product code	
Other name	Hexyon®, Hexaxim®, Hexacima®
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received 0.5 mL IM injection of hexavalent DTaP-IPV-HB-PRP~T combined vaccine at 3, 5 and 12 months of age.

Investigational medicinal product name	4CMenB vaccine
Investigational medicinal product code	
Other name	Bexsero®
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received 0.5 mL IM injection of 4CMenB vaccine at 4, 6 and 13 months of age.

Investigational medicinal product name	PCV13 vaccine
Investigational medicinal product code	
Other name	Prevenar® 13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received 0.5 mL IM injection of PCV13 vaccine at 3, 5, and 12 months of age.

Number of subjects in period 1	Group 1: Co-administration	Group 2: Sequential administration
Started	201	196
Completed	186	175
Not completed	15	21
Adverse event, non-fatal	1	-
Protocol deviation	3	5
Unspecified	1	-
Lost to follow-up	2	4
Withdrawal by parent/guardian	8	12

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: Co-administration
Reporting group description:	
Participants received 0.5 milliliter (mL) intramuscular (IM) injection of hexavalent DTaP-IPV-HB-PRP~T combined vaccine administered concomitantly with 0.5 mL IM injection each of pneumococcal polysaccharide conjugate (13-valent, adsorbed) (PCV13) vaccine and 4CMenB vaccine at 3, 5, and 12 months of age.	
Reporting group title	Group 2: Sequential administration
Reporting group description:	
Participants received 0.5 mL IM injection of hexavalent DTaP-IPV-HB-PRP~T combined vaccine administered concomitantly with 0.5 mL IM injection of PCV13 vaccine at 3, 5, and 12 months of age and a sequential administration of 0.5 mL IM injection of 4CMenB vaccine at 4, 6, and 13 months of age.	

Reporting group values	Group 1: Co-administration	Group 2: Sequential administration	Total
Number of subjects	201	196	397
Age Categorical			
Units: Subjects			
Age Continuous			
Units: weeks			
arithmetic mean	12.9	12.8	
standard deviation	± 1.40	± 1.33	-
Gender Categorical			
Units: Subjects			
Female	94	91	185
Male	107	105	212

End points

End points reporting groups

Reporting group title	Group 1: Co-administration

Reporting group description:

Participants received 0.5 milliliter (mL) intramuscular (IM) injection of hexavalent DTaP-IPV-HB-PRP~T combined vaccine administered concomitantly with 0.5 mL IM injection each of pneumococcal polysaccharide conjugate (13-valent, adsorbed) (PCV13) vaccine and 4CMenB vaccine at 3, 5, and 12 months of age.

Reporting group title	Group 2: Sequential administration

Reporting group description:

Participants received 0.5 mL IM injection of hexavalent DTaP-IPV-HB-PRP~T combined vaccine administered concomitantly with 0.5 mL IM injection of PCV13 vaccine at 3, 5, and 12 months of age and a sequential administration of 0.5 mL IM injection of 4CMenB vaccine at 4, 6, and 13 months of age.

Primary: Percentage of Participants who Achieved Anti-Hepatitis B Surface Antigen (HBsAg) Antibodies Concentration Above Predefined Threshold

End point title	Percentage of Participants who Achieved Anti-Hepatitis B Surface Antigen (HBsAg) Antibodies Concentration Above Predefined Threshold

End point description:

Anti-HBsAg Ab were measured by the commercially available VITROS ECi/ECiQ immunodiagnostic system using chemiluminescence detection technology. The percentage of participants with an anti-HBsAg Ab concentration >=10 milli international units per mL (mIU/mL) was assessed. Percentages are rounded off to the tenth decimal place. Analysis was performed on per protocol analysis set (PPAS) which was a subset of the full analysis set (FAS: a subset of randomized participants who received at least 1 dose of the study vaccine) that included participants who did not present with any of the protocol deviations.

End point type	Primary

End point timeframe:

Day 30 post-dose 3 of DTaP-IPV-HB-PRP~T combined vaccine (Month 13)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	97		
Units: percentage of participants				
number (confidence interval 95%)	98.0 (94.2 to 99.6)	95.9 (89.8 to 98.9)		

Statistical analyses

Statistical analysis title	Difference in percentage of participants
Comparison groups	Group 1: Co-administration v Group 2: Sequential administration

Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in percentage of participants
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	8.3

Notes:

[1] - Non-inferiority concluded if the lower limit of 2-sided 95% confidence interval (CI) of difference between groups was greater than -10%

Primary: Percentage of Participants who Achieved Anti-polyribosyl Ribitol Phosphate (PRP) Antibodies Concentration Above Predefined Threshold

End point title	Percentage of Participants who Achieved Anti-polyribosyl Ribitol Phosphate (PRP) Antibodies Concentration Above Predefined Threshold

End point description:

Anti-PRP Ab were measured using a Farr-type radioimmunoassay (RIA). The percentage of participants with an anti-PRP Ab concentration >=1.0 microgram [mcg]/mL was assessed. Percentages are rounded off to the tenth decimal place. Analysis was performed on PPAS which was a subset of the FAS that included participants who did not present with any of the protocol deviations.

End point type	Primary

End point timeframe:

Day 30 post-dose 3 of DTaP-IPV-HB-PRP~T combined vaccine (Month 13)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	97		
Units: percentage of participants				
number (confidence interval 95%)	86.6 (80.0 to 91.6)	94.8 (88.4 to 98.3)		

Statistical analyses

Statistical analysis title	Difference in percentage of participants
Comparison groups	Group 1: Co-administration v Group 2: Sequential administration
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in percentage of participants
Point estimate	-8.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.3
upper limit	-0.4

Notes:

[2] - Non-inferiority concluded if the lower limit of 2-sided 95% CI of difference between groups was greater than -10%

Secondary: Percentage of Participants who Achieved Antibodies Against all Antigens of DTaP-IPV-HB-PRP~T Combined Vaccine Above Predefined Thresholds

End point title	Percentage of Participants who Achieved Antibodies Against all Antigens of DTaP-IPV-HB-PRP~T Combined Vaccine Above Predefined Thresholds

End point description:

The following cut-off values were considered:
- >=0.01 IU/mL, >=0.1 IU/mL, and >=1.0 IU/mL for anti-D and anti-T Ab concentrations
- >=8 (1/dilution) for anti-poliovirus 1, 2, and 3 Ab titers
- >=lower limit of quantification (LLOQ) and >=4 times (*) LLOQ for anti-pertussis (PT) and anti-filamentous hemagglutinin (FHA) Ab concentrations
- >=0.15 mcg/mL and >=1.0 mcg/mL for anti-PRP Ab concentrations
- >=10 mIU/mL and >=100 mIU/mL for anti-HBsAg Ab concentrations.

The Ab concentrations against diphtheria, pertussis, tetanus antigens were assayed using electrochemiluminescence (ECL) immunoassay method. Anti-poliovirus types 1, 2, and 3 was measured by a neutralization assay. Percentages are rounded off to the tenth decimal place. Analysis was performed on PPAS which was a subset of the FAS that included participants who did not present with any of the protocol deviations. Here 'n'= number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

Pre-dose 1 (Month 3) and Day 30 post-dose 3 of DTaP-IPV-HB-PRP~T combined vaccine (Month 13)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	97		
Units: percentage of participants				
number (confidence interval 95%)				
Anti-D, >=0.01 IU/mL, Month 3 (n=149,97)	93.3 (88.0 to 96.7)	92.8 (85.7 to 97.0)		
Anti-D, >=0.1 IU/mL, Month 3 (n=149,97)	55.7 (47.3 to 63.8)	48.5 (38.2 to 58.8)		
Anti-D, >=1.0 IU/mL, Month 3 (n=149,97)	4.0 (1.5 to 8.6)	5.2 (1.7 to 11.6)		
Anti-D, >=0.01 IU/mL, Month 13 (n=149,97)	100 (97.6 to 100)	100 (96.3 to 100)		
Anti-D, >=0.1 IU/mL, Month 13 (n=149,97)	100 (97.6 to 100)	100 (96.3 to 100)		
Anti-D, >=1.0 IU/mL, Month 13 (n=149,97)	92.6 (87.2 to 96.3)	96.9 (91.2 to 99.4)		
Anti-T, >=0.01 IU/mL, Month 3 (n=149,96)	99.3 (96.3 to 100)	100 (96.2 to 100)		
Anti-T, >=0.1 IU/mL, Month 3 (n=149,96)	95.3 (90.6 to 98.1)	92.7 (85.6 to 97.0)		
Anti-T, >=1.0 IU/mL, Month 3 (n=149,96)	55.7 (47.3 to 63.8)	46.9 (36.6 to 57.3)		

Anti-T, >= 0.01 IU/mL, Month 13 (n=149,97)	100 (97.6 to 100)	100 (96.3 to 100)		
Anti-T, >=0.1 IU/mL, Month 13 (n=149,97)	100 (97.6 to 100)	100 (96.3 to 100)		
Anti-T, >=1.0 IU/mL, Month 13 (n=149,97)	90.6 (84.7 to 94.8)	95.9 (89.8 to 98.9)		
Anti-Polio 1, Month 3 (n=91,60)	36.3 (26.4 to 47.0)	41.7 (29.1 to 55.1)		
Anti-Polio 1, Month 13 (n=128,95)	100 (97.2 to 100)	100 (96.2 to 100)		
Anti-Polio 2, Month 3 (n=107,64)	64.5 (54.6 to 73.5)	79.7 (67.8 to 88.7)		
Anti-Polio 2, Month 13 (n=129,96)	100 (97.2 to 100)	100 (96.2 to 100)		
Anti-Polio 3, Month 3 (n=113,70)	46.0 (36.6 to 55.6)	44.3 (32.4 to 56.7)		
Anti-Polio 3, Month 13 (n=131,96)	100 (97.2 to 100)	100 (96.2 to 100)		
Anti-PT, >=LLOQ, Month 3 (n=149,96)	100 (97.6 to 100)	100 (96.2 to 100)		
Anti-PT, >=4*LLOQ, Month 3 (n=149,96)	100 (97.6 to 100)	100 (96.2 to 100)		
Anti-PT, >=LLOQ, Month 13 (n=149,97)	100 (97.6 to 100)	100 (96.3 to 100)		
Anti-PT, >=4*LLOQ, Month 13 (n=149,97)	100 (97.6 to 100)	100 (96.3 to 100)		
Anti-FHA, >=LLOQ, Month 3 (n=148,94)	100 (97.5 to 100)	100 (96.2 to 100)		
Anti-FHA, >=4*LLOQ, Month 3 (n=148,94)	100 (97.5 to 100)	100 (96.2 to 100)		
Anti-FHA, >=LLOQ, Month 13 (n=149,97)	100 (97.6 to 100)	100 (96.3 to 100)		
Anti-FHA, >=4*LLOQ, Month 13 (n=149,97)	100 (97.6 to 100)	100 (96.3 to 100)		
Anti-PRP, >=0.15 mcg/mL, Month 3 (n=149,97)	26.8 (19.9 to 34.7)	26.8 (18.3 to 36.8)		
Anti-PRP, >=1 mcg/mL, Month 3 (n=149,97)	2.7 (0.7 to 6.7)	2.1 (0.3 to 7.3)		
Anti-PRP, >=0.15 mcg/mL, Month 13 (n=149,97)	98.0 (94.2 to 99.6)	99.0 (94.4 to 100)		
Anti-HBsAg, >=10 mIU/mL, Month 3 (n=146,95)	41.1 (33.0 to 49.5)	31.6 (22.4 to 41.9)		
Anti-HBsAg, >=100 mIU/mL, Month 3 (n=146,95)	16.4 (10.8 to 23.5)	11.6 (5.9 to 19.8)		
Anti-HBsAg, >=100 mIU/mL, Month 13 (n=149,97)	90.6 (84.7 to 94.8)	82.5 (73.4 to 89.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentrations (GMCs) of Antibodies Against all Antigens of the DTaP-IPV-HB-PRP~T Combined Vaccine Except Polio 1, 2 and 3

End point title	Geometric Mean Concentrations (GMCs) of Antibodies Against all Antigens of the DTaP-IPV-HB-PRP~T Combined Vaccine Except Polio 1, 2 and 3

End point description:

GMCs of Abs against diphtheria, pertussis, tetanus antigens were assayed using ECL immunoassay

method. GMCs of Abs against PRP were measured using a Farr-type RIA. Anti-HBsAg Ab were measured by the commercially available VITROSECi/ECiQ immunodiagnostic system using chemiluminescence detection technology. Individual Ab concentrations for D, T, PT, FHA, PRP, and HBsAg are presented. Analysis was performed on PPAS which was a subset of the FAS that included participants who did not present with any of the protocol deviations. Here 'n'= number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

Pre-dose 1 (Month 3) and Day 30 post-dose 3 of DTaP-IPV-HB-PRP~T combined vaccine (Month 13)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	97		
Units: units/mL				
geometric mean (confidence interval 95%)				
Anti-D, Month 3 (n=149,97)	0.107 (0.083 to 0.137)	0.102 (0.075 to 0.139)		
Anti-D, Month 13 (n=149,97)	2.45 (2.22 to 2.70)	2.73 (2.39 to 3.11)		
Anti-T, Month 3 (n=149,96)	0.968 (0.773 to 1.21)	0.841 (0.613 to 1.16)		
Anti-T, Month 13 (n=149,97)	3.59 (3.11 to 4.14)	4.62 (3.84 to 5.56)		
Anti-PT, Month 3 (n=149,96)	6.55 (5.20 to 8.26)	5.04 (3.78 to 6.71)		
Anti-PT, Month 13 (n=149,97)	101 (91.0 to 112)	98.3 (84.5 to 114)		
Anti-FHA, Month 3 (n=148,94)	34.6 (27.6 to 43.3)	23.2 (16.0 to 33.7)		
Anti-FHA, Month 13 (n=149,97)	149 (132 to 167)	152 (133 to 173)		
Anti-PRP, Month 3 (n=149,97)	0.073 (0.060 to 0.090)	0.068 (0.055 to 0.086)		
Anti-PRP, Month 13 (n=149,97)	6.41 (4.89 to 8.40)	10.0 (7.55 to 13.3)		
Anti-HBsAg, Month 3 (n=146,95)	10.9 (8.08 to 14.6)	7.87 (5.52 to 11.2)		
Anti-HBsAg, Month 13 (n=149,97)	1296 (957 to 1754)	1037 (657 to 1638)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Antibodies Against Polio 1, 2 and 3

End point title	Geometric Mean Titers (GMTs) of Antibodies Against Polio 1, 2 and 3

End point description:

Anti-poliovirus types 1, 2, and 3 were measured by a neutralization assay. Individual Ab titers for poliovirus types 1, 2, and 3 are presented. Analysis was performed on PPAS which was a subset of the

FAS that included participants who did not present with any of the protocol deviations. Only those participants with data collected at specified timepoint are reported. Here 'n'= number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

Pre-dose 1 (Month 3) and Day 30 post-dose 3 of DTaP-IPV-HB-PRP~T combined vaccine (Month 13)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	131	96		
Units: 1/dilution				
geometric mean (confidence interval 95%)				
Anti-polio 1, Month 3 (n=91,60)	5.68 (4.41 to 7.32)	5.93 (4.49 to 7.82)		
Anti-polio 1, Month 13 (n=128,95)	875 (730 to 1049)	1738 (1377 to 2193)		
Anti-polio 2, Month 3 (n=107,64)	11.7 (9.21 to 14.8)	14.9 (11.4 to 19.6)		
Anti-polio 2, Month 13 (n=129,96)	2299 (1877 to 2816)	3263 (2695 to 3950)		
Anti-polio 3, Month 3 (n=113,70)	7.15 (5.74 to 8.90)	6.50 (5.06 to 8.36)		
Anti-polio 3, Month 13 (n=131,96)	1511 (1213 to 1881)	1933 (1460 to 2560)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Ratio (GMRs) of Antibodies Against all Antigens of the DTaP-IPV-HB-PRP~T Combined Vaccine

End point title	Geometric Mean Ratio (GMRs) of Antibodies Against all Antigens of the DTaP-IPV-HB-PRP~T Combined Vaccine

End point description:

GMR was the ratio of the individual titers post vaccination over pre-vaccination (30 days post-dose 3 over pre-dose 1). GMRs for D, T, poliovirus types 1, 2, and 3, PT, FHA, PRP, and HBsAg are presented. Analysis was performed on PPAS which was a subset of the FAS that included participants who did not present with any of the protocol deviations. Here 'n'= number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

Pre-dose 1 (Month 3) and Day 30 post-dose 3 of DTaP-IPV-HB-PRP~T combined vaccine (Month 13)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	97		
Units: ratio				
geometric mean (confidence interval 95%)				
Anti-D (n=149,97)	22.9 (17.1 to 30.8)	26.8 (18.5 to 38.9)		
Anti-T (n=149,96)	3.71 (2.83 to 4.87)	5.62 (3.90 to 8.09)		
Anti-Polio 1 (n=83,60)	163 (110 to 242)	289 (183 to 456)		
Anti-Polio 2 (n=98,64)	212 (146 to 308)	204 (139 to 300)		
Anti-Polio 3 (n=104,70)	219 (155 to 308)	298 (196 to 455)		
Anti-PT (n=149,96)	15.4 (11.5 to 20.6)	19.6 (13.6 to 28.4)		
Anti-FHA (n=148,94)	4.32 (3.28 to 5.70)	6.61 (4.20 to 10.4)		
Anti-PRP (n=149,97)	87.4 (61.5 to 124)	146 (104 to 206)		
Anti-HBsAg (n=146,95)	125 (79.6 to 195)	133 (74.1 to 238)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Seroconversion for Anti-pertussis Toxoid and Anti-filamentous Hemagglutinin Adhesion

End point title	Percentage of Participants With Seroconversion for Anti-pertussis Toxoid and Anti-filamentous Hemagglutinin Adhesion

End point description:

The Ab concentrations against pertussis antigens were assayed using ECL immunoassay method. Seroconversion was defined as >=4-fold increase from pre-dose 1 to post-dose 3 Ab concentrations. Percentages are rounded off to the tenth decimal place. Analysis was performed on PPAS which was a subset of the FAS that included participants who did not present with any of the protocol deviations. Only those participants with data collected at specified timepoints are reported. Here 'n'= number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

From pre-dose 1 (Month 3) up to Day 30 post-dose 3 of DTaP-IPV-HB-PRP~T combined vaccine (Month 13)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	96		
Units: percentage of participants				
number (confidence interval 95%)				
Anti-PT (n=149,96)	71.8 (63.9 to 78.9)	78.1 (68.5 to 85.9)		
Anti-FHA (n=148,94)	48.0 (39.7 to 56.3)	54.3 (43.7 to 64.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Antibodies Against 4-component Meningococcal B Vaccine Measured by Serum Bactericidal Assay Using Human Complement (hSBA) Above Predefined Threshold

End point title	Percentage of Participants With Antibodies Against 4-component Meningococcal B Vaccine Measured by Serum Bactericidal Assay Using Human Complement (hSBA) Above Predefined Threshold

End point description:

Functional Ab activity against a panel of different nesseiria meningitidis antigens (neisseria adhesin A [NadA], factor H binding protein [fHbp] and outer membrane vesicles containing outer membrane protein [PorA P1.4]) were measured using an hSBA assay. Cut-off value was >=5 (1/dilution) Ab titers. Percentages are rounded off to the tenth decimal place. Analysis was performed on PPAS which was a subset of the FAS that included participants who did not present with any of the protocol deviations. Only those participants with data collected at specified timepoints are reported. Here 'n'= number of participants with data collected for each specified category. 99999=no participants experiencing the endpoint.

End point type	Secondary

End point timeframe:

Pre-dose 1 (Month 3) and Day 30 post-dose 3 of 4CMenB vaccine (Month 13 for Group 1; Month 14 for Group 2)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	127	94		
Units: percentage of participants				
number (confidence interval 95%)				
Anti-NadA, Month 3 (n=123,83)	0.8 (0 to 4.4)	99999 (99999 to 99999)		
Anti-NadA, Month 13 or 14 (n=127,93)	100 (97.1 to 100)	100 (96.1 to 100)		
Anti-fHbp, Month 3 (n=123,83)	4.1 (1.3 to 9.2)	2.4 (0.3 to 8.4)		
Anti-fHbp, Month 13 or 14 (n=127,94)	98.4 (94.4 to 99.8)	100 (96.2 to 100)		
Anti-PorA P1.4, Month 3 (n=123,83)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Anti-PorA P1.4, Month 13 or 14 (n=127,94)	97.6 (93.3 to 99.5)	98.9 (94.2 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Vaccine Response to Pertussis Toxoid and Filamentous Hemagglutinin Adhesion

End point title	Percentage of Participants With a Vaccine Response to Pertussis Toxoid and Filamentous Hemagglutinin Adhesion

End point description:

The Ab concentrations against pertussis antigens were assayed using ECL immunoassay method. Vaccine response was defined as post-dose 3 Ab concentrations >=4 * LLOQ, if pre-dose 1 Ab concentrations <4 * LLOQ or post-dose 3 Ab concentration >=pre-dose 1 Ab concentration, if pre-dose 1 Ab concentrations >=4 * LLOQ. Percentages are rounded off to the tenth decimal place. Analysis was performed on PPAS which was a subset of the FAS that included participants who did not present with any of the protocol deviations. Only those participants with data collected at specified timepoints are reported. Here 'n'= number of participants with data collected for a particular category.

End point type	Secondary

End point timeframe:

Pre-dose 1 (Month 3) and Day 30 post-dose 3 of DTaP-IPV-HB-PRP~T combined vaccine (Month 13)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	96		
Units: percentage of participants				
number (confidence interval 95%)				
Anti-PT (n=149,96)	97.3 (93.3 to 99.3)	95.8 (89.7 to 98.9)		
Anti-FHA (n=148,94)	81.1 (73.8 to 87.0)	76.6 (66.7 to 84.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers of Antibodies Against Antigens of the 4-component Meningococcal B Vaccine

End point title	Geometric Mean Titers of Antibodies Against Antigens of the 4-component Meningococcal B Vaccine

End point description:

Functional Ab activity against a panel of different N. meningitidis antigens (NadA, fHbp and PorA P1.4) were measured using an hSBA assay. Analysis was performed on PPAS which was a subset of the FAS that included participants who did not present with any of the protocol deviations. Only those

participants with data collected at specified timepoints are reported. Here 'n'= number of participants with data collected for each specified category. -99999 and 99999=not calculated.

End point type	Secondary

End point timeframe:

Pre-dose 1 (Month 3) and Day 30 post-dose 3 of 4CMenB vaccine (Month 13 for Group 1; Month 14 for Group 2)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	127	94		
Units: 1/dilution				
geometric mean (confidence interval 95%)				
Anti-NadA, Month 3 (n=123,83)	2.06 (1.96 to 2.15)	2.00 (-99999 to 99999)		
Anti-NadA, Month 13 or 14 (n=127,93)	2412 (2029 to 2868)	3040 (2411 to 3834)		
Anti-fHbp, Month 3 (n=123,83)	2.33 (2.16 to 2.51)	2.17 (2.03 to 2.33)		
Anti-fHbp, Month 13 or 14 (n=127,94)	68.0 (57.8 to 79.9)	111 (91.8 to 135)		
Anti-PorA P1.4, Month 3 (n=123,83)	2.00 (-99999 to 99999)	2.00 (-99999 to 99999)		
Anti-PorA P1.4, Month 13 or 14 (n=127,94)	50.9 (41.3 to 62.7)	102 (79.9 to 130)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titer Ratio (GMTRs) of Antibodies Against Antigens of the 4-component Meningococcal B Vaccine (4CMenB)

End point title	Geometric Mean Titer Ratio (GMTRs) of Antibodies Against Antigens of the 4-component Meningococcal B Vaccine (4CMenB)

End point description:

GMTR was the ratio of the individual titers post-vaccination over pre-vaccination (Day 30 post-dose 3 over pre-dose 1). Functional Ab activity against a panel of different N. meningitidis strains (NadA, fHbp and PorA P1.4) were measured using an hSBA assay. Analysis was performed on PPAS which was a subset of the FAS that included participants who did not present with any of the protocol deviations. Only those participants with data collected at specified timepoints are reported. Here 'n'= number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

Pre-dose 1 (Month 3) and Day 30 post-dose 3 of 4CMenB vaccine (Month 13 for Group 1; Month 14 for Group 2)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	82		
Units: ratio				
geometric mean (confidence interval 95%)				
Anti-NadA (n=111,81)	1212 (1008 to 1458)	1518 (1188 to 1939)		
Anti-fHbp (n=111,82)	29.9 (24.7 to 36.1)	50.5 (40.5 to 63.0)		
Anti-PorA P1.4 (n=111,82)	26.7 (21.3 to 33.5)	52.2 (40.3 to 67.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentrations of Antibodies Against Pneumococcal Capsular Polysaccharide (PnPS) Antigens of the Pneumococcal Polysaccharide Conjugate Vaccine (13-valent, Adsorbed) Vaccine

End point title	Geometric Mean Concentrations of Antibodies Against Pneumococcal Capsular Polysaccharide (PnPS) Antigens of the Pneumococcal Polysaccharide Conjugate Vaccine (13-valent, Adsorbed) Vaccine

End point description:

Anti-pneumococcal Ab was assessed by pneumococcal capsular polysaccharide (PnPS) immunoglobulin G (IgG) ECL assay which is used to quantitate the amount of anti-streptococcus pneumoniae PS (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F) Ab in human serum. Analysis was performed on PPAS which was a subset of the FAS that included participants who did not present with any of the protocol deviations. GMC for the study population was calculated. Only those participants with data collected at specified timepoint are reported. Here 'n'= number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

Day 30 post-dose 3 of PCV13 vaccine (Month 13)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	94		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (n=116,94)	5.44 (4.64 to 6.38)	3.72 (3.15 to 4.39)		
Serotype 3 (n=117,94)	1.10 (0.962 to 1.25)	0.929 (0.810 to 1.07)		
Serotype 4 (n=116,94)	3.23 (2.82 to 3.69)	2.65 (2.25 to 3.12)		

Serotype 5 (n=116,94)	3.59 (3.13 to 4.13)	2.83 (2.43 to 3.31)		
Serotype 6A (n=117,94)	11.0 (9.76 to 12.4)	8.12 (6.97 to 9.47)		
Serotype 6B (n=119,94)	6.49 (5.55 to 7.59)	5.38 (4.46 to 6.49)		
Serotype 7F (n=119,94)	5.48 (4.93 to 6.08)	4.52 (3.98 to 5.13)		
Serotype 9V (n=117,94)	5.28 (4.61 to 6.05)	4.07 (3.44 to 4.81)		
Serotype 14 (n=119,94)	10.9 (9.11 to 13.1)	10.1 (8.58 to 11.9)		
Serotype 18C (n=115,94)	3.38 (2.98 to 3.84)	2.82 (2.43 to 3.28)		
Serotype 19A (n=116,94)	8.12 (6.92 to 9.53)	5.73 (4.77 to 6.89)		
Serotype 19F (n=117,94)	10.5 (9.06 to 12.1)	7.29 (6.24 to 8.52)		
Serotype 23F (n=118,94)	3.23 (2.78 to 3.75)	2.75 (2.25 to 3.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Vaccine Response to Pneumococcal Capsular Polysaccharide Antigens

End point title	Percentage of Participants With a Vaccine Response to Pneumococcal Capsular Polysaccharide Antigens

End point description:

The PnPS IgG ECL assay is used to quantitate the amount of anti-Streptococcus pneumoniae PS (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F) Ab in human serum. Vaccine response was defined as Day 30 post-dose 3 Ab concentration >=0.35 mcg/mL. Percentages are rounded off to the tenth decimal place. Analysis was performed on PPAS which was a subset of the FAS that included participants who did not present with any of the protocol deviations. Only those participants with data collected at specified timepoint are reported. Here 'n'= number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

Day 30 post-dose 3 of PCV13 vaccine (Month 13)

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	94		
Units: percentage of participants				
number (confidence interval 95%)				
Serotype 1 (n=116,94)	100 (96.9 to 100)	100 (96.2 to 100)		
Serotype 3 (n=117,94)	92.3 (85.9 to 96.4)	95.7 (89.5 to 98.8)		

Serotype 4 (n=116,94)	100 (96.9 to 100)	100 (96.2 to 100)		
Serotype 5 (n=116,94)	100 (96.9 to 100)	98.9 (94.2 to 100)		
Serotype 6A (n=117,94)	100 (96.9 to 100)	100 (96.2 to 100)		
Serotype 6B (n=119,94)	100 (96.9 to 100)	100 (96.2 to 100)		
Serotype 7F (n=119,94)	100 (96.9 to 100)	100 (96.2 to 100)		
Serotype 9V (n=117,94)	100 (96.9 to 100)	100 (96.2 to 100)		
Serotype 14 (n=119,94)	99.2 (95.4 to 100)	100 (96.2 to 100)		
Serotype 18C (n=115,94)	100 (96.8 to 100)	100 (96.2 to 100)		
Serotype 19A (n=116,94)	100 (96.9 to 100)	98.9 (94.2 to 100)		
Serotype 19F (n=117,94)	100 (96.9 to 100)	100 (96.2 to 100)		
Serotype 23F (n=118,94)	98.3 (94.0 to 99.8)	98.9 (94.2 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Immediate Unsolicited Adverse Events

End point title	Number of Participants With Immediate Unsolicited Adverse Events

End point description:

An AE was any untoward medical occurrence in a participant or in a clinical investigation participant administered a medicinal product and which did not necessarily have a causal relationship with this treatment. Immediate events were recorded to capture medically relevant unsolicited systemic AEs (including those related to the product administered) that occurred within the first 30 minutes after vaccination. An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the case report book (CRB) in terms of diagnosis and/or onset window post-vaccination and included both serious adverse events (SAEs) and non-serious unsolicited AEs. Analysis was performed on the safety analysis set (SafAS) which included those participants who received at least 1 dose of the study vaccine (i.e., 1 dose of the hexavalent vaccine) and had any safety data available.

End point type	Secondary

End point timeframe:

Up to 30 minutes post each vaccination

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	192		
Units: participants	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Solicited Injection Site and Systemic Reactions

End point title	Number of Participants With Solicited Injection Site and Systemic Reactions

End point description:

A solicited reaction was a "pre-listed" adverse reaction (sign or symptom) observed and reported under the conditions (nature and onset) prelisted in the protocol and CRB and were considered to be related to the product administered. An injection site reaction was an adverse reaction at and around the injection site which were commonly inflammatory reactions. Solicited injection site reactions included tenderness, erythema and swelling around the injection site. Solicited systemic reactions included fever, vomiting, abnormal crying, drowsiness, appetite loss, and irritability. Analysis was performed on SafAS which included those participants who received at least 1 dose of the study vaccine (i.e., 1 dose of the hexavalent vaccine) and had any safety data available. Only those participants with data collected at specified timepoint are reported.

End point type	Secondary

End point timeframe:

Up to 7 days post each vaccination

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	191		
Units: participants				
Solicited injection site reactions	177	176		
Solicited systemic reactions	186	186		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Unsolicited Non-serious Adverse Events

End point title	Number of Participants With Unsolicited Non-serious Adverse Events

End point description:

An AE was any untoward medical occurrence in a clinical investigation participant administered a medicinal product, and which did not necessarily have a causal relationship with this treatment. An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the CRB in terms of diagnosis and/or onset window post-vaccination. Unsolicited non-serious AEs are reported. Analysis was performed on SafAS which included those participants who received at least 1 dose of the study vaccine (i.e., 1 dose of the hexavalent vaccine) and had any safety data available.

End point type	Secondary

End point timeframe:

Up to 30 days post each vaccination

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	192		
Units: participants	107	134		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Serious Adverse Events (SAEs) and Adverse Events of Special Interest (AESIs)

End point title	Number of Participants With Serious Adverse Events (SAEs) and Adverse Events of Special Interest (AESIs)

End point description:

An SAE was any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was an important medical event. An AESI (serious or non-serious) was defined as one of scientific and medical concern specific to the Sponsor's product or program, for which ongoing monitoring and rapid communication by the Investigator to the Sponsor was appropriate. The following AE were captured as AESI throughout the study: extensive limb swelling, hypotonic hyporesponsive episode, convulsions (whether febrile or not), anaphylactic reactions, apnea, and severe neurological conditions. Analysis was performed on SafAS.

End point type	Secondary

End point timeframe:

From Day 0 (Month 3) up to Month 13 for Group 1 and Month 14 for Group 2

End point values	Group 1: Co-administration	Group 2: Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	192		
Units: participants				
Any SAE	10	8		
Any AESI	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 0 (Month 3) up to Month 13 for Group 1 and Month 14 for Group 2

Adverse event reporting additional description:

Analysis was performed on SafAS which included those participants who received at least 1 dose of the study vaccine (i.e., 1 dose of the hexavalent vaccine) and had any safety data available.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Group 2: Sequential administration

Reporting group description:

Participants received 0.5 mL IM injection of hexavalent DTaP-IPV-HB-PRP~T combined vaccine administered concomitantly with 0.5 mL IM injection of PCV13 vaccine at 3, 5, and 12 months of age and a sequential administration of 0.5 mL IM injection of 4CMenB vaccine at 4, 6, and 13 months of age.

Reporting group title	Group 1: Co-administration

Reporting group description:

Participants received 0.5 mL IM injection of hexavalent DTaP-IPV-HB-PRP~T combined vaccine administered concomitantly with 0.5 mL IM injection each of PCV13 vaccine and 4CMenB vaccine at 3, 5, and 12 months of age.

Serious adverse events	Group 2: Sequential administration	Group 1: Co-administration	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 192 (4.17%)	10 / 194 (5.15%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Hand Fracture			
subjects affected / exposed	0 / 192 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Aortic Valve Stenosis			
subjects affected / exposed	0 / 192 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic Shock			

subjects affected / exposed	1 / 192 (0.52%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 192 (0.52%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 192 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 192 (1.04%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 192 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 192 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19			
subjects affected / exposed	0 / 192 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	1 / 192 (0.52%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	3 / 192 (1.56%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			
subjects affected / exposed	0 / 192 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 192 (0.00%)	2 / 194 (1.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis			
subjects affected / exposed	0 / 192 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Syncytial Virus Infection			
subjects affected / exposed	1 / 192 (0.52%)	0 / 194 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Syncytial Virus Bronchiolitis			
subjects affected / exposed	1 / 192 (0.52%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Bacterial			
subjects affected / exposed	0 / 192 (0.00%)	1 / 194 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Group 2: Sequential administration	Group 1: Co-administration	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	188 / 192 (97.92%)	191 / 194 (98.45%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	164 / 192 (85.42%)	164 / 194 (84.54%)	
occurrences (all)	549	370	
General disorders and administration site conditions			
Injection Site Pain			
subjects affected / exposed	158 / 192 (82.29%)	169 / 194 (87.11%)	
occurrences (all)	739	999	
Injection Site Erythema			
subjects affected / exposed	141 / 192 (73.44%)	147 / 194 (75.77%)	
occurrences (all)	534	695	
Crying			
subjects affected / exposed	168 / 192 (87.50%)	171 / 194 (88.14%)	
occurrences (all)	590	411	
Pyrexia			
subjects affected / exposed	120 / 192 (62.50%)	146 / 194 (75.26%)	
occurrences (all)	242	276	
Injection Site Swelling			
subjects affected / exposed	117 / 192 (60.94%)	138 / 194 (71.13%)	
occurrences (all)	398	545	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	60 / 192 (31.25%)	49 / 194 (25.26%)	
occurrences (all)	107	67	
Teething			
subjects affected / exposed	10 / 192 (5.21%)	8 / 194 (4.12%)	
occurrences (all)	20	9	
Diarrhoea			
subjects affected / exposed	15 / 192 (7.81%)	11 / 194 (5.67%)	
occurrences (all)	16	14	
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	37 / 192 (19.27%)	18 / 194 (9.28%)	
occurrences (all)	45	20	
Rhinorrhoea			
subjects affected / exposed	11 / 192 (5.73%)	5 / 194 (2.58%)	
occurrences (all)	12	5	
Psychiatric disorders			
Irritability			
subjects affected / exposed	172 / 192 (89.58%)	177 / 194 (91.24%)	
occurrences (all)	703	446	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	13 / 192 (6.77%)	8 / 194 (4.12%)	
occurrences (all)	15	9	
Ear Infection			
subjects affected / exposed	10 / 192 (5.21%)	1 / 194 (0.52%)	
occurrences (all)	11	1	
Conjunctivitis			
subjects affected / exposed	12 / 192 (6.25%)	6 / 194 (3.09%)	
occurrences (all)	13	6	
Covid-19			
subjects affected / exposed	16 / 192 (8.33%)	13 / 194 (6.70%)	
occurrences (all)	16	13	
Nasopharyngitis			
subjects affected / exposed	20 / 192 (10.42%)	14 / 194 (7.22%)	
occurrences (all)	32	15	
Upper Respiratory Tract Infection			
subjects affected / exposed	23 / 192 (11.98%)	11 / 194 (5.67%)	
occurrences (all)	39	12	
Rhinitis			
subjects affected / exposed	26 / 192 (13.54%)	20 / 194 (10.31%)	
occurrences (all)	33	23	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	134 / 192 (69.79%)	133 / 194 (68.56%)	
occurrences (all)	316	254	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 July 2020	Updated version following the Italian Medicines Agency (AIFA) feedback.
29 January 2021	Update of responsible personnel list and study plan.
21 January 2022	Enrollment of participants in study A3L00057 was slower than anticipated. Therefore, to limit the duration of the study, additional sites in 1 European country where the tested vaccines (Hexyon, Bexsero, Prevenar 13) were licensed (Finland) were added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported