Clinical trial results:
A phase IIIb multi-centre, open, controlled study to assess the immunogenicity, reactogenicity and safety of GlaxoSmithKline (GSK) Biologicals' Haemophilus influenzae type b – meningococcal serogroup C conjugate (Hib-MenC) vaccine (Menitorix) in preterm and full-term infants when co-administered with GSK Biologicals' DTPa-HBV-IPV vaccine (Infanrix penta) and with Wyeth's 7-valent pneumococcal conjugate vaccine (Prevenar) and given according to a 2, 4 and 6 months of age primary vaccination schedule and when given as a booster dose with concomitant GSK Biologicals' DTPa-IPV vaccine (Infanrix IPV) and Wyeth's Prevenar in the second year of life.
Estudio fase IIIb abierto, multicéntrico, controlado, para evaluar la inmunogenicidad, reactogenicidad y seguridad de la vacuna conjugada frente a Haemophilus Influenzae tipo b y Meningococo del serogrupo C (Hib-MenC) (Menitorix) de GSK Biologicals en niños prematuros y nacidos a término cuando se administra simultáneamente con la vacuna DTPa-HBV-IPV de GSK Biologicals (Infanrix penta) y con la vacuna conjugada antineumocócica 7-valente de Wyeth (Prevenar) administrada como pauta primaria de vacunación a los 2, 4 y 6 meses de edad y cuando se administra como dosis de recuerdo simultáneamente con la vacuna DTPa-IPV de GSK Biologicals (Infanrix IPV) y Prevenar en el segundo año de vida.

Summary

EudraCT number	2007-001167-29
Trial protocol	ES
Global end of trial date	30 December 2008

Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	23 January 2015

Trial information

Trial identification

Sponsor protocol code	110215, 110217

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00586612
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'institut 89, Rixensart, Belgium, 1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 32 2 656 81 11, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 32 2 656 81 11, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 April 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 December 2008
Global end of trial reached?	Yes
Global end of trial date	30 December 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary vaccination
At one month after the third dose (Post dose 3) in preterm and full-term infants:
•To evaluate the immunogenicity of GSK Biologicals' Hib-MenC vaccine when given concomitantly with GSK Biologicals' DTPa-HBV-IPV vaccine and Wyeth's 7-valent pneumococcal vaccine, in terms of percentage of subjects with:
- Anti-PRP concentration >=0.15 microg/ml
- rSBA-MenC titre >=1:8

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 December 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 313
Worldwide total number of subjects	313
EEA total number of subjects	313

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)	313
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:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

Period 1 title	Primary phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Preterm group

Arm description:

Subjects born after a gestation period of less than or equal to 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.

Arm type	Experimental
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study and 1 dose in the Booster study.

Investigational medicinal product name	Infanrix™ penta
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study

Investigational medicinal product name	Prevenar™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study and 1 dose in the Booster study.

Investigational medicinal product name	Infanrix™ IPV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 1 dose in the Booster study.

Arm title	Full-term group

Arm description:

Subjects born after a gestation period of more than 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.

Arm type	Active comparator
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study and 1 dose in the Booster study.

Investigational medicinal product name	Infanrix™ penta
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study

Investigational medicinal product name	Prevenar™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study and 1 dose in the Booster study.

Investigational medicinal product name	Infanrix™ IPV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 1 dose in the Booster study.

Number of subjects in period 1	Preterm group	Full-term group
Started	163	150
Completed	162	147
Not completed	1	3
Consent withdrawn by subject	-	2
Lost to follow-up	-	1
Protocol deviation	1	-

Period 2

Period 2 title	Booster phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Preterm group

Arm description:

Subjects born after a gestation period of less than or equal to 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.

Arm type	Experimental
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study and 1 dose in the Booster study.

Investigational medicinal product name	Infanrix™ penta
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study

Investigational medicinal product name	Prevenar™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study and 1 dose in the Booster study.

Investigational medicinal product name	Infanrix™ IPV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 1 dose in the Booster study.

Arm title	Full-term group

Arm description:

Subjects born after a gestation period of more than 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.

Arm type	Active comparator
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study and 1 dose in the Booster study.

Investigational medicinal product name	Infanrix™ penta
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study

Investigational medicinal product name	Prevenar™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 3 doses in the primary study and 1 dose in the Booster study.

Investigational medicinal product name	Infanrix™ IPV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 1 dose in the Booster study.

Number of subjects in period 2[1]	Preterm group	Full-term group
Started	154	144
Completed	151	143
Not completed	3	1
Lost to follow-up	3	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all the subjects enrolled in the Primary phase started the Booster phase.

Baseline characteristics

Reporting groups	
Reporting group title	Preterm group
Reporting group description:	
Subjects born after a gestation period of less than or equal to 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.	
Reporting group title	Full-term group
Reporting group description:	
Subjects born after a gestation period of more than 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.	

Reporting group values	Preterm group	Full-term group	Total
Number of subjects	163	150	313
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: weeks			
geometric mean	8.9	8.8	
standard deviation	± 1.15	± 0.79	-
Gender categorical			
Units: Subjects			
Female	77	65	142
Male	86	85	171

End points

End points reporting groups

Reporting group title	Preterm group
Reporting group description:	
Subjects born after a gestation period of less than or equal to 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.	
Reporting group title	Full-term group
Reporting group description:	
Subjects born after a gestation period of more than 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.	
Reporting group title	Preterm group
Reporting group description:	
Subjects born after a gestation period of less than or equal to 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.	
Reporting group title	Full-term group
Reporting group description:	
Subjects born after a gestation period of more than 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.	

Primary: Number of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration greater than or equal to 0.15 micrograms per milliliter (µg/mL)

End point title	Number of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration greater than or equal to 0.15 micrograms per milliliter (µg/mL)[1]
End point description:	
Anti-PRP antibody concentration greater than or equal to 0.15 µg/mL is indicative of protection.	
End point type	Primary
End point timeframe:	
One month after the third vaccination	

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: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	142		
Units: Subjects				
(anti-PRP)	139	141		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer greater than or equal to 1:8

End point title	Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer greater than or equal to 1:8[2]

End point description:

rSBA-MenC titer greater than or equal to 1:8 is indicative of protection.

End point type	Primary

End point timeframe:

One month after the third vaccination

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: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	140		
Units: Subjects				
(rSBA-MenC)	142	140		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-Polyribosylribitol phosphate (anti-PRP) antibody concentration greater than or equal to the cut-off values

End point title	Number of subjects with Anti-Polyribosylribitol phosphate (anti-PRP) antibody concentration greater than or equal to the cut-off values

End point description:

Anti-PRP antibody cut-off values assessed include 0.15 micrograms per milliliter (µg/mL) and 1 µg/mL.

End point type	Secondary

End point timeframe:

Before vaccination (at Day 0)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	138		
Units: Subjects				
≥ 0.15 µg/mL	38	43		
≥ 1.0 µg/mL	5	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subject with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration greater than or equal to 1 microgram per milliliter

End point title	Number of subject with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration greater than or equal to 1 microgram per milliliter
End point description:	
Anti-PRP antibody cut-off value assessed include 1 microgram per milliliter (µg/mL).	
End point type	Secondary
End point timeframe:	
One month after the third vaccination	

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	142		
Units: Subjects				
(anti-PRP)	133	134		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer greater than or equal to the cut-off values

End point title	Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer greater than or equal to the cut-off values
End point description:	
rSBA-MenC titer cut-off values assessed include 1:8, 1:32 and 1:128.	
End point type	Secondary
End point timeframe:	
Before vaccination (at Day 0)	

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	137		
Units: Subjects				
≥ 1:8	16	23		
≥ 1:32	5	11		
≥ 1:128	0	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer greater than or equal to the cut-off values

End point title	Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer greater than or equal to the cut-off values

End point description:

rSBA-MenC titer cut-off values assessed include 1:32 and 1:128.

End point type	Secondary

End point timeframe:

One month after the third vaccination

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	140		
Units: Subjects				
≥ 1:32	142	139		
≥ 1:128	135	136		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-polysaccharide C (anti-PSC) antibody concentration greater than or equal to (≥) the cut-off values

End point title	Number of subjects with Anti-polysaccharide C (anti-PSC) antibody concentration greater than or equal to (≥) the cut-off values

End point description:

Anti-PSC antibody cut-off values assessed include 0.3 micrograms per milliliter (µg/mL) and 2 µg/mL.

End point type	Secondary

End point timeframe:

Before vaccination (at Day 0)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	137		
Units: Subjects				
≥ 0.3 µg/mL	23	36		
≥ 2.0 µg/mL	3	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-polysaccharide C (anti-PSC) antibody concentration greater than or equal to (≥) the cut-off values

End point title	Number of subjects with Anti-polysaccharide C (anti-PSC) antibody concentration greater than or equal to (≥) the cut-off values

End point description:

Anti-PSC antibody cut-off values assessed include 0.3 micrograms per milliliter (µg/mL) and 2 µg/mL.

End point type	Secondary

End point timeframe:

One month after the third dose

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	141		
Units: Subjects				
≥ 0.3 µg/mL	140	141		
≥ 2.0 µg/mL	127	136		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentration greater than or equal to (≥) the cut-off values

End point title	Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentration greater than or equal to (≥) the cut-off values

End point description:

Anti-HBs antibody cut-off values assessed include 10 milli-international units per milliliter (mIU/mL) and 100 mIU/mL.

End point type	Secondary

End point timeframe:

Before vaccination (at Day 0)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	118		
Units: Subjects				
≥ 10 mIU/mL	89	78		
≥ 100 mIU/mL	3	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentration greater than or equal to (≥) the cut-off values

End point title	Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentration greater than or equal to (≥) the cut-off values

End point description:

Anti-HBs antibody cut-off values assessed include 10 milli-international units per milliliter (mIU/mL) and 100 mIU/mL.

End point type	Secondary

End point timeframe:

One month after the third dose

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	129		
Units: Subjects				
≥ 10 mIU/mL	128	129		
≥ 100 mIU/mL	109	117		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosylribitol phosphate (anti-PRP) and anti-polysaccharide C (anti-PSC) concentration

End point title	Anti-polyribosylribitol phosphate (anti-PRP) and anti-polysaccharide C (anti-PSC) concentration

End point description:

Anti-PRP and anti-PSC concentrations are given as geometric mean concentrations (GMCs) expressed micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

Before vaccination (at Day 0)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	138		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP (n=140, 138)	0.116 (0.101 to 0.133)	0.14 (0.117 to 0.167)		
Anti-PSC (n=142, 137)	0.19 (0.17 to 0.22)	0.25 (0.21 to 0.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosylribitol phosphate (anti-PRP) and anti-polysaccharide C (anti-PSC) concentration

End point title	Anti-polyribosylribitol phosphate (anti-PRP) and anti-polysaccharide C (anti-PSC) concentration

End point description:

Anti-PRP and anti-PSC concentrations are given as geometric mean concentrations (GMCs) expressed micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

One month after the third dose

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	142		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP (n= 140, 142)	10.437 (8.398 to 12.97)	10.473 (8.547 to 12.833)		
Anti-PSC (n= 140, 141)	6.34 (5.57 to 7.22)	7.46 (6.67 to 8.34)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B surface antigen (anti-HBs) concentration

End point title	Anti-hepatitis B surface antigen (anti-HBs) concentration

End point description:

Anti-HBs concentrations are given as geometric mean concentrations (GMCs) expressed in milli-international units per milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

Before vaccination (at Day 0)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	118		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-hepatitis B surface antigen (anti-HBs)	24.79 (19.82 to 31)	16.67 (13.52 to 20.56)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B surface antigen (anti-HBs) concentration

End point title	Anti-hepatitis B surface antigen (anti-HBs) concentration

End point description:

Anti-HBs concentrations are given as geometric mean concentrations (GMCs) expressed in milli-international units per milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

One month after the third dose

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	129		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-hepatitis B surface antigen (anti-HBs)	372.3 (299.98 to 462.04)	586.58 (473.8 to 726.21)		

Statistical analyses

No statistical analyses for this end point

Secondary: Meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer

End point title	Meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer
End point description:	
rSBA-MenC titers are given as geometric mean titers (GMTs).	
End point type	Secondary
End point timeframe:	
Before vaccination (at Day 0)	

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	137		
Units: Titer				
geometric mean (confidence interval 95%)				
(rSBA-MenC)	4.9 (4.5 to 5.5)	5.9 (4.9 to 6.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer

End point title	Meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer
End point description:	
rSBA-MenC titers are given as geometric mean titers (GMTs).	
End point type	Secondary
End point timeframe:	
One month after the third dose	

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	140		
Units: titre				
geometric mean (confidence interval 95%)				
(rSBA-MenC)	1055.9 (859.1 to 1297.7)	1346.2 (1130.4 to 1603.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms

End point title	Number of subjects reporting solicited local symptoms

End point description:

Solicited local symptoms assessed include pain, redness and swelling and are presented across doses.

End point type	Secondary

End point timeframe:

During the 4-day follow-up period after any primary vaccination dose

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	150		
Units: Subjects				
Pain	106	100		
Redness	94	123		
Swelling	91	113		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general symptoms

End point title	Number of subjects reporting solicited general symptoms

End point description:

Solicited general symptoms assessed include drowsiness, fever, irritability/fussiness and loss of appetite and are presented across doses.

End point type	Secondary

End point timeframe:

During the 4-day follow-up period after any primary vaccination dose

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	150		
Units: Subjects				
Drowsiness	111	102		
Fever	89	85		
Irritability/fussiness	128	105		
Loss of appetite	99	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events (AEs)

End point title	Number of subjects reporting unsolicited adverse events (AEs)

End point description:

Unsolicited AE covers any AE reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms.

End point type	Secondary

End point timeframe:

Within 31 days after each primary vaccination

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	150		
Units: Subjects				
(AEs)	56	72		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

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

End point description:

SAEs assessed include medical occurrences that result in death, is life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

Throughout the entire primary vaccination phase

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	150		
Units: Subjects				
(SAEs)	11	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration greater than or equal to 0.15 migrogram per milliliter (µg/mL)

End point title	Number of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration greater than or equal to 0.15 migrogram per milliliter (µg/mL)

End point description:

Anti-PRP antibody cut-off value assessed was 0.15 migrogram per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

Prior to (Month 14) and one month after the booster vaccination (Month 15)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	134		
Units: Subjects				
Pre-booster (n= 133; 130)	116	117		
Post-booster (n= 132; 134)	132	134		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration greater than or equal to 1.0 migrogram per milliliter (µg/mL)

End point title	Number of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration greater than or equal to 1.0

	migrogram per milliliter (µg/mL)

End point description:

Anti-PRP antibody cut-off value assessed was 1.0 migrogram per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

Prior to (Month 14) and one month after the booster vaccination (Month 15)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	134		
Units: Subjects				
Pre-booster (n= 133; 130)	53	53		
Post-booster (n= 132; 134)	132	134		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer greater than or equal to the cut-off values

End point title	Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer greater than or equal to the cut-off values

End point description:

rSBA-MenC titer cut-off values assessed include 1:8, 1:32 and 1:128.

End point type	Secondary

End point timeframe:

Prior to (Month 14) and one month after the booster vaccination (Month 15)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	137		
Units: Subjects				
≥ 1:8 pre-booster (n= 134; 134)	102	117		
≥ 1:8 post-booster (n= 133; 137)	132	136		
≥ 1:32 pre-booster (n= 134; 134)	95	115		
≥ 1:32 post-booster (n= 133; 137)	132	136		
≥ 1:128 pre-booster (n= 134; 134)	69	85		
≥ 1:128 post-booster (n= 133; 137)	131	136		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polysaccharide C (anti-PSC) antibody concentration greater than or equal to the cut-off values

End point title	Number of subjects with anti-polysaccharide C (anti-PSC) antibody concentration greater than or equal to the cut-off values

End point description:

Anti-PSC antibody cut-off values assessed include 0.3 micrograms per milliliter (µg/mL) and 2.0 µg/mL.

End point type	Secondary

End point timeframe:

Prior to (Month 14) and one month after the booster vaccination (Month 15)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	129		
Units: Subjects				
≥ 0.3 µg/mL pre-booster (n= 130; 127)	74	92		
≥ 0.3 µg/mL post-booster (n= 117; 129)	116	129		
≥ 2.0 µg/mL pre-booster (n= 130; 127)	11	11		
≥ 2.0 µg/mL post-booster (n= 117; 129)	105	124		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentration greater than or equal to the cut-off values

End point title	Number of subjects with anti-hepatitis B surface antigen (anti-HBs) antibody concentration greater than or equal to the cut-off values

End point description:

Anti-HBs antibody cut-off values assessed include 10 milli-international units per milliliter (mIU/mL) and 100 mIU/mL. Note: the protocol planned an analysis on HBs after the booster dose, but this analysis was not performed as the vaccines administered as booster doses did not contain HBs component.

End point type	Secondary

End point timeframe:

Prior to (Month 14) the booster vaccination

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125	116		
Units: Subjects				
≥ 10 mIU/mL pre-booster	121	113		
≥ 100 mIU/mL pre-booster	61	71		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosylribitol phosphate (anti-PRP) and anti-polysaccharide C (anti-PSC) concentration

End point title	Anti-polyribosylribitol phosphate (anti-PRP) and anti-polysaccharide C (anti-PSC) concentration

End point description:

Anti-PRP and anti-PSC concentrations are given as geometric mean concentrations (GMCs) in micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

Prior to (Month 14) and one month after the booster vaccination (Month 15)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	134		
Units: µg/mL				
geometric mean (confidence interval 95%)				
anti-PRP pre-booster (n= 133; 130)	0.706 (0.565 to 0.881)	0.777 (0.622 to 0.972)		
anti-PRP post-booster (n= 132; 134)	50.343 (41.627 to 60.884)	54.625 (45.325 to 65.834)		
anti-PSC pre-booster (n= 130; 127)	0.42 (0.35 to 0.51)	0.56 (0.47 to 0.67)		
anti-PSC post-booster (n= 117; 129)	10.06 (8.14 to 12.45)	11.31 (9.6 to 13.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B surface antigen (anti-HBs) concentration

End point title	Anti-hepatitis B surface antigen (anti-HBs) concentration

End point description:

Anti-HBs concentrations are given as geometric mean concentrations (GMCs) in milli-international units

per milliliter (mIU/mL). Note: Planned analysis in the protocol of HBs after the booster dose was not performed as booster vaccines did not contain HBs component.

End point type	Secondary

End point timeframe:

Prior to (Month 14) the booster vaccination

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125	116		
Units: :mIU/mL				
geometric mean (confidence interval 95%)				
(anti-HBs)	95.9 (75.6 to 121.5)	145.6 (112.1 to 189.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer

End point title	Meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer

End point description:

rSBA-MenC titers are given as geometric mean titers (GMTs).

End point type	Secondary

End point timeframe:

Prior to (Month 14) and one month after the booster vaccination (Month 15)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	137		
Units: titre				
geometric mean (confidence interval 95%)				
Pre-booster (n= 134; 134)	79.3 (56.3 to 111.8)	147.8 (110.9 to 197.1)		
Post-booster (n= 133; 137)	4883.1 (3783.1 to 6302.9)	5288.8 (4244.9 to 6589.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited symptoms (local and general)

End point title	Number of subjects reporting solicited symptoms (local and general)

End point description:

Solicited local symptoms assessed include pain, redness and swelling. Solicited general symptoms assessed include drowsiness, fever, irritability/fussiness and loss of appetite.

End point type	Secondary

End point timeframe:

During the 4-day follow-up period following booster vaccination

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	144		
Units: Subjects				
Pain	82	98		
Redness	77	109		
Swelling	67	94		
Drowsiness	33	46		
Fever	43	53		
Irritability	70	69		
Loss of appetite	34	50		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events (AEs)

End point title	Number of subjects reporting unsolicited adverse events (AEs)

End point description:

Unsolicited AE covers any AE reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms.

End point type	Secondary

End point timeframe:

Within 31 days after the booster vaccination (month 15)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	144		
Units: Subjects				
(AEs)	34	42		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

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

End point description:

SAEs assessed include medical occurrences that result in death, is life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject. Period 1 is defined as 31 days after last primary vaccination until administration of booster dose (Month 14). Period 2 is defined as the administration of the booster dose until the end of the study (Month 15).

End point type	Secondary

End point timeframe:

31 days after last primary vaccination until administration of booster dose (Month 14) and from the administration of the booster dose until the end of the study (Month 15)

End point values	Preterm group	Full-term group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	144		
Units: Subjects				
Period 1	10	2		
Period 2	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For SAEs: the whole study period (Day 0 - Month 15); For frequent adverse events: solicited adverse events a 4-day period after vaccination, unsolicited adverse events a 31-day period after vaccination.

Adverse event reporting additional description:

Solicited adverse events after primary and booster vaccination are put as separate adverse events. In the description field of these adverse events it is specified to which vaccination phase they belong.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Preterm group

Reporting group description:

Subjects born after a gestation period of less than or equal to 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.

Reporting group title	Full-term group

Reporting group description:

Subjects born after a gestation period of more than 36 weeks and who received 3 doses (at 2, 4 and 6 months of age) of Menitorix™, Infanrix™ penta and Prevenar™ and a booster dose of Menitorix™, Infanrix™ IPV and Prevenar™ at 16-18 months of age.

Serious adverse events	Preterm group	Full-term group	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 163 (13.50%)	10 / 150 (6.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 150 (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			
Apnoea			
subjects affected / exposed	1 / 163 (0.61%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			

subjects affected / exposed	4 / 163 (2.45%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	6 / 163 (3.68%)	2 / 150 (1.33%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 163 (2.45%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 163 (0.61%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 163 (1.84%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candidiasis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 163 (0.61%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	1 / 163 (0.61%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningococcal sepsis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 163 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 163 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 163 (0.61%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 163 (0.00%)	2 / 150 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	1 / 163 (0.61%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	1 / 163 (0.61%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 163 (0.61%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 163 (0.61%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	1 / 163 (0.61%)	0 / 150 (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	Preterm group	Full-term group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	128 / 163 (78.53%)	123 / 150 (82.00%)	
General disorders and administration site conditions			
Injection site nodule			
subjects affected / exposed	3 / 163 (1.84%)	24 / 150 (16.00%)	
occurrences (all)	3	24	

Pain (After primary vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed	106 / 163 (65.03%)	100 / 150 (66.67%)	
occurrences (all)	106	100	
Redness (After primary vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed	94 / 163 (57.67%)	123 / 150 (82.00%)	
occurrences (all)	94	123	
Swelling (After primary vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed	91 / 163 (55.83%)	123 / 150 (82.00%)	
occurrences (all)	91	123	
Drowsiness (After primary vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed	111 / 163 (68.10%)	102 / 150 (68.00%)	
occurrences (all)	111	102	
Fever (After primary vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed	89 / 163 (54.60%)	85 / 150 (56.67%)	
occurrences (all)	89	85	
Irritability/fussiness (After primary vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed	128 / 163 (78.53%)	105 / 150 (70.00%)	
occurrences (all)	128	105	
Loss of appetite (After primary vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed	99 / 163 (60.74%)	100 / 150 (66.67%)	
occurrences (all)	99	100	
Pain (After booster vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	82 / 154 (53.25%)	98 / 144 (68.06%)	
occurrences (all)	82	98	
Redness (After booster vaccination)			

alternative assessment type: Systematic			
subjects affected / exposed[2]	77 / 154 (50.00%)	109 / 144 (75.69%)	
occurrences (all)	77	109	
Swelling (After booster vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed[3]	67 / 154 (43.51%)	94 / 144 (65.28%)	
occurrences (all)	67	94	
Drowsiness (After booster vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed[4]	33 / 154 (21.43%)	46 / 144 (31.94%)	
occurrences (all)	33	46	
Fever (After booster vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed[5]	43 / 154 (27.92%)	53 / 144 (36.81%)	
occurrences (all)	43	53	
Irritability/fussiness (After booster vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed[6]	70 / 154 (45.45%)	69 / 144 (47.92%)	
occurrences (all)	70	69	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	9 / 163 (5.52%)	6 / 150 (4.00%)	
occurrences (all)	9	6	
Infections and infestations			
Injection site haematoma			
subjects affected / exposed	1 / 163 (0.61%)	9 / 150 (6.00%)	
occurrences (all)	1	9	
Loss of appetite (After booster vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed[7]	34 / 154 (22.08%)	69 / 144 (47.92%)	
occurrences (all)	34	69	
Upper respiratory tract infection			
subjects affected / exposed	7 / 163 (4.29%)	11 / 150 (7.33%)	
occurrences (all)	7	11	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total Vaccinated cohort, only on subjects with their symptom sheets completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported