Clinical trial results:
A phase III open-label randomised study to evaluate the immunogenicity and safety of the concomitant administration of a new Hexavalent DTaP-IPV-HB-Hib combined vaccine (Hexavalent vaccine) given at 2, 3, and 4 months of age with a meningococcal serogroup C conjugate (MenC) vaccine given at 2 and 4 months of age.

Short title:
Concomitant administration of a new hexavalent vaccine (Hexavalent vaccine) with a meningococcal serogroup C conjugate vaccine in healthy infants during primary series immunisation followed by booster vaccination

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2012-005547-24
Trial protocol	FI
Global end of trial date	11 February 2015

Results information

Result version number	v1
This version publication date	13 April 2016
First version publication date	18 March 2015

Trial information

Trial identification

Sponsor protocol code	HXM01C

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01839175
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur MSD SNC
Sponsor organisation address	162 avenue Jean Jaurès - CS 50712, Lyon Cedex 07, France, 69367
Public contact	Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C., ClinicalTrialsDisclosure@spmsd.com
Scientific contact	Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C., ClinicalTrialsDisclosure@spmsd.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	Interim
Date of interim/final analysis	29 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 July 2014
Global end of trial reached?	Yes
Global end of trial date	11 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

PRIMARY SERIES (Period 2):
- To demonstrate that the concomitant administration of the hexavalent vaccine given at 2, 3 and 4 months of age with a meningococcal serogroup C conjugate (MenC) vaccine given at 2 and 4 months of age is non inferior to the administration of the hexavalent vaccine without a MenC vaccine concomitantly in term of seroprotection rate for hepatitis B one month after the third dose of the hexavalent vaccine.
- To demonstrate that the concomitant administration of a MenC vaccine given at 2 and 4 months of age with the hexavalent vaccine given at 2, 3 and 4 months of age induces an acceptable response for MenC in term of seroprotection rate (SPR) one month after the second dose of MenC.

BOOSTER:
To describe the immunogenicity of a booster dose of the hexavalent vaccine and of a meningococcal group ACWY conjugate vaccine either co-administered at 12 months of age or given separately.

Protection of trial subjects:

Subjects in the study received three injections during primary series (period 2) and one injection during the booster part of a single dose of the study vaccine DTaP-IPV-HB-Hib supplied in a prefilled 0.5 mL syringe that was administered by qualified study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After each vaccination, subjects were also kept under observation for 30 minutes to ensure their safety. Appropriate equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

Not Applicable

Evidence for comparator:

The control group complies with the recommended vaccination schedules for all vaccines (i.e. Study vaccine and routine vaccines) as per their respective Summaries of Product Characteristics (SmPCs).

Actual start date of recruitment	29 April 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 350
Worldwide total number of subjects	350
EEA total number of subjects	350

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)	350
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:

Study subjects were enrolled from 29 April 2013 to 09 August 2013 in 11 clinical centers in Finland.

Pre-assignment

Screening details:

A total of 354 subjects were screened out of which 350 subjects who met all the inclusion but none of the exclusion criteria were randomised and vaccinated.

Period 1

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

Blinding implementation details:

This was an open-label study as the number of vaccines administered in each group was different at several visits. Blinding would have required a placebo injection which was not deemed necessary since the primary endpoints were based on immunological criteria. Serology tests for the hexavalent vaccine antigens were performed by laboratory staff blinded to subject group.

Arms

Are arms mutually exclusive?	Yes
Arm title	Hexavalent vaccine co-administered with MenC vaccine

Arm description:

Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with one dose each at 2, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.

Arm type	Experimental
Investigational medicinal product name	Hexyon (Hexavalent vaccine)
Investigational medicinal product code	DTaP-IPV-HB-Hib
Other name	Hexacima / Hexaxim
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route, one dose at 2, 3, and 4 months of age.

Investigational medicinal product name	NeisVac-C
Investigational medicinal product code	MenC vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route, one dose at 2, and 4 months of age.

Arm title	Hexavalent vaccine without MenC vaccine

Arm description:

Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.

Arm type	Active comparator

Investigational medicinal product name	Hexyon (Hexavalent vaccine)
Investigational medicinal product code	DTaP-IPV-HB-Hib
Other name	Hexacima / Hexaxim
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route, one dose at 2, 3, and 4 months of age.

Number of subjects in period 1	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine
Started	175	175
Completed	175	175

Period 2

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

Blinding implementation details:

This was an open-label study as the number of vaccines administered in each group was different at several visits. Blinding would have required a placebo injection which was not deemed necessary since the primary endpoints were based on immunological criteria. Serology tests for the hexavalent vaccine antigens were performed by laboratory staff blinded to subject group.

Arms

Are arms mutually exclusive?	Yes
Arm title	Hexavalent vaccine co-administered with MenC vaccine

Arm description:

Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with one dose each at 2, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.

Arm type	Experimental
Investigational medicinal product name	Hexyon (Hexavalent vaccine)
Investigational medicinal product code	DTaP-IPV-HB-Hib
Other name	Hexacima / Hexaxim
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route, one dose at 2, 3, and 4 months of age.

Investigational medicinal product name	NeisVac-C
Investigational medicinal product code	MenC vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route, one dose at 2, and 4 months of age.

Arm title	Hexavalent vaccine without MenC vaccine

Arm description:

Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age. Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.

Arm type	Active comparator
Investigational medicinal product name	Hexyon (Hexavalent vaccine)
Investigational medicinal product code	DTaP-IPV-HB-Hib
Other name	Hexacima / Hexaxim
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route, one dose at 2, 3, and 4 months of age.

Number of subjects in period 2	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine
Started	175	175
Completed	173	172
Not completed	2	4
Adverse event, non-fatal	1	2
Transferred to other arm/group	1	-
Lost to follow-up	-	2
Joined	0	1
Transferred in from other group/arm	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Hexavalent vaccine co-administered with MenC vaccine
Reporting group description:	
Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with one dose each at 2, and 4 months of age. Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.	
Reporting group title	Hexavalent vaccine without MenC vaccine
Reporting group description:	
Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age. Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.	

Reporting group values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine	Total
Number of subjects	175	175	350
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	175	175	350
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: days			
arithmetic mean	62.8	63.2	
standard deviation	± 7	± 7	-
Gender categorical Units: Subjects			
Female	83	82	165
Male	92	93	185

End points

End points reporting groups

Reporting group title	Hexavalent vaccine co-administered with MenC vaccine
Reporting group description:	
Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with one dose each at 2, and 4 months of age. Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.	
Reporting group title	Hexavalent vaccine without MenC vaccine
Reporting group description:	
Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age. Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.	
Reporting group title	Hexavalent vaccine co-administered with MenC vaccine
Reporting group description:	
Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with one dose each at 2, and 4 months of age. Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.	
Reporting group title	Hexavalent vaccine without MenC vaccine
Reporting group description:	
Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age. Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.	

Primary: Seroprotection against Hepatitis B one month after vaccination with either Hexavalent vaccine co-administered with MenC vaccine or Hexavalent vaccine without MenC vaccine

End point title	Seroprotection against Hepatitis B one month after vaccination with either Hexavalent vaccine co-administered with MenC vaccine or Hexavalent vaccine without MenC vaccine
End point description:	
Percentage of subjects with an anti-Hepatitis B surface antigen (Hep B) concentration ≥10 mIU/mL (measured by hepatitis B enhanced Chemiluminescence assay) Analysis was done on the per protocol set.	
End point type	Primary
End point timeframe:	
One month post-dose 3 of Hexavalent vaccine.	

End point values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	160	155		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-Hep B ≥10 mIU/mL	97.5 (93.7 to 99.3)	96.1 (91.8 to 98.6)		

Statistical analyses

Statistical analysis title	non-inferiority of the immune response

Statistical analysis description:

To demonstrate the non-inferiority of the immune response of the concomitant administration of the Hexavalent vaccine co-administered with MenC vaccine as compared to the Hexavalent vaccine without Men C vaccine one month after the third dose.

Comparison groups	Hexavalent vaccine co-administered with MenC vaccine v Hexavalent vaccine without MenC vaccine
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	Wilson score Method without cc
Parameter estimate	Difference in percentages of subjects
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.92
upper limit	5.95

Notes:

[1] - The immune response of Hexavalent vaccine co-administered with MenC vaccine was considered as non-inferior to Hexavalent vaccine without MenC vaccine if the lower bound of the two-sided 95.0% Confidence Intervals (CI) of the difference in the percentages of subjects with anti-Hep B ≥10 mIU/mL measured one month after the third dose is greater than -10%. CI was based on the Wilson score method without continuity correction (cc).

Primary: Seroprotection for MenC one month after vaccination with two doses of MenC

End point title	Seroprotection for MenC one month after vaccination with two doses of MenC[2]

End point description:

Percentages of subjects with an anti-MenC titre ≥8 (1/dilution (dil)) (measured by Serum Bactericidal Antibody assay with rabbit complement) one month after two doses of MenC vaccine.
Analysis was done on the per protocol set.
The immune response to MenC vaccine was considered as acceptable if the lower bound of the two-sided 95.0% CI of the percentage of subjects with anti-MenC ≥8 (1/dil) one month after the second dose is greater than 90%

End point type	Primary

End point timeframe:

One month post-dose 2 of MenC vaccine.

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 immune response to MenC vaccine was considered as acceptable if the lower bound of the two-sided 95.0% CI of the percentage of subjects with anti-MenC ≥8 (1/dil) one month after the second dose is greater than 90%. No comparison between arms was planned.

End point values	Hexavalent vaccine co-administered with MenC vaccine			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-MenC≥8 (1/dil)	100 (97.7 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Response rates for all Hexavalent vaccine antigens one month after 3 doses of Hexavalent vaccine co-administered with MenC vaccine or 3 doses of Hexavalent vaccine without MenC vaccine

End point title	Response rates for all Hexavalent vaccine antigens one month after 3 doses of Hexavalent vaccine co-administered with MenC vaccine or 3 doses of Hexavalent vaccine without MenC vaccine

End point description:

Percentages of subjects with an anti-Hep B concentration ≥10 mIU/mL (measured by Hep B enhanced Chemiluminescence assay), with an anti-PRP concentration ≥0.15ug/mL for Hib by Farr type radioimmunoassay, with an anti-D concentration ≥0.01 IU/mL and ≥0.1 IU/mL for diphtheria by Micrometabolic Inhibition Test (MIT), with an anti-T concentration ≥0.01 IU/mL and ≥0.1 IU/mL for tetanus by enzyme linked immunosorbent assay (ELISA), with an anti-IPV titre ≥8 (1/dil) for poliovirus types 1, 2, and 3 by MIT, with an anti-PT vaccine response (VR), with an anti-FHA VR, with 4-fold increase for PT and FHA by ELISA (EU/mL).
Pertussis vaccine response (VR) is defined as:
- If pre-vaccination antibody concentration was <4*LLOQ, then the post-vaccination antibody concentration was to be ≥4*LLOQ,
- If pre-vaccination antibody concentration was ≥4*LLOQ, then the post-vaccination antibody concentration was to be ≥pre-immunisation levels
Analysis was done on the per protocol set

End point type	Secondary

End point timeframe:

One month post-dose 3 of Hexavalent vaccine.

End point values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	160		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-Hep B ≥10 mIU/mL (N=160, 155)	97.5 (93.7 to 99.3)	96.1 (91.8 to 98.6)		
Anti-PRP ≥0.15 ug/mL (N=160, 158)	98.1 (94.6 to 99.6)	94.3 (89.5 to 97.4)		

Anti-D ≥ 0.01 IU/mL (N=160, 158)	100 (97.7 to 100)	99.4 (96.5 to 100)		
Anti-D≥ 0.1 IU/mL (N=160, 158)	35 (27.6 to 42.9)	41.1 (33.4 to 49.2)		
Anti-T ≥ 0.01 IU/mL (N=159, 156)	100 (97.7 to 100)	100 (97.7 to 100)		
Anti-T ≥ 0.1 IU/mL (N=159, 156)	100 (97.7 to 100)	99.4 (96.5 to 100)		
Anti-IPV1 (N=159, 152)	100 (97.7 to 100)	98.7 (95.3 to 99.8)		
Anti-IPV2 (N=159, 152)	100 (97.7 to 100)	100 (97.6 to 100)		
Anti-IPV3 (N=159, 152)	100 (97.7 to 100)	99.3 (96.4 to 100)		
Anti-PT VR (N=154, 154)	98.7 (95.4 to 99.8)	100 (97.6 to 100)		
Anti-PT 4-fold (N=154, 154)	88.3 (82.2 to 92.9)	88.3 (82.2 to 92.9)		
Anti-FHA VR (N=154, 153)	99.4 (96.4 to 100)	100 (97.6 to 100)		
Anti-FHA 4-fold (N=154, 153)	89.6 (83.7 to 93.9)	91.5 (85.9 to 95.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Response rates for MenC one month after vaccination with one dose or two doses of MenC Vaccine.

End point title	Response rates for MenC one month after vaccination with one dose or two doses of MenC Vaccine.

End point description:

Percentages of subjects with an anti-MenC titre ≥8 (1/dilution (dil)) or with an anti-MenC titre ≥128 (1/dil) (measured by Serum Bactericidal Antibody assay with rabbit complement) one month after one dose or one month after two doses of MenC vaccine.
Analysis was done on the per protocol set.

End point type	Secondary

End point timeframe:

One month post-dose 1 or post-dose 2 of MenC vaccine.

End point values	Hexavalent vaccine co-administered with MenC vaccine			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-MenC ≥8 (1/dil) post-dose 1 (N=157)	99.4 (96.5 to 100)			
Anti-MenC ≥128 (1/dil) post-dose 1 (N=157)	98.1 (94.5 to 99.6)			

Anti-MenC ≥8 (1/dil) post-dose 2 (N=162)	100 (97.7 to 100)			
Anti-MenC ≥128 (1/dil) post-dose 2 (N=162)	96.3 (92.1 to 98.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers or Concentrations of Antibodies one month after 3 doses of Hexavalent vaccine co-administered with MenC vaccine or 3 doses of Hexavalent vaccine without MenC vaccine

End point title	Geometric Mean Titers or Concentrations of Antibodies one month after 3 doses of Hexavalent vaccine co-administered with MenC vaccine or 3 doses of Hexavalent vaccine without MenC vaccine

End point description:

Antibody titers or concentrations were measured for hepatitis B (Hep B) by enhanced chemiluminescence detection (mIU/mL), for Haemophilus influenzae type b (PRP) by Farr type radioimmunoassay (ug/mL), for diphtheria (D) by Micrometabolic Inhibition Test (IU/mL), for tetanus by enzyme linked immunosorbent assay (IU/mL), for poliovirus (IPV) types 1, 2, and 3 by Micrometabolic Inhibition Test (1/dil), for pertussis toxoid (PT) and filamentous hemagglutinin (FHA) by enzyme linked immunosorbent assay (ELISA in EU/mL)).
Analysis was done on the per protocol set.

End point type	Secondary

End point timeframe:

One month post-dose 3 of Hexavalent vaccine.

End point values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	160		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Hep B (N=160, 155)	242.75 (195.05 to 302.11)	267.58 (212.65 to 336.7)		
Anti-PRP (N=160, 158)	3.49 (2.88 to 4.24)	1.89 (1.49 to 2.38)		
Anti-D (N=160, 158)	0.08 (0.07 to 0.1)	0.09 (0.08 to 0.1)		
Anti-T (N=159, 156)	1.17 (1.07 to 1.29)	0.78 (0.7 to 0.87)		
Anti-IPV1 (N=159, 152)	92.49 (75.06 to 113.97)	126.84 (101.46 to 158.56)		
Anti-IPV2 (N=159, 152)	90.9 (73.23 to 112.83)	104.72 (82.66 to 132.67)		

Anti-IPV3 (N=159, 152)	173.3 (138.2 to 217.31)	250.78 (197.56 to 318.34)		
Anti-PT (N=160, 159)	129.74 (118.93 to 141.52)	139.91 (126.98 to 154.15)		
Anti-FHA (N=158, 156)	123.54 (112.47 to 135.69)	147.77 (134.82 to 161.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers of Antibodies one month after 1 dose or 2 doses of MenC vaccine co-administered with Hexavalent vaccine

End point title	Geometric Mean Titers of Antibodies one month after 1 dose or 2 doses of MenC vaccine co-administered with Hexavalent vaccine

End point description:

Antibody titers were measured by Serum Bactericidal Antibody assay with rabbit complement (1/dil) one month after one dose or two doses of MenC vaccine
Analysis was done on the per protocol set.

End point type	Secondary

End point timeframe:

One month post-dose 1 or post-dose 2 of MenC vaccine.

End point values	Hexavalent vaccine co-administered with MenC vaccine			
Subject group type	Reporting group			
Number of subjects analysed	162			
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-MenC post-dose 1 (N=157)	885.17 (737.06 to 1063.04)			
Anti-MenC post-dose 2 (N=162)	579.64 (505.36 to 664.84)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Solicited Injection Site or Systemic Reactions After Hexavalent vaccine co-administered with MenC vaccine or

Hexavalent vaccine without MenC

End point title	Number of Subjects Reporting Solicited Injection Site or Systemic Reactions After Hexavalent vaccine co-administered with MenC vaccine or Hexavalent vaccine without MenC

End point description:

Solicited Injection Site Reactions: Erythema, Pain, and Swelling; Solicited Systemic Reactions: Crying, Decreased appetite, Irritability, Pyrexia, Somnolence, and Vomiting within 7 days after any hexavalent vaccine injection with or without MenC vaccine. Analysis was done on the safety analysis set, i.e. all subjects who received at least one dose of the hexavalent vaccine and had any safety follow-up data.

End point type	Secondary

End point timeframe:

Day 0 up to 7 days following any dose.

End point values	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent vaccine without MenC vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	176		
Units: Number of subjects				
number (not applicable)				
Solicited reaction any dose	174	176		
Solicited Injection site reaction	155	130		
Solicited Injection site after Hexavalent vaccine	147	130		
Erythema after Hexavalent vaccine	95	97		
Pain after Hexavalent vaccine	120	109		
Swelling after Hexavalent vaccine	60	61		
Solicited Injection site after MenC vaccine	124	0		
Erythema after MenC vaccine	78	0		
Pain after MenC vaccine	106	0		
Swelling after MenC vaccine	45	0		
Solicited systemic reaction	174	176		
Crying	148	125		
Decreased appetite	98	96		
Irritability	166	166		
Pyrexia	126	127		
Somnolence	144	151		
Vomiting	63	47		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited adverse events were collected from Day 0 up to 30 days after each vaccination. Serious adverse events were collected from the first vaccination and up to the last visit.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Hexavalent vaccine co-administered with MenC vaccine

Reporting group description:

Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age co-administered with 2 doses of MenC vaccine with one dose each at 2, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age

Reporting group title	Hexavalent without MenC

Reporting group description:

Subjects received 3 doses of hexavalent vaccine with one dose each at 2, 3, and 4 months of age.
Subjects received also routine vaccination: RotaTeq at 2, 3, and 4 months of age and Prevenar 13 at 2, and 4 months of age.

Serious adverse events	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent without MenC	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 174 (2.30%)	2 / 176 (1.14%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin neoplasm bleeding			
subjects affected / exposed	0 / 174 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 174 (0.57%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			

subjects affected / exposed	1 / 174 (0.57%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 174 (0.00%)	1 / 176 (0.57%)	
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	1 / 174 (0.57%)	0 / 176 (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	1 / 174 (0.57%)	0 / 176 (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	Hexavalent vaccine co-administered with MenC vaccine	Hexavalent without MenC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	105 / 174 (60.34%)	108 / 176 (61.36%)	
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	9 / 174 (5.17%)	7 / 176 (3.98%)	
occurrences (all)	11	7	
Injection site induration			
subjects affected / exposed	14 / 174 (8.05%)	9 / 176 (5.11%)	
occurrences (all)	25	10	
Pyrexia			
subjects affected / exposed	5 / 174 (2.87%)	10 / 176 (5.68%)	
occurrences (all)	6	11	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	14 / 174 (8.05%)	12 / 176 (6.82%)	
occurrences (all)	17	15	
Flatulence			
subjects affected / exposed	7 / 174 (4.02%)	9 / 176 (5.11%)	
occurrences (all)	7	12	
Teething			
subjects affected / exposed	9 / 174 (5.17%)	5 / 176 (2.84%)	
occurrences (all)	12	5	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 174 (5.17%)	9 / 176 (5.11%)	
occurrences (all)	12	9	
Infections and infestations			
Rhinitis			
subjects affected / exposed	24 / 174 (13.79%)	26 / 176 (14.77%)	
occurrences (all)	34	32	
Upper respiratory tract infection			
subjects affected / exposed	25 / 174 (14.37%)	27 / 176 (15.34%)	
occurrences (all)	29	27	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 November 2013	Amendment 1 to Protocol (leading to Version 2.0) was produced to provide details regarding the booster vaccination at 12 to 13 months of age with hexavalent vaccine, 13-valent pneumococcal polysaccharide conjugate vaccine and meningococcal C containing vaccine.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

None reported

Notes: