Clinical trial results:
A Phase 2, Open-label, Controlled, Multi-center Study to Evaluate Meningococcal ACWY Antibody Response in Children Aged 40 and 60 Months who Have Previously Received Novartis MenACWY Conjugate Vaccine as Infants

Summary

EudraCT number	2007-004978-16
Trial protocol	GB
Global end of trial date	20 September 2010

Results information

Result version number	v1 (current)
This version publication date	11 May 2016
First version publication date	18 November 2014

Trial information

Trial identification

Sponsor protocol code	V59P5E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00601731
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics S.r.l.
Sponsor organisation address	Via fiorentina 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines and Diagnostics S.r.l., RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics S.r.l., RegistryContactVaccinesUS@novartis.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 March 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 September 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immunity against meningococcal serogroups A, C, W-135 and Y at 40 and 60 months of age in children who were vaccinated with MenACWY Ad- at 2, 4 and 12 months of age, in terms of percentage of participants with human SBA (hSBA) titers ≥ 1:8 for each of meningococcal serogroups A, C, W-135 and Y (Men A, C, W, Y).

Protection of trial subjects:

Study vaccines were not administered to individuals with known hypersensitivity to any component of the vaccines. An oral temperature ≥38.0°C (≥100.4°F) or serious active infection was a reason for delaying vaccination. Standard immunization practices were observed and care was taken to administer the injection intramuscularly. As with all injectable vaccines, appropriate medical treatment and supervision was readily available in case of rare anaphylactic reactions following administration of the study vaccine. Epinephrine 1:1000 and diphenhydramine was available in case of any anaphylactic reactions. Care was taken to ensure that the vaccine is not injected into a blood vessel.

Background therapy:

In Canada, a preschool booster of MMR and DTaP/IPV was given out of study at the 60-month visit, if not already given in the routine Public Health program after 48 months of age.

Evidence for comparator: -

Actual start date of recruitment	05 February 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 186
Country: Number of subjects enrolled	Canada: 196
Worldwide total number of subjects	382
EEA total number of subjects	186

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	382
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:

Subjects were enrolled at 2 centers in Canada and 1 center in the UK.

Pre-assignment

Screening details:

Attempts were made to contact the parents of the 274 UK children and 263 Canadian children who completed V59P5 study, to enroll their child in this follow-on study.

Period 1

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

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	UK Site

Arm description:

UK vaccine group that received primary vaccine schedule of MenACWY (adjuvanted and unadjuvanted) vaccine at 2 and 4 or 2, 3 and 4 months with booster at 12 months of age, enrolled at either 40 or 60 months of age into the current study as follow-on participants.

Arm type	Experimental
Investigational medicinal product name	MenACWY Conjugate Vaccine
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 or 4 doses of 0.5 millilitres

Arm title	UK Control

Arm description:

Newly enrolled age-matched subjects that received a complete vaccination course of routine monovalent MenC conjugate vaccine at 2, 3 and 4 months of age without any booster vaccination.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Canada Sites

Arm description:

Canadian vaccine group that received primary vaccination with MenACWY (adjuvanted and unadjuvanted) vaccine at 2,4 months of age with 12 month booster or at 2, 4, 6 months with or without a booster vaccination.

Arm type	Experimental
Investigational medicinal product name	MenACWY Conjugate Vaccine
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 or 4 doses of 0.5 millilitres

Arm title	Canada Control

Arm description:

Newly enrolled age-matched subjects that received the complete vaccination course of routine monovalent MenC conjugate vaccine at 2 and 12 months or only at 12 months of age.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	UK Site	UK Control	Canada Sites
Started	143	43	166
Completed	120	43	151
Not completed	23	0	15
Consent withdrawn by subject	10	-	3
Lost to follow-up	13	-	12

Number of subjects in period 1	Canada Control
Started	30
Completed	29
Not completed	1
Consent withdrawn by subject	-
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	UK Site
Reporting group description:	
UK vaccine group that received primary vaccine schedule of MenACWY (adjuvanted and unadjuvanted) vaccine at 2 and 4 or 2, 3 and 4 months with booster at 12 months of age, enrolled at either 40 or 60 months of age into the current study as follow-on participants.	
Reporting group title	UK Control
Reporting group description:	
Newly enrolled age-matched subjects that received a complete vaccination course of routine monovalent MenC conjugate vaccine at 2, 3 and 4 months of age without any booster vaccination.	
Reporting group title	Canada Sites
Reporting group description:	
Canadian vaccine group that received primary vaccination with MenACWY (adjuvanted and unadjuvanted) vaccine at 2,4 months of age with 12 month booster or at 2, 4, 6 months with or without a booster vaccination.	
Reporting group title	Canada Control
Reporting group description:	
Newly enrolled age-matched subjects that received the complete vaccination course of routine monovalent MenC conjugate vaccine at 2 and 12 months or only at 12 months of age.	

Reporting group values	UK Site	UK Control	Canada Sites
Number of subjects	143	43	166
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: months			
arithmetic mean	44.3	62	42.5
standard deviation	± 6.4	± 0.2	± 4.5
Gender categorical Units: Subjects			
Female	74	20	85
Male	69	23	81

Reporting group values	Canada Control	Total	
Number of subjects	30	382	
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: months			
arithmetic mean	60.6		
standard deviation	± 0.6	-	
Gender categorical			
Units: Subjects			
Female	15	194	
Male	15	188	

Subject analysis sets

Subject analysis set title	UK2,3,4,12+, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 3, and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4,12+, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4C/12+, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of monovalent MenC-CRM conjugate vaccine at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4,12-, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 12 months of age.

Subject analysis set title	UK Control, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Newly enrolled age-matched subjects that received a complete vaccination course of routine monovalent MenC conjugate vaccine at 2, 3 and 4 months of age without any booster vaccination.

Subject analysis set title	Ca2,4,6+, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 4 and 6 months of age without any booster vaccination.

Subject analysis set title	Ca2,4,6+/12PS, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM1 conjugate vaccine with adjuvant at 2, 4 and 6 months of age followed by a reduced booster vaccination of quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Subject analysis set title	Ca2,4,12+, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	Ca2,4+/12PS, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a reduced booster vaccination of quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Subject analysis set title	Ca2,4,12-, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a booster vaccination of the quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 12 months of age.

Subject analysis set title	Ca2,4-/12PS, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a reduced booster vaccination of the quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Subject analysis set title	Ca Control, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Newly enrolled age-matched subjects that received a complete vaccination course of routine monovalent MenC conjugate vaccine at 2 and 12 months or only at 12 months of age.

Subject analysis set title	UK2,3,4,12+, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 3, and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4,12+, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4C/12+, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of monovalent MenC-CRM conjugate vaccine at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4,12-, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without

adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 12 months of age.

Subject analysis set title	Ca2,4,6+, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 4 and 6 months of age without any booster vaccination.

Subject analysis set title	Ca2,4,6+/12PS, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 4 and 6 months of age followed by a reduced booster vaccination of quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Subject analysis set title	Ca2,4,12+, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	Ca2,4+/12PS, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a reduced booster vaccination of quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Subject analysis set title	Ca2,4,12-, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a booster vaccination of the quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 12 months of age.

Subject analysis set title	Ca2,4-/12PS, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a reduced booster vaccination of the quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Reporting group values	UK2,3,4,12+, 60 Months	UK2,4,12+, 60 Months	UK2,4C/12+, 60 Months
Number of subjects	33	35	18
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age continuous			
Units: months			
arithmetic mean	61.3	61.4	61.2
standard deviation	± 0.8	± 0.8	± 0.8
Gender categorical			
Units: Subjects			
Female	11	19	12
Male	22	16	6

Reporting group values	UK2,4,12-, 60 Months	UK Control, 60 Months	Ca2,4,6+, 60 Months
Number of subjects	31	42	27
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: months			
arithmetic mean	61.5	62	60.3
standard deviation	± 0.6	± 0.2	± 0.5
Gender categorical			
Units: Subjects			
Female	18	19	19
Male	13	23	8

Reporting group values	Ca2,4,6+/12PS, 60 Months	Ca2,4,12+, 60 Months	Ca2,4+/12PS, 60 Months
Number of subjects	25	23	25
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: months			
arithmetic mean	60.6	60.3	60.2
standard deviation	± 1	± 0.6	± 0.4

Gender categorical Units: Subjects			
Female	12	13	10
Male	13	10	15

Reporting group values	Ca2,4,12-, 60 Months	Ca2,4-/12PS, 60 Months	Ca Control, 60 Months
Number of subjects	23	24	30
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: months			
arithmetic mean	60.7	60.4	60.6
standard deviation	± 0.7	± 0.5	± 0.6
Gender categorical Units: Subjects			
Female	12	12	15
Male	11	12	15

Reporting group values	UK2,3,4,12+, 40 Months	UK2,4,12+, 40 Months	UK2,4C/12+, 40 Months
Number of subjects	33	37	17
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: months			
arithmetic mean	42.5	42.6	42.6
standard deviation	± 0.6	± 0.6	± 0.5
Gender categorical Units: Subjects			
Female	13	19	12
Male	20	18	5

Reporting group values	UK2,4,12-, 40 Months	Ca2,4,6+, 40 Months	Ca2,4,6+/12PS, 40 Months
Number of subjects	34	28	23
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: months			
arithmetic mean	40.6	42	41.8
standard deviation	± 0.8	± 1	± 1.2
Gender categorical			
Units: Subjects			
Female	19	19	9
Male	15	9	14

Reporting group values	Ca2,4,12+, 40 Months	Ca2,4+/12PS, 40 Months	Ca2,4,12-, 40 Months
Number of subjects	27	28	25
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: months			
arithmetic mean	42	41.6	40.7
standard deviation	± 0.9	± 1	± 1
Gender categorical			
Units: Subjects			
Female	15	10	12
Male	12	18	13

Reporting group values	Ca2,4-/12PS, 40 Months		
Number of subjects	24		

Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: months			
arithmetic mean	40.9		
standard deviation	± 1.1		
Gender categorical Units: Subjects			
Female	13		
Male	11		

End points

End points reporting groups

Reporting group title	UK Site

Reporting group description:

UK vaccine group that received primary vaccine schedule of MenACWY (adjuvanted and unadjuvanted) vaccine at 2 and 4 or 2, 3 and 4 months with booster at 12 months of age, enrolled at either 40 or 60 months of age into the current study as follow-on participants.

Reporting group title	UK Control

Reporting group description:

Newly enrolled age-matched subjects that received a complete vaccination course of routine monovalent MenC conjugate vaccine at 2, 3 and 4 months of age without any booster vaccination.

Reporting group title	Canada Sites

Reporting group description:

Canadian vaccine group that received primary vaccination with MenACWY (adjuvanted and unadjuvanted) vaccine at 2,4 months of age with 12 month booster or at 2, 4, 6 months with or without a booster vaccination.

Reporting group title	Canada Control

Reporting group description:

Newly enrolled age-matched subjects that received the complete vaccination course of routine monovalent MenC conjugate vaccine at 2 and 12 months or only at 12 months of age.

Subject analysis set title	UK2,3,4,12+, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 3, and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4,12+, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4C/12+, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of monovalent MenC-CRM conjugate vaccine at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4,12-, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 12 months of age.

Subject analysis set title	UK Control, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Newly enrolled age-matched subjects that received a complete vaccination course of routine monovalent MenC conjugate vaccine at 2, 3 and 4 months of age without any booster vaccination.

Subject analysis set title	Ca2,4,6+, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 4 and 6 months of age without any booster vaccination.

Subject analysis set title	Ca2,4,6+/12PS, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM1 conjugate vaccine with adjuvant at 2, 4 and 6 months of age followed by a reduced booster vaccination of quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Subject analysis set title	Ca2,4,12+, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	Ca2,4+/12PS, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a reduced booster vaccination of quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Subject analysis set title	Ca2,4,12-, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a booster vaccination of the quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 12 months of age.

Subject analysis set title	Ca2,4-/12PS, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a reduced booster vaccination of the quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Subject analysis set title	Ca Control, 60 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Newly enrolled age-matched subjects that received a complete vaccination course of routine monovalent MenC conjugate vaccine at 2 and 12 months or only at 12 months of age.

Subject analysis set title	UK2,3,4,12+, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 3, and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4,12+, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4C/12+, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of monovalent MenC-CRM conjugate vaccine at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	UK2,4,12-, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without

adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 12 months of age.

Subject analysis set title	Ca2,4,6+, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 4 and 6 months of age without any booster vaccination.

Subject analysis set title	Ca2,4,6+/12PS, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 4 and 6 months of age followed by a reduced booster vaccination of quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Subject analysis set title	Ca2,4,12+, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Subject analysis set title	Ca2,4+/12PS, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a reduced booster vaccination of quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Subject analysis set title	Ca2,4,12-, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a booster vaccination of the quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 12 months of age.

Subject analysis set title	Ca2,4-/12PS, 40 Months
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a reduced booster vaccination of the quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Primary: Percentages of subjects with human Serum Bactericidal Assay (hSBA) ≥ 1:8 for each of meningococcal serogroups A, C, W and Y

End point title	Percentages of subjects with human Serum Bactericidal Assay (hSBA) ≥ 1:8 for each of meningococcal serogroups A, C, W and Y[1]

End point description:

Percentages of subjects with human Serum Bactericidal Assay (hSBA) ≥1:8 as measured by serum bactericidal activity at 40 months and 60 months of age and associated 95% Clopper-Pearson CIs were computed for each of the serogroups within each of the vaccinated groups and in age-matched control subjects.

End point type	Primary

End point timeframe:

40 months and 60 months of age

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: Statisical analyses are not applicable for this end point.

End point values	UK2,3,4,12+, 60 Months	UK2,4,12+, 60 Months	UK2,4C/12+, 60 Months	UK2,4,12-, 60 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33[2]	35[3]	18[4]	31
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	9 (2 to 24)	11 (3 to 27)	11 (1 to 35)	3 (0.082 to 17)
Serogroup C	34 (19 to 53)	32 (17 to 51)	59 (33 to 82)	45 (27 to 64)
Serogroup W	69 (50 to 84)	85 (68 to 95)	78 (52 to 94)	84 (66 to 95)
Serogroup Y	61 (42 to 77)	71 (53 to 85)	71 (44 to 90)	42 (25 to 61)

Notes:

[2] - No. subjects serogroup C: 32
No. subjects serogroup W: 32
[3] - No. subjects serogroup C: 34
No. subjects serogroup W: 34
No. subjects serogroup Y: 34
[4] - No. subjects serogroup C: 17
No. subjects serogroup Y: 17

End point values	UK Control, 60 Months	Ca2,4,6+, 60 Months	Ca2,4,6+/12PS, 60 Months	Ca2,4,12+, 60 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	27[5]	25[6]	23[7]
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	0 (0 to 8)	0 (0 to 13)	0 (0 to 14)	4 (0 to 22)
Serogroup C	29 (16 to 45)	14 (3 to 36)	13 (3 to 32)	14 (3 to 35)
Serogroup W	36 (22 to 52)	31 (14 to 52)	44 (24 to 65)	57 (34 to 77)
Serogroup Y	29 (16 to 45)	30 (14 to 50)	24 (9 to 45)	43 (23 to 66)

Notes:

[5] - No. subjects serogroup C: 21
No. subjects serogroup W: 26
[6] - No. subjects serogroup C: 24
[7] - No. subjects serogroup C: 22

End point values	Ca2,4+/12PS, 60 Months	Ca2,4,12-, 60 Months	Ca2,4-/12PS, 60 Months	Ca Control, 60 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25[8]	23[9]	24[10]	30[11]
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	4 (0 to 20)	4 (0 to 22)	0 (0 to 14)	3 (0.084 to 17)
Serogroup C	24 (8 to 47)	27 (11 to 50)	46 (26 to 67)	53 (34 to 72)
Serogroup W	42 (22 to 63)	81 (58 to 95)	67 (45 to 84)	34 (18 to 54)
Serogroup Y	22 (7 to 44)	57 (34 to 78)	57 (34 to 77)	10 (2 to 27)

Notes:

[8] - No. subjects serogroup C: 21
No. subjects serogroup W: 24
No. subjects serogroup Y: 23
[9] - No. subjects serogroup C: 22
No. subjects serogroup Y: 21
No. subjects serogroup W: 21
[10] - No. subjects serogroup Y: 23
[11] - No. subjects serogroup W: 29

End point values	UK2,3,4,12+,	UK2,4,12+, 40	UK2,4C/12+,	UK2,4,12-, 40

	40 Months	Months	40 Months	Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33[12]	37[13]	17	34[14]
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	27 (13 to 46)	8 (2 to 22)	29 (10 to 56)	3 (0.074 to 15)
Serogroup C	41 (24 to 59)	47 (30 to 65)	71 (44 to 90)	33 (18 to 52)
Serogroup W	73 (54 to 87)	69 (52 to 84)	71 (44 to 90)	74 (56 to 87)
Serogroup Y	76 (58 to 89)	61 (43 to 77)	76 (50 to 93)	53 (35 to 90)

Notes:

[12] - No. subjects serogroup C: 32

[13] - No. subjects serogroup C: 36
No. subjects serogroup W: 36
No. subjects serogroup Y: 36

[14] - No. subjects serogroup C: 33

End point values	Ca2,4,6+, 40 Months	Ca2,4,6+/12PS, 40 Months	Ca2,4,12+, 40 Months	Ca2,4+/12PS, 40 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28[15]	23[16]	27[17]	28[18]
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	0 (0 to 12)	4 (0 to 22)	7 (1 to 24)	0 (0 to 12)
Serogroup C	20 (6 to 44)	14 (3 to 35)	31 (14 to 52)	35 (17 to 56)
Serogroup W	29 (13 to 49)	48 (27 to 69)	59 (39 to 78)	43 (24 to 63)
Serogroup Y	32 (16 to 52)	26 (10 to 48)	44 (25 to 65)	21 (8 to 41)

Notes:

[15] - No. subjects serogroup C: 20

[16] - No. subjects serogroup C: 22

[17] - No. subjects serogroup C: 26

[18] - No. subjects serogroup C: 26

End point values	Ca2,4,12-, 40 Months	Ca2,4-/12PS, 40 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25[19]	24		
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	8 (1 to 26)	0 (0 to 14)		
Serogroup C	38 (19 to 59)	46 (26 to 67)		
Serogroup W	72 (51 to 88)	58 (37 to 78)		
Serogroup Y	64 (43 to 82)	63 (41 to 81)		

Notes:

[19] - No. subjects serogroup C: 24

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with hSBA ≥1:4 for each of meningococcal serogroups A, C, W and Y

End point title	Percentages of subjects with hSBA ≥1:4 for each of

	meningococcal serogroups A, C, W and Y

End point description:

Percentages of subjects with hSBA ≥1:4 as measured by serum bactericidal activity at 40 months and 60 months of age and associated 95% Clopper-Pearson CIs were computed for each of the serogroups within each of the vaccinated groups and in age-matched control subjects.

End point type	Secondary

End point timeframe:

40 months and 60 months of age

End point values	UK2,3,4,12+, 60 Months	UK2,4,12+, 60 Months	UK2,4C/12+, 60 Months	UK2,4,12-, 60 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33[20]	35[21]	18[22]	31
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A	15 (5 to 32)	11 (3 to 27)	22 (6 to 48)	3 (0.082 to 17)
Serogroup C	50 (32 to 68)	44 (27 to 62)	71 (44 to 90)	52 (33 to 70)
Serogroup W	69 (50 to 84)	85 (69 to 95)	83 (59 to 96)	84 (66 to 95)
Serogroup Y	73 (54 to 87)	79 (62 to 91)	76 (50 to 93)	55 (36 to 73)

Notes:

[20] - No. subjects serogroup C: 32
No. subjects serogroup W: 32
[21] - No. subjects serogroup C: 34
No. subjects serogroup W: 34
No. subjects serogroup Y: 34
[22] - No. subjects serogroup C: 17
No. subjects serogroup Y: 17

End point values	UK Control, 60 Months	Ca2,4,6+, 60 Months	Ca2,4,6+/12PS, 60 Months	Ca2,4,12+, 60 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	27[23]	25[24]	23[25]
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A	0 (0 to 8)	4 (0.094 to 19)	0 (0 to 14)	9 (1 to 28)
Serogroup C	40 (26 to 57)	24 (8 to 47)	29 (13 to 51)	32 (14 to 55)
Serogroup W	36 (22 to 52)	31 (14 to 52)	52 (31 to 72)	61 (39 to 80)
Serogroup Y	33 (20 to 50)	48 (29 to 68)	40 (21 to 61)	57 (34 to 77)

Notes:

[23] - No. subjects serogroup C: 21
No. subjects serogroup W: 26
[24] - No. subjects serogroup C: 24

[25] - No. subjects serogroup C: 22

End point values	Ca2,4+/12PS, 60 Months	Ca2,4,12-, 60 Months	Ca2,4-/12PS, 60 Months	Ca Control, 60 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25[26]	23[27]	24[28]	30[29]
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A	4 (0 to 20)	9 (1 to 28)	0 (0 to 14)	7 (1 to 22)
Serogroup C	48 (26 to 70)	59 (36 to 79)	58 (37 to 78)	67 (47 to 83)

Serogroup W	50 (29 to 71)	81 (58 to 95)	67 (45 to 84)	34 (18 to 54)
Serogroup Y	35 (16 to 57)	62 (38 to 82)	61 (39 to 80)	13 (4 to 31)

Notes:

[26] - No. subjects serogroup C: 21
No. subjects serogroup W: 24
No. subjects serogroup Y: 23

[27] - No. subjects serogroup C: 22
No. subjects serogroup W: 21
No. subjects serogroup Y: 21

[28] - No. subjects serogroup Y: 23

[29] - No. subjects serogroup W: 29

End point values	UK2,3,4,12+, 40 Months	UK2,4,12+, 40 Months	UK2,4C/12+, 40 Months	UK2,4,12-, 40 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33[30]	37[31]	17	34[32]
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A	30 (16 to 49)	8 (2 to 22)	29 (10 to 56)	3 (0.074 to 15)
Serogroup C	47 (29 to 65)	53 (35 to 70)	71 (44 to 90)	42 (25 to 61)
Serogroup W	73 (54 to 87)	69 (52 to 84)	71 (44 to 90)	85 (69 to 95)
Serogroup Y	76 (58 to 89)	78 (61 to 90)	88 (64 to 99)	71 (53 to 85)

Notes:

[30] - No. subjects serogroup C: 32

[31] - No. subjects serogroup C: 36
No. subjects serogroup W: 36
No. subjects serogroup Y: 36

[32] - No. subjects serogroup C: 33

End point values	Ca2,4,6+, 40 Months	Ca2,4,6+/12PS, 40 Months	Ca2,4,12+, 40 Months	Ca2,4+/12PS, 40 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28[33]	23[34]	27[35]	28[36]
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A	0 (0 to 12)	4 (0 to 22)	11 (2 to 29)	7 (1 to 24)
Serogroup C	20 (6 to 44)	14 (3 to 35)	38 (20 to 59)	54 (33 to 73)
Serogroup W	29 (13 to 49)	52 (31 to 73)	63 (42 to 81)	54 (34 to 72)
Serogroup Y	50 (31 to 69)	35 (16 to 57)	59 (39 to 78)	43 (24 to 63)

Notes:

[33] - No. subjects serogroup C: 20

[34] - No. subjects serogroup C: 22

[35] - No. subjects serogroup C: 26

[36] - No. subjects serogroup C: 26

End point values	Ca2,4,12-, 40 Months	Ca2,4-/12PS, 40 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25[37]	24		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A	8 (1 to 26)	0 (0 to 14)		
Serogroup C	54 (33 to 74)	54 (33 to 74)		
Serogroup W	72 (51 to 88)	71 (49 to 87)		
Serogroup Y	68 (46 to 85)	63 (41 to 81)		

Notes:
[37] - No. subjects serogroup C: 24

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) in subjects within each site and in age-matched control subjects for each of meningococcal serogroups A, C, W and Y

End point title	Geometric Mean Titers (GMTs) in subjects within each site and in age-matched control subjects for each of meningococcal serogroups A, C, W and Y

End point description:

End point type	Secondary

End point timeframe:
40 months and 60 months of age

End point values	UK2,3,4,12+, 60 Months	UK2,4,12+, 60 Months	UK2,4C/12+, 60 Months	UK2,4,12-, 60 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33[38]	35[39]	18[40]	31
Units: titer				
geometric mean (confidence interval 95%)				
Serogroup A	2.6 (2.12 to 3.19)	2.69 (2.21 to 3.28)	2.85 (2.16 to 3.75)	2.11 (1.71 to 2.61)
Serogroup C	4.98 (3.28 to 7.55)	4.69 (3.13 to 7.04)	14 (8.15 to 26)	6.77 (4.43 to 10)
Serogroup W	18 (10 to 32)	35 (20 to 60)	34 (16 to 72)	26 (15 to 45)
Serogroup Y	11 (6.87 to 18)	17 (10 to 27)	16 (8.03 to 32)	7.24 (4.35 to 12)

Notes:
[38] - No. subjects serogroup C: 32
No. subjects serogroup W: 32
[39] - No. subjects serogroup C: 34
No. subjects serogroup W: 34
No. subjects serogroup Y: 34
[40] - No. subjects serogroup C: 17
No. subjects serogroup Y: 17

End point values	UK Control, 60 Months	Ca2,4,6+, 60 Months	Ca2,4,6+/12PS, 60 Months	Ca2,4,12+, 60 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	27[41]	25[42]	23[43]
Units: titer				
geometric mean (confidence interval 95%)				
Serogroup A	2 (1.67 to 2.39)	2.08 (1.77 to 2.45)	2 (1.69 to 2.36)	2.37 (1.99 to 2.82)

Serogroup C	3.93 (2.73 to 5.65)	2.75 (1.77 to 4.26)	2.86 (1.9 to 4.3)	3.22 (2.11 to 4.92)
Serogroup W	6.51 (3.99 to 11)	3.77 (2.14 to 6.64)	7.26 (4.08 to 13)	10 (5.77 to 19)
Serogroup Y	4.36 (2.81 to 6.75)	5.24 (3.32 to 8.27)	4.49 (2.79 to 7.22)	6.44 (3.94 to 11)

Notes:

[41] - No. subjects serogroup C: 21
No. subjects serogroup W: 26
[42] - No. subjects serogroup C: 24

[43] - No. subjects serogroup C: 22

End point values	Ca2,4+/12PS, 60 Months	Ca2,4,12-, 60 Months	Ca2,4-/12PS, 60 Months	Ca Control, 60 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25[44]	23[45]	24[46]	30[47]
Units: titer				
geometric mean (confidence interval 95%)				
Serogroup A	2.2 (1.86 to 2.6)	2.36 (1.98 to 2.8)	2 (1.69 to 2.37)	2.24 (1.91 to 2.62)
Serogroup C	4.02 (2.6 to 6.21)	4.85 (3.17 to 7.4)	6.27 (4.18 to 9.41)	9.46 (6.48 to 14)
Serogroup W	7.02 (3.9 to 13)	24 (13 to 45)	19 (11 to 35)	5.02 (2.88 to 8.73)
Serogroup Y	3.73 (2.27 to 6.12)	11 (6.57 to 18)	11 (6.88 to 18)	2.82 (1.8 to 4.42)

Notes:

[44] - No. subjects serogroup C: 21
No. subjects serogroup W: 24
No. subjects serogroup Y: 23
[45] - No. subjects serogroup C: 22
No. subjects serogroup W: 21
No. subjects serogroup Y: 21
[46] - No. subjects serogroup Y: 23

[47] - No. subjects serogroup W: 29

End point values	UK2,3,4,12+, 40 Months	UK2,4,12+, 40 Months	UK2,4C/12+, 40 Months	UK2,4,12-, 40 Months
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33[48]	37[49]	17	34[50]
Units: titer				
geometric mean (confidence interval 95%)				
Serogroup A	3.75 (2.76 to 5.11)	2.58 (1.93 to 3.45)	4.33 (2.82 to 6.66)	2.08 (1.54 to 2.82)
Serogroup C	6.43 (3.85 to 11)	7.02 (4.33 to 11)	23 (11 to 46)	4.29 (2.59 to 7.11)
Serogroup W	23 (13 to 42)	27 (15 to 47)	22 (9.65 to 50)	26 (14 to 46)
Serogroup Y	22 (13 to 38)	15 (9.16 to 26)	27 (13 to 58)	9.33 (5.48 to 16)

Notes:

[48] - No. subjects serogroup C: 32

[49] - No. subjects serogroup C: 36
No. subjects serogroup W: 36
No. subjects serogroup Y: 36
[50] - No. subjects serogroup C: 33

End point values	Ca2,4,6+, 40 Months	Ca2,4,6+/12PS, 40	Ca2,4,12+, 40 Months	Ca2,4+/12PS, 40 Months

		Months		
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28[51]	23[52]	27[53]	28[54]
Units: titer				
geometric mean (confidence interval 95%)				
Serogroup A	2.01 (1.69 to 2.39)	2.17 (1.79 to 2.62)	2.56 (2.15 to 3.05)	2.11 (1.77 to 2.5)
Serogroup C	3.18 (1.98 to 5.1)	2.68 (1.71 to 4.2)	4.17 (2.77 to 6.27)	5.45 (3.62 to 8.2)
Serogroup W	3.86 (2.15 to 6.93)	6.77 (3.55 to 13)	12 (6.72 to 22)	7.55 (4.22 to 14)
Serogroup Y	5.54 (3.39 to 9.06)	4.3 (2.49 to 7.4)	7.41 (4.5 to 12)	3.96 (2.42 to 6.46)

Notes:

[51] - No. subjects serogroup C: 20

[52] - No. subjects serogroup C: 22

[53] - No. subjects serogroup C: 26

[54] - No. subjects serogroup C: 26

End point values	Ca2,4,12-, 40 Months	Ca2,4-/12PS, 40 Months		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25[55]	24		
Units: titer				
geometric mean (confidence interval 95%)				
Serogroup A	2.41 (2.01 to 2.89)	2 (1.66 to 2.4)		
Serogroup C	4.98 (3.26 to 7.62)	6.45 (4.22 to 9.86)		
Serogroup W	23 (13 to 43)	16 (8.63 to 30)		
Serogroup Y	13 (7.47 to 21)	11 (6.2 to 18)		

Notes:

[55] - No. subjects serogroup C: 24

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

6 months

Adverse event reporting additional description:

The medically significant AEs and SAEs were collected among the subjects during the 6-month follow-up after the vaccination visit.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	UK2,3,4,12+

Reporting group description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 3, and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Reporting group title	UK2,4,12+

Reporting group description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Reporting group title	UK2,4C/12+

Reporting group description:

UK vaccine group receiving primary vaccine of monovalent MenC-CRM conjugate vaccine at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Reporting group title	UK2,4,12-

Reporting group description:

UK vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 12 months of age.

Reporting group title	UK Control

Reporting group description:

Newly enrolled age-matched subjects that received a complete vaccination course of routine monovalent MenC conjugate vaccine at 2, 3 and 4 months of age without any booster vaccination.

Reporting group title	Ca2,4,6+

Reporting group description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2, 4 and 6 months of age without any booster vaccination.

Reporting group title	Ca2,4,6+/12PS

Reporting group description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM1 conjugate vaccine with adjuvant at 2, 4 and 6 months of age followed by a reduced booster vaccination of quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Reporting group title	Ca2,4,12+

Reporting group description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a booster dose of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 12 months of age.

Reporting group title	Ca2,4+/12PS

Reporting group description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine with adjuvant at 2 and 4 months of age followed by a reduced booster vaccination of quadrivalent

MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Reporting group title	Ca2,4,12-

Reporting group description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a booster vaccination of the quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 12 months of age.

Reporting group title	Ca2,4-/12PS

Reporting group description:

Canadian vaccine group receiving primary vaccine of quadrivalent MenACWY-CRM conjugate vaccine without adjuvant at 2 and 4 months of age followed by a reduced booster vaccination of the quadrivalent MenACWY polysaccharide vaccine (1/5 dose) at 12 months of age.

Reporting group title	Ca Control

Reporting group description:

Newly enrolled age-matched subjects that received a complete vaccination course of routine monovalent MenC conjugate vaccine at 2 and 12 months or only at 12 months of age.

Serious adverse events	UK2,3,4,12+	UK2,4,12+	UK2,4C/12+
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 33 (3.03%)	1 / 33 (3.03%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 33 (0.00%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Asperger's disorder			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Lower respiratory tract infection			
subjects affected / exposed	1 / 33 (3.03%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	UK2,4,12-	UK Control	Ca2,4,6+
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 29 (10.34%)	0 / 26 (0.00%)	1 / 28 (3.57%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	1 / 29 (3.45%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Asperger's disorder			

subjects affected / exposed	1 / 29 (3.45%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ca2,4,6+/12PS	Ca2,4,12+	Ca2,4+/12PS
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			

subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Asperger's disorder			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ca2,4,12-	Ca2,4-/12PS	Ca Control
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	1 / 25 (4.00%)	0 / 23 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			

subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 22 (0.00%)	1 / 25 (4.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Asperger's disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	UK2,3,4,12+	UK2,4,12+	UK2,4C/12+
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 33 (12.12%)	3 / 33 (9.09%)	5 / 16 (31.25%)
Injury, poisoning and procedural complications			
Head injury			

subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Infections and infestations			
Otitis media			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
H1N1 Influenza			
subjects affected / exposed	3 / 33 (9.09%)	1 / 33 (3.03%)	0 / 16 (0.00%)
occurrences (all)	3	1	0
Impetigo			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Lower respiratory tract infection			
subjects affected / exposed	3 / 33 (9.09%)	2 / 33 (6.06%)	1 / 16 (6.25%)
occurrences (all)	2	2	1
Varicella			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Foot and mouth disease			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Non-serious adverse events	UK2,4,12-	UK Control	Ca2,4,6+
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 29 (6.90%)	0 / 26 (0.00%)	1 / 28 (3.57%)
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 29 (3.45%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			

Lymphadenitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Otitis media			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
H1N1 Influenza			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Impetigo			
subjects affected / exposed	1 / 29 (3.45%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Varicella			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Foot and mouth disease			
subjects affected / exposed	0 / 29 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Ca2,4,6+/12PS	Ca2,4,12+	Ca2,4+/12PS
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 25 (4.00%)	3 / 24 (12.50%)	1 / 26 (3.85%)
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Infections and infestations			
Otitis media			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Pneumonia			
subjects affected / exposed	0 / 25 (0.00%)	3 / 24 (12.50%)	0 / 26 (0.00%)
occurrences (all)	0	3	0
H1N1 Influenza			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Impetigo			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Varicella			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Foot and mouth disease			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Ca2,4,12-	Ca2,4-/12PS	Ca Control
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 22 (9.09%)	2 / 25 (8.00%)	0 / 23 (0.00%)
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Otitis media			

subjects affected / exposed	2 / 22 (9.09%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	3	0	0
Pneumonia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 25 (4.00%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
H1N1 Influenza			
subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 22 (0.00%)	1 / 25 (4.00%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Varicella			
subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Foot and mouth disease			
subjects affected / exposed	0 / 22 (0.00%)	0 / 25 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/22394992