Clinical trial results:
Tweede Immunisatie Men C (TIM)-studie

Summary

EudraCT number	2011-000375-13
Trial protocol	NL
Global end of trial date	19 November 2014

Results information

Result version number	v1 (current)
This version publication date	07 October 2026
First version publication date	07 October 2026

Trial information

Trial identification

Sponsor protocol code	LIS-144

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	METC-nummer: R-11.09E/TIM , ABR-nummer: NL35207.100.11 , Clinical Trial Register Nummer: NTR 3521

Notes:

Sponsors

Sponsor organisation name	RIVM
Sponsor organisation address	PO Box 1, Bilthoven, Netherlands, 3720 BA
Public contact	Clinical Expertise Centre, RIVM, mensgebonden-onderzoek@rivm.nl
Scientific contact	Clinical Expertise Centre, RIVM, mensgebonden-onderzoek@rivm.nl

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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 November 2014
Global end of trial reached?	Yes
Global end of trial date	19 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the appropriate age for a second immunization with the Meningococcal C conjugated vaccine.

Protection of trial subjects:

During this study the subjects will receive one dose of NeisVac-C™(Registration number: RVG 26343). NeisVac-C™ is a registered vaccine and currently used in the Dutch NIP for all children aged 14 months. Furthermore, the vaccine has already been used in the Netherlands (and other countries) in the same age group (children 10, 12 and 15 years of age) during the catch-up campaign in 2002. During the catch-up campaign over 3 million children were vaccinated and only 1512 developed an adverse reaction. It is therefore unlikely that serious side effects will occur that can lead to premature termination of the study.

The invasive study procedures (vaccination and venapunctures) will be carried out by experienced and qualified persons according to standard operating procedures. A local anesthetic (Xylocaine spray) can be used to minimize the pain of the venapuncture.

Furthermore, the burden and risk of blood and saliva sampling is considered low. Blood collection could result in a small bruise at the location of injection, which will disappear within a few days.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 May 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 268
Worldwide total number of subjects	268
EEA total number of subjects	268

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)	91
Adolescents (12-17 years)	177
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Persons of 10-15 years of age (year 1996-2002) who have previously received one MenCC vaccination and are living in or around Utrecht (Leidsche Rijn) (n=4500, 1500 per age group) were invited for participation in the study. Recruitment was done via an invitation letter to the parents. First inclusion: 3-Oct-2011.

Pre-assignment

Screening details:

Inclusion and exclusion was checked by the PI:
inclusion
-10-, 12, 15-years received primary vaccination MenCC; good general health; Received all regular vaccines of Dutch NIP
exclusion:
-acute illness; antibiotic use; serious disease, allergy to vaccin; immune deficiency; neurologic disorder; pregnancy; previous Meningococcal disease

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	10 year olds

Arm description:

immune response to a second MenCC vaccination in age group 10 years old

Arm type	Experimental
Investigational medicinal product name	NeisVac-C™
Investigational medicinal product code	RVG 26343
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

One dose of 0.5 ml for intramuscular injection contains 10 microgram of Neisseria meningitidis group C (strain C11) polysaccharide (de-O-acetylated). The polysaccharide is conjugated to 10-20 micrograms of tetanus toxoid and is adsorbed to aluminium hydroxide (0.5 mg). Other additive products are sodium chloride and water for injections.
The NeisVac-C™ vaccine (0.5 ml) is injected intramuscularly in the upper arm. This is a customary and well-accepted route of administration of this vaccine.

Arm title	12 year olds

Arm description:

immune response to a second MenCC vaccination in age group 12 years old

Arm type	Experimental
Investigational medicinal product name	NeisVac-C™
Investigational medicinal product code	RVG 26343
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

One dose of 0.5 ml for intramuscular injection contains 10 microgram of Neisseria meningitidis group C (strain C11) polysaccharide (de-O-acetylated). The polysaccharide is conjugated to 10-20 micrograms of tetanus toxoid and is adsorbed to aluminium hydroxide (0.5 mg). Other additive products are sodium

chloride and water for injections.
The NeisVac-C™ vaccine (0.5 ml) is injected intramuscularly in the upper arm. This is a customary and well-accepted route of administration of this vaccine.

Arm title	15 year olds
Arm description:	
immune response to a second MenCC vaccination in age group 15 years old	
Arm type	Experimental
Investigational medicinal product name	NeisVac-C™
Investigational medicinal product code	RVG 26343
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

One dose of 0.5 ml for intramuscular injection contains 10 microgram of Neisseria meningitidis group C (strain C11) polysaccharide (de-O-acetylated). The polysaccharide is conjugated to 10-20 micrograms of tetanus toxoid and is adsorbed to aluminium hydroxide (0.5 mg). Other additive products are sodium chloride and water for injections.
The NeisVac-C™ vaccine (0.5 ml) is injected intramuscularly in the upper arm. This is a customary and well-accepted route of administration of this vaccine.

Number of subjects in period 1	10 year olds	12 year olds	15 year olds
Started	91	91	86
T1 (1 month after T0)	88	90	85
T2 (1 year after T0)	85	89	83
T3 (3 years after T0) (follow-up)	66	76	59
Completed	66	76	59
Not completed	25	15	27
Didn't want to participate with the follow-up	19	13	24
No blood	3	-	-
Lost to follow-up	3	2	3

Baseline characteristics

Reporting groups	
Reporting group title	10 year olds
Reporting group description:	
immune response to a second MenCC vaccination in age group 10 years old	
Reporting group title	12 year olds
Reporting group description:	
immune response to a second MenCC vaccination in age group 12 years old	
Reporting group title	15 year olds
Reporting group description:	
immune response to a second MenCC vaccination in age group 15 years old	

Reporting group values	10 year olds	12 year olds	15 year olds
Number of subjects	91	91	86
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	91	0	0
Adolescents (12-17 years)	0	91	86
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	9.9	12.0	15.0
standard deviation	± 0.3	± 0.3	± 0.3
Gender categorical Units: Subjects			
Female	53	44	41
Male	38	47	45

Reporting group values	Total		
Number of subjects	268		
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)	91		
Adolescents (12-17 years)	177		
Adults (18-64 years)	0		

From 65-84 years	0		
85 years and over	0		

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	138		
Male	130		

End points

End points reporting groups

Reporting group title	10 year olds
Reporting group description:	
immune response to a second MenCC vaccination in age group 10 years old	
Reporting group title	12 year olds
Reporting group description:	
immune response to a second MenCC vaccination in age group 12 years old	
Reporting group title	15 year olds
Reporting group description:	
immune response to a second MenCC vaccination in age group 15 years old	
Subject analysis set title	Age group 10 at T0
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Age group 10 T0	
Subject analysis set title	Age group 10 at T1
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Age group 10 T1	
Subject analysis set title	Age group 10 at T2
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Age group 10 at T2	
Subject analysis set title	Age group 12 at T0
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Age group 12 at T0	
Subject analysis set title	Age group 12 at T1
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Age group 12 at T1	
Subject analysis set title	Age group 12 at T2
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Age group 12 at T2	
Subject analysis set title	Age group 15 at T0
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Age group 15 at T0	
Subject analysis set title	Age group 15 at T1
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Age group 15 at T1	
Subject analysis set title	Age group 15 at T2
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Age group 15 at T2	
Subject analysis set title	Age group 10 at T3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Age group 10 years old, sample T3

Subject analysis set title	Age group 12 at T3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Age group 12 years old , sample T3

Subject analysis set title	Age group 15 at T3
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Age group 15 years old, sample T3

Primary: Geometric Mean Titers (GMTs) of MenC SBA levels at T0

End point title	Geometric Mean Titers (GMTs) of MenC SBA levels at T0

End point description:

Geometric Mean Titers (GMTs) of Meningococcal Serogroup C (MenC) Specific Serum Bactericidal Antibody (SBA) prior to (T0) the MenC Conjugate Booster.

End point type	Primary

End point timeframe:

T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	91	86	
Units: GMT				
geometric mean (confidence interval 95%)	4.0 (2.9 to 5.4)	8.2 (5.3 to 12.6)	13.1 (8.1 to 21.0)	

Statistical analyses

Statistical analysis title	GMT MenC SBA levels analysis 10 vs. 12 at T0

Statistical analysis description:

Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T0 were determined using the Mann-Whitney U test. Differences between groups in SBA GMTs at T1 and T2 were determined with linear regression analyses, adjusting for titers at T0. P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.006 [1]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMT MenC SBA levels analysis 10 vs. 15 at T0

Statistical analysis description:

Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T0

were determined using the Mann-Whitney U test. Differences between groups in SBA GMTs at T1 and T2 were determined with linear regression analyses, adjusting for titers at T0.

Comparison groups	15 year olds v 10 year olds
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [2]
Method	Wilcoxon (Mann-Whitney)

Notes:

[2] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMT MenC SBA levels analysis 12 vs. 15 at T0

Statistical analysis description:

Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T0 were determined using the Mann-Whitney U test. Differences between groups in SBA GMTs at T1 and T2 were determined with linear regression analyses, adjusting for titers at T0.

Comparison groups	12 year olds v 15 year olds
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.459 [3]
Method	Wilcoxon (Mann-Whitney)

Notes:

[3] - P-values were adjusted for three comparisons with Bonferroni correction.

Primary: Geometric Mean Titers (GMTs) of MenC SBA levels at T1

End point title	Geometric Mean Titers (GMTs) of MenC SBA levels at T1

End point description:

Geometric Mean Titers (GMTs) of Meningococcal Serogroup C (MenC) Specific Serum Bactericidal Antibody (SBA) 1 Month (T1) after the MenC Conjugate Booster.

End point type	Primary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	89[4]	85	
Units: GMT				
geometric mean (confidence interval 95%)	31.564 (26.899 to 37.038)	45.175 (38.608 to 52.859)	47.289 (40.422 to 55.322)	

Notes:

[4] - 1 insufficient blood sample

Statistical analyses

Statistical analysis title	GMT MenC SBA levels analysis 10 vs. 12 at T1

Statistical analysis description:

Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T0

were determined using the Mann-Whitney U test. Differences between groups in SBA GMTs at T1 and T2 were determined with linear regression analyses, adjusting for titers at T0.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.021 [5]
Method	Regression, Linear

Notes:

[5] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMT MenC SBA levels analysis 10 vs. 15 at T1

Statistical analysis description:

Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T0 were determined using the Mann-Whitney U test. Differences between groups in SBA GMTs at T1 and T2 were determined with linear regression analyses, adjusting for titers at T0.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.003 [6]
Method	Regression, Linear

Notes:

[6] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMT MenC SBA levels analysis 12 vs. 15 at T1

Statistical analysis description:

Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T0 were determined using the Mann-Whitney U test. Differences between groups in SBA GMTs at T1 and T2 were determined with linear regression analyses, adjusting for titers at T0.

Comparison groups	12 year olds v 15 year olds
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [7]
Method	Regression, Linear

Notes:

[7] - P-values were adjusted for three comparisons with Bonferroni correction.

Primary: Geometric Mean Titers (GMTs) of MenC SBA levels at T2

End point title	Geometric Mean Titers (GMTs) of MenC SBA levels at T2

End point description:

Geometric Mean Titers (GMTs) of Meningococcal Serogroup C (MenC) Specific Serum Bactericidal Antibody (SBA) 1 Year (T2) after the MenC Conjugate Booster.

End point type	Primary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	89	83	
Units: GMT				
geometric mean (confidence interval 95%)	1.987 (1.602 to 2.247)	4.165 (3.444 to 5.038)	6.292 (5.272 to 7.509)	

Statistical analyses

Statistical analysis title	GMT MenC SBA levels analysis 10 vs. 12 at T2

Statistical analysis description:

Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T0 were determined using the Mann-Whitney U test. Differences between groups in SBA GMTs at T1 and T2 were determined with linear regression analyses, adjusting for titers at T0.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [8]
Method	Regression, Linear

Notes:

[8] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMT MenC SBA levels analysis 10 vs. 15 at T2

Statistical analysis description:

Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T0 were determined using the Mann-Whitney U test. Differences between groups in SBA GMTs at T1 and T2 were determined with linear regression analyses, adjusting for titers at T0.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [9]
Method	Regression, Linear

Notes:

[9] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMT MenC SBA levels analysis 12 vs. 15 at T2

Statistical analysis description:

Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T0 were determined using the Mann-Whitney U test. Differences between groups in SBA GMTs at T1 and T2 were determined with linear regression analyses, adjusting for titers at T0.

Comparison groups	12 year olds v 15 year olds
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.021 [10]
Method	Regression, Linear

Notes:

[10] - P-values were adjusted for three comparisons with Bonferroni correction.

Primary: Proportion of Participants with an SBA titer >=8 at T0

End point title	Proportion of Participants with an SBA titer >=8 at T0

End point description:

Percentage of Participants with an SBA titer >=8 prior to (T0) the MenC Conjugate Booster. Proportion and 95% confidence intervals (95%CIs) of participants with an SBA titer >=8 were calculated using the Agresti-Coull method.

End point type	Primary

End point timeframe:

T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	91	86	
Units: proportion >=8				
arithmetic mean (confidence interval 95%)	19 (12 to 28)	34 (25 to 45)	45 (35 to 56)	

Statistical analyses

Statistical analysis title	SBA titer >=8 analysis 10 vs. 12 at T0

Statistical analysis description:

An SBA titer >=8 was considered as international correlate of protection. Differences between groups in proportion of participants with an SBA titer >=8 was determined with Chi square test

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.057 [11]
Method	Chi-squared

Notes:

[11] - P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	SBA titer >=8 analysis 10 vs. 15 at T0

Statistical analysis description:

An SBA titer >=8 was considered as international correlate of protection. Differences between groups in proportion of participants with an SBA titer >=8 was determined with Chi square test

Comparison groups	10 year olds v 15 year olds

Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [12]
Method	Chi-squared

Notes:

[12] - P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	SBA titer >=8 analysis 12 vs. 15 at T0

Statistical analysis description:

An SBA titer >=8 was considered as international correlate of protection. Differences between groups in proportion of participants with an SBA titer >=8 was determined with Chi square test

Comparison groups	12 year olds v 15 year olds
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.375 [13]
Method	Chi-squared

Notes:

[13] - P-values were adjusted for three comparisons with Bonferroni correction

Primary: Proportion of Participants with an SBA titer >=8 at T1

End point title	Proportion of Participants with an SBA titer >=8 at T1

End point description:

Percentage of Participants with an SBA titer >=8 1 month (T1) after the MenC Conjugate Booster. Proportion and 95% confidence intervals (95%CIs) of participants with an SBA titer >=8 were calculated using the Agresti-Coull method.

End point type	Primary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	90	85	
Units: proportion >=8				
arithmetic mean (confidence interval 95%)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)	

Statistical analyses

Statistical analysis title	SBA titer >=8 analysis 10 vs. 12 at T1

Statistical analysis description:

An SBA titer >=8 was considered as international correlate of protection. Differences between groups in proportion of participants with an SBA titer >=8 was determined with Chi square test

Comparison groups	10 year olds v 12 year olds

Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [14]
Method	Chi-squared

Notes:

[14] - P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	SBA titer >=8 analysis 10 vs. 15 at T1

Statistical analysis description:

An SBA titer >=8 was considered as international correlate of protection. Differences between groups in proportion of participants with an SBA titer >=8 was determined with Chi square test

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [15]
Method	Chi-squared

Notes:

[15] - P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	SBA titer >=8 analysis 12 vs. 15 at T1

Statistical analysis description:

An SBA titer >=8 was considered as international correlate of protection. Differences between groups in proportion of participants with an SBA titer >=8 was determined with Chi square test

Comparison groups	12 year olds v 15 year olds
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [16]
Method	Chi-squared

Notes:

[16] - P-values were adjusted for three comparisons with Bonferroni correction

Primary: Proportion of Participants with an SBA titer >=8 at T2

End point title	Proportion of Participants with an SBA titer >=8 at T2

End point description:

Percentage of Participants with an SBA titer >=8 1 year (T2) after the MenC Conjugate Booster. Proportion and 95% confidence intervals (95%CIs) of participants with an SBA titer >=8 were calculated using the Agresti-Coull method.

End point type	Primary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	89	83	
Units: proportion >=8				
arithmetic mean (confidence interval 95%)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)	

Statistical analyses

Statistical analysis title	SBA titer >=8 analysis 10 vs. 12 at T2

Statistical analysis description:

An SBA titer >=8 was considered as international correlate of protection. Differences between groups in proportion of participants with an SBA titer >=8 was determined with Chi square test

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [17]
Method	Chi-squared

Notes:

[17] - P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	SBA titer >=8 analysis 10 vs. 15 at T2

Statistical analysis description:

An SBA titer >=8 was considered as international correlate of protection. Differences between groups in proportion of participants with an SBA titer >=8 was determined with Chi square test

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [18]
Method	Chi-squared

Notes:

[18] - P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	SBA titer >=8 analysis 12 vs. 15 at T2

Statistical analysis description:

An SBA titer >=8 was considered as international correlate of protection. Differences between groups in proportion of participants with an SBA titer >=8 was determined with Chi square test

Comparison groups	12 year olds v 15 year olds
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [19]
Method	Chi-squared

Notes:

[19] - P-values were adjusted for three comparisons with Bonferroni correction

Primary: Geometric Mean Titers (GMTs) of MenC SBA levels at T3	
End point title	Geometric Mean Titers (GMTs) of MenC SBA levels at T3
End point description:	
Geometric Mean Titers (GMTs) of Meningococcal Serogroup C (MenC) Specific Serum Bactericidal Antibody (SBA) 3 years (T3) after the MenC Conjugate Booster vaccination.	
End point type	Primary
End point timeframe:	
T3	

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	75	58	
Units: GMT				
geometric mean (confidence interval 95%)	619 (489 to 782)	1992 (1568 to 2531)	3678 (2966 to 4562)	

Statistical analyses

Statistical analysis title	GMT MenC SBA levels analysis 10 vs. 12 at T3
Statistical analysis description:	
Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T3 were determined with linear regression analyses, adjusting for titers at T0. P-values were adjusted for three comparisons with Bonferroni correction.	
Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [20]
Method	Regression, Linear

Notes:

[20] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMT MenC SBA levels analysis 10 vs. 15 at T3
Statistical analysis description:	
Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T3 were determined with linear regression analyses, adjusting for titers at T0. P-values were adjusted for three comparisons with Bonferroni correction.	
Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [21]
Method	Regression, Linear

Notes:

[21] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMT MenC SBA levels analysis 12 vs. 15 at T3

Statistical analysis description:

Differences between groups in Serum Bactericidal Antibody (SBA) Geometric Mean Titers (GMTs) at T3 were determined with linear regression analyses, adjusting for titers at T0. P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.006 [22]
Method	Regression, Linear

Notes:

[22] - P-values were adjusted for three comparisons with Bonferroni correction.

Primary: Proportion of Participants with an SBA titer >=8 at T3

End point title	Proportion of Participants with an SBA titer >=8 at T3

End point description:

Percentage of Participants with an SBA titer >8 3 years (T3) after the MenC Conjugate Booster. Proportions with 95% CI of participants
with an rSBA >=8 were calculated using the Wilson score interval with continuity correction.

End point type	Primary

End point timeframe:

T3

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	75	58	
Units: proportion >8				
number (confidence interval 95%)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)	

Statistical analyses

Statistical analysis title	Proportion GMT SBA >=8 10 vs. 12 at T3

Statistical analysis description:

Differences in proportion of participants GMT SBA >-=8 at T3 were tested with the Chi-square test.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1
Method	Chi-squared

Statistical analysis title	Proportion GMT SBA >=8 10 vs. 15 at T3

Statistical analysis description:	
Differences in proportion of participants GMT SBA >-=8 at T3 were tested with the Chi-square test.	
Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1
Method	Chi-squared

Statistical analysis title	Proportion GMT SBA >=8 12 vs. 15 at T3
Statistical analysis description:	
Differences in proportion of participants GMT SBA >-=8 at T3 were tested with the Chi-square test.	
Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1
Method	Chi-squared

Secondary: GMC MenC-PS specific IgG antibodies at T0	
End point title	GMC MenC-PS specific IgG antibodies at T0
End point description:	
Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G (IgG) prior to (T0) the MenC Conjugate Booster.	
End point type	Secondary
End point timeframe:	
T0	

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	91	86	
Units: ug/mL				
geometric mean (confidence interval 95%)	0.26 (0.22 to 0.31)	0.32 (0.26 to 0.39)	0.40 (0.31 to 0.51)	

Statistical analyses

Statistical analysis title	GMC Men C IgG antibodies analysis 10 vs. 12 at T0

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG were determined with linear regression analyses, adjusting for concentrations at T0. GMC ratios indicate the level of increase (T1/T0) or decrease (T1/T2)

between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.444 [23]
Method	t-test, 2-sided

Notes:

[23] - linear regression analyses, adjusting for concentrations at T0. Differences in GMC ratios between groups were determined with independent sample t-tests. P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	GMC Men C IgG antibodies analysis 10 vs. 15 at T0

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG were determined with linear regression analyses, adjusting for concentrations at T0. GMC ratios indicate the level of increase (T1/T0) or decrease (T1/T2)
between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.018 [24]
Method	t-test, 2-sided

Notes:

[24] - linear regression analyses, adjusting for concentrations at T0. Differences in GMC ratios between groups were determined with independent sample t-tests. P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	GMC Men C IgG antibodies analysis 12 vs. 15 at T0

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG were determined with linear regression analyses, adjusting for concentrations at T0. GMC ratios indicate the level of increase (T1/T0) or decrease (T1/T2)
between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	12 year olds v 15 year olds
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.579 [25]
Method	t-test, 2-sided

Notes:

[25] - linear regression analyses, adjusting for concentrations at T0. Differences in GMC ratios between groups were determined with independent sample t-tests. P-values were adjusted for three comparisons with Bonferroni correction

Secondary: GMC MenC-PS specific IgG antibodies at T1

End point title	GMC MenC-PS specific IgG antibodies at T1

End point description:

Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS)

Specific Immunoglobulin G (IgG) 1 Month (T1) after the MenC Conjugate Booster.

End point type	Secondary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	90	85	
Units: ug/mL				
geometric mean (confidence interval 95%)	134 (117.0 to 153.4)	193.6 (168.2 to 222.3)	174.3 (147.5 to 206.0)	

Statistical analyses

Statistical analysis title	GMC Men C IgG antibodies analysis 10 vs. 12 at T1

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG were determined with linear regression analyses, adjusting for concentrations at T0. GMC ratios indicate the level of increase (T1/T0) or decrease (T1/T2)
between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [26]
Method	Regression, Linear

Notes:

[26] - P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	GMC Men C IgG antibodies analysis 10 vs. 15 at T1

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG were determined with linear regression analyses, adjusting for concentrations at T0. GMC ratios indicate the level of increase (T1/T0) or decrease (T1/T2)
between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.063 [27]
Method	Regression, Linear

Notes:

[27] - P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	GMC Men C IgG antibodies analysis 12 vs. 15 at T1

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG were determined with linear regression analyses, adjusting for concentrations at T0. GMC ratios indicate the level of increase (T1/T0) or decrease (T1/T2)
between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	12 year olds v 15 year olds
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [28]
Method	Regression, Linear

Notes:

[28] - P-values were adjusted for three comparisons with Bonferroni correction

Secondary: GMC MenC-PS specific IgG antibodies at T2

End point title	GMC MenC-PS specific IgG antibodies at T2

End point description:

Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G (IgG) 1 Year (T2) after the MenC Conjugate Booster.

End point type	Secondary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	89	83	
Units: ug/mL				
geometric mean (confidence interval 95%)	12.2 (10.2 to 14.4)	23.3 (19.3 to 28.0)	33.7 (28.4 to 39.9)	

Statistical analyses

Statistical analysis title	GMC Men C IgG antibodies analysis 10 vs. 12 at T2

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG were determined with linear regression analyses, adjusting for concentrations at T0. GMC ratios indicate the level of increase (T1/T0) or decrease (T1/T2)
between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds

Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [29]
Method	Regression, Linear

Notes:

[29] - P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	GMC Men C IgG antibodies analysis 10 vs. 15 at T2

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG were determined with linear regression analyses, adjusting for concentrations at T0. GMC ratios indicate the level of increase (T1/T0) or decrease (T1/T2)
between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [30]
Method	Regression, Linear

Notes:

[30] - P-values were adjusted for three comparisons with Bonferroni correction

Statistical analysis title	GMC Men C IgG antibodies analysis 12 vs. 15 at T2

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG were determined with linear regression analyses, adjusting for concentrations at T0. GMC ratios indicate the level of increase (T1/T0) or decrease (T1/T2)
between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	12 year olds v 15 year olds
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.033 [31]
Method	Regression, Linear

Notes:

[31] - P-values were adjusted for three comparisons with Bonferroni correction

Secondary: Men-C PS specific IgG memory B-cell responses at T0

End point title	Men-C PS specific IgG memory B-cell responses at T0

End point description:

Frequency of circulating MenC-PS-specific IgG memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells

End point type	Secondary

End point timeframe:

T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	13	14	
Units: MenC-specific memory B cells				
geometric mean (confidence interval 95%)	0.10 (0.03 to 0.39)	0.08 (0.01 to 0.41)	0.26 (0.06 to 1.18)	

Statistical analyses

Statistical analysis title	Men-C PS IgG memory B cells T0 10 vs. 12 years old
Statistical analysis description:	
Mann-Whitney U test on circulating MenC-PS-specific memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.	
Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.7418
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C PS IgG memory B cells T0 10 vs. 15 years old
Statistical analysis description:	
Mann-Whitney U test on circulating MenC-PS-specific memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.	
Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.465
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C PS IgG memory B cells T0 12 vs. 15 years old
Statistical analysis description:	
Mann-Whitney U test on circulating MenC-PS-specific memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.	
Comparison groups	15 year olds v 12 year olds

Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3933
Method	Wilcoxon (Mann-Whitney)

Secondary: Men-C PS specific IgG memory B-cell responses at T1

End point title	Men-C PS specific IgG memory B-cell responses at T1

End point description:

Frequency of circulating MenC-PS-specific IgG memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells

End point type	Secondary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	14	18	
Units: MenC-specific memory B cells				
geometric mean (confidence interval 95%)	45.27 (31.03 to 66.06)	140.87 (116.76 to 169.96)	68.26 (45.47 to 102.45)	

Statistical analyses

Statistical analysis title	Men-C IgG memory B cells T1 10 vs. 12 years old

Statistical analysis description:

Frequency of circulating MenC-PS-specific memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C IgG memory B cells T1 10 vs. 15 years old

Statistical analysis description:

Frequency of circulating MenC-PS-specific memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells

Comparison groups	10 year olds v 15 year olds

Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1131
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C IgG memory B cells T1 12 vs. 15 years old
Statistical analysis description:	
Frequency of circulating MenC-PS-specific memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells	
Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0031
Method	Wilcoxon (Mann-Whitney)

Secondary: Men-C PS specific IgG memory B-cell responses at T2	
End point title	Men-C PS specific IgG memory B-cell responses at T2
End point description:	
Frequency of circulating MenC-PS-specific IgG memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells	
End point type	Secondary
End point timeframe:	
T2	

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	14	18	
Units: MenC-specific memory B cells				
geometric mean (confidence interval 95%)	5.08 (1.39 to 18.63)	24.45 (15.93 to 37.51)	11.76 (4.27 to 32.42)	

Statistical analyses

Statistical analysis title	Men-C PS IgG memory B cells T2 10 vs. 12 years old
Statistical analysis description:	
Frequency of circulating MenC-PS-specific IgG memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.	
Comparison groups	10 year olds v 12 year olds

Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0214
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C PS IgG memory B cells T2 10 vs. 15 years old

Statistical analysis description:

Frequency of circulating MenC-PS-specific IgG memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1625
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C PS IgG memory B cells T2 12 vs. 15 year old

Statistical analysis description:

Frequency of circulating MenC-PS-specific IgG memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.4139
Method	Wilcoxon (Mann-Whitney)

Secondary: GMC MenC-PS specific IgA in serum at T0

End point title	GMC MenC-PS specific IgA in serum at T0

End point description:

Geometric mean concentrations (GMCs) of MenC-polysaccharide specific IgA in serum prior to (T0) the MenC conjugate booster vaccination.

End point type	Secondary

End point timeframe:

T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81[32]	86[33]	75[34]	
Units: ng/mL				
geometric mean (confidence interval 95%)	13.3 (10.0 to 17.6)	24.7 (17.4 to 35.0)	36.1 (25.5 to 51.0)	

Notes:

[32] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[33] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[34] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgA in serum 10 vs. 12 at T0

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in serum at T0 between age groups were made using the Mann–Whitney U test. Comparisons between age groups at T1 and T2 were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.051 [35]
Method	Wilcoxon (Mann-Whitney)

Notes:

[35] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in serum 10 vs. 15 at T0

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in serum at T0 between age groups were made using the Mann–Whitney U test. Comparisons between age groups at T1 and T2 were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [36]
Method	Wilcoxon (Mann-Whitney)

Notes:

[36] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in serum 12 vs. 15 at T0

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in serum at T0 between age groups were made using the Mann–Whitney U test. Comparisons between age groups at T1 and T2 were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds

Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.21 [37]
Method	Wilcoxon (Mann-Whitney)

Notes:

[37] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC MenC-PS specific IgA in serum at T1

End point title	GMC MenC-PS specific IgA in serum at T1

End point description:

Geometric mean concentrations (GMCs) of MenC-polysaccharide specific IgA in serum 1 month (T1) after the MenC conjugate booster vaccination.

End point type	Secondary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83[38]	86[39]	75[40]	
Units: ng/mL				
geometric mean (confidence interval 95%)	7464 (5827 to 9560)	18641 (15308 to 22700)	21290 (16598 to 27309)	

Notes:

[38] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[39] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[40] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgA in serum 10 vs. 12 at T1

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in serum at T1 between age groups were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [41]
Method	Regression, Linear

Notes:

[41] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in serum 10 vs. 15 at T1

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in serum at T1 between age groups were made using linear

regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [42]
Method	Regression, Linear

Notes:

[42] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in serum 12 vs. 15 at T0

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in serum at T1 between age groups were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [43]
Method	Regression, Linear

Notes:

[43] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC MenC-PS specific IgA in serum at T2

End point title	GMC MenC-PS specific IgA in serum at T2

End point description:

Geometric mean concentrations (GMCs) of MenC-polysaccharide specific IgA in serum 1 Year (T2) after the MenC conjugate booster vaccination.

End point type	Secondary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83[44]	86[45]	75[46]	
Units: ng/mL				
geometric mean (confidence interval 95%)	730 (568 to 938)	2243 (1773 to 2838)	3557 (2749 to 4601)	

Notes:

[44] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[45] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[46] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgA in serum 10 vs. 12 at T2

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in serum at T2 between age groups were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [47]
Method	Regression, Linear

Notes:

[47] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in serum 10 vs. 15 at T2

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in serum at T2 between age groups were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [48]
Method	Regression, Linear

Notes:

[48] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in serum 12 vs. 15 at T2

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in serum at T2 between age groups were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.174 [49]
Method	Regression, Linear

Notes:

[49] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC MenC-PS specific IgA in saliva at T0

End point title	GMC MenC-PS specific IgA in saliva at T0

End point description:

Geometric mean concentrations (GMCs) of MenC-polysaccharide specific IgA in saliva prior to (T0) the MenC conjugate booster vaccination.

End point type	Secondary

End point timeframe:

T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81[50]	86[51]	75[52]	
Units: ng/mL				
geometric mean (confidence interval 95%)	4.8 (4.1 to 5.6)	6.5 (5.3 to 7.9)	9.0 (7.4 to 11.0)	

Notes:

[50] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[51] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[52] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgA in saliva 10 vs. 12 at T0

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in saliva at T0 between age groups were made using the Mann–Whitney U test.
All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.159 [53]
Method	Wilcoxon (Mann-Whitney)

Notes:

[53] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in saliva 10 vs. 15 at T0

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in saliva at T0 between age groups were made using the Mann–Whitney U test.
All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [54]
Method	Wilcoxon (Mann-Whitney)

Notes:

[54] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in saliva 12 vs. 15 at T0

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in saliva at T0 between age groups were made using the Mann–Whitney U test.
All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds

Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.03 [55]
Method	Wilcoxon (Mann-Whitney)

Notes:

[55] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC MenC-PS specific IgA in saliva at T1

End point title	GMC MenC-PS specific IgA in saliva at T1

End point description:

Geometric mean concentrations (GMCs) of MenC-polysaccharide specific IgA in saliva 1 Month (T1) after the MenC conjugate booster vaccination.

End point type	Secondary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83[56]	86[57]	75[58]	
Units: ng/mL				
geometric mean (confidence interval 95%)	35.4 (25.2 to 49.7)	87.1 (67.7 to 112.2)	99.2 (70.4 to 139.6)	

Notes:

[56] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[57] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[58] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgA in saliva 10 vs. 12 at T1

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in saliva at T1 between age groups were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [59]
Method	Regression, Linear

Notes:

[59] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in saliva 10 vs. 15 at T1

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in saliva at T1 between age groups were made using linear

regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [60]
Method	Regression, Linear

Notes:

[60] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in saliva 12 vs. 15 at T1

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in saliva at T1 between age groups were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [61]
Method	Regression, Linear

Notes:

[61] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC MenC-PS specific IgA in saliva at T2	
End point title	GMC MenC-PS specific IgA in saliva at T2

End point description:

Geometric mean concentrations (GMCs) of MenC-polysaccharide specific IgA in saliva 1 Year (T2) after the MenC conjugate booster vaccination.

End point type	Secondary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83[62]	86[63]	75[64]	
Units: ng/mL				
geometric mean (confidence interval 95%)	12.4 (9.6 to 15.9)	25.1 (19.7 to 32.1)	28.5 (21.9 to 37.0)	

Notes:

[62] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[63] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.
[64] - Only participants with sufficient amounts of saliva and serum available to perform all measurements.

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgA in saliva 10 vs. 12 at T2

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in saliva at T2 between age groups were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.006 [65]
Method	Regression, Linear

Notes:

[65] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in saliva 10 vs. 15 at T2

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in saliva at T2 between age groups were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.057 [66]
Method	Regression, Linear

Notes:

[66] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgA in saliva 12 vs. 15 at T2

Statistical analysis description:

Comparisons of GMC MenC-PS specific IgA in saliva at T2 between age groups were made using linear regression analyses with correction for values at T0. All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [67]
Method	Regression, Linear

Notes:

[67] - All p-values for these analyses were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC MenC-PS specific IgG1 antibodies at T0

End point title	GMC MenC-PS specific IgG1 antibodies at T0

End point description:

Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 1 (IgG1).

End point type	Secondary

End point timeframe:

T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	91	86	
Units: ug/mL				
geometric mean (confidence interval 95%)	0.34 (0.29 to 0.41)	0.34 (0.27 to 0.44)	0.34 (0.27 to 0.43)	

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgG1 10 vs. 12 at T0

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	12 year olds v 10 year olds
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [68]
Method	Regression, Linear

Notes:

[68] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG1 10 vs. 15 at T0

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [69]
Method	Regression, Linear

Notes:

[69] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG1 12 vs. 15 at T0

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds

Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [70]
Method	Regression, Linear

Notes:

[70] - P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC MenC-PS specific IgG1 antibodies at T1

End point title	GMC MenC-PS specific IgG1 antibodies at T1

End point description:

Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 1 (IgG1).

End point type	Secondary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	90	85	
Units: ug/mL				
geometric mean (confidence interval 95%)	158.6 (138.2 to 181.9)	213.4 (183.4 to 248.3)	168.7 (139.5 to 203.9)	

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgG1 10 vs. 12 at T1

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.015 [71]
Method	Regression, Linear

Notes:

[71] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG1 10 vs. 15 at T1

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [72]
Method	Regression, Linear

Notes:

[72] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG1 12 vs. 15 at T1

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.174 [73]
Method	Regression, Linear

Notes:

[73] - P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC MenC-PS specific IgG1 antibodies at T2

End point title	GMC MenC-PS specific IgG1 antibodies at T2

End point description:

Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 1 (IgG1).

End point type	Secondary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	89	83	
Units: ug/mL				
geometric mean (confidence interval 95%)	13.21 (11.32 to 15.42)	22.22 (18.51 to 26.68)	26.29 (22.39 to 30.88)	

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgG1 10 vs. 12 at T2

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds

Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [74]
Method	Regression, Linear

Notes:

[74] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG1 10 vs. 15 at T2

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [75]
Method	Regression, Linear

Notes:

[75] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG1 12 vs. 15 at T2

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.531 [76]
Method	Regression, Linear

Notes:

[76] - P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC MenC-PS specific IgG2 antibodies at T0

End point title	GMC MenC-PS specific IgG2 antibodies at T0

End point description:

Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 2 (IgG2).

End point type	Secondary

End point timeframe:

T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82[77]	86[78]	86	
Units: ug/mL				
geometric mean (confidence interval 95%)	0.09 (0.08 to 0.11)	0.13 (0.11 to 0.17)	0.16 (0.12 to 0.21)	

Notes:

[77] - Concentration IgG2 too low to measure in nine participants; GMC IgG2 presented from 82 participants
[78] - Concentration IgG2 too low to measure in five participants; GMC IgG2 presented from 86 participants.

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgG2 10 vs. 12 at T0

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.024 [79]
Method	Regression, Linear

Notes:

[79] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG2 10 vs. 15 at T0

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.003 [80]
Method	Regression, Linear

Notes:

[80] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG2 12 vs. 15 at T0

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds

Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [81]
Method	Regression, Linear

Notes:

[81] - P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC MenC-PS specific IgG2 antibodies at T1

End point title	GMC MenC-PS specific IgG2 antibodies at T1

End point description:

Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 2 (IgG2).

End point type	Secondary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	90	85	
Units: ug/mL				
geometric mean (confidence interval 95%)	14.0 (11.1 to 187.7)	28.0 (23.3 to 33.6)	30.5 (23.9 to 38.9)	

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgG2 10 vs. 12 at T1

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.003 [82]
Method	Regression, Linear

Notes:

[82] - * P-values were adjusted for three comparisons with Bonferroni

Statistical analysis title	GMC MenC-PS specific IgG2 10 vs. 15 at T1

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [83]
Method	Regression, Linear

Notes:

[83] - * P-values were adjusted for three comparisons with Bonferroni

Statistical analysis title	GMC MenC-PS specific IgG2 12 vs. 15 at T1

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [84]
Method	Regression, Linear

Notes:

[84] - * P-values were adjusted for three comparisons with Bonferroni

Secondary: GMC MenC-PS specific IgG2 antibodies at T2

End point title	GMC MenC-PS specific IgG2 antibodies at T2

End point description:

Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 2 (IgG2).

End point type	Secondary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	89	83	
Units: ug/mL				
geometric mean (confidence interval 95%)	1.28 (1.02 to 1.59)	3.23 (2.54 to 4.12)	5.32 (3.99 to 7.10)	

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgG2 10 vs. 12 at T2

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
* P-values were adjusted for three comparisons with Bonferroni correction. Extensive results of the crude a

Comparison groups	10 year olds v 12 year olds

Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [85]
Method	Regression, Linear

Notes:

[85] - * P-values were adjusted for three comparisons with Bonferroni

Statistical analysis title	GMC MenC-PS specific IgG2 10 vs. 15 at T2

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
* P-values were adjusted for three comparisons with Bonferroni correction. Extensive results of the crude a

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [86]
Method	Regression, Linear

Notes:

[86] - * P-values were adjusted for three comparisons with Bonferroni

Statistical analysis title	GMC MenC-PS specific IgG2 12 vs. 15 at T2

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
* P-values were adjusted for three comparisons with Bonferroni correction. Extensive results of the crude a

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.531 [87]
Method	Regression, Linear

Notes:

[87] - * P-values were adjusted for three comparisons with Bonferroni

Secondary: Ratio MenC-PS specific IgG1/IgG2 antibodies at T0

End point title	Ratio MenC-PS specific IgG1/IgG2 antibodies at T0

End point description:

Ratio of the Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 1 (IgG1) and Immunoglobulin G Subclass 2 (IgG2) at T0.

End point type	Secondary

End point timeframe:

T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	82[88]	86[89]	86	
Units: ratio IgG1 / IgG2				
number (confidence interval 95%)	3.98 (3.23 to 4.91)	2.71 (2.23 to 3.30)	2.17 (1.68 to 2.79)	

Notes:

[88] - Concentration IgG2 too low to measure in nine participants; ratio presented from 82 participants

[89] - Concentration IgG2 too low to measure in five participants; ratio presented from 86 participants

Statistical analyses

Statistical analysis title	MenC-PS IgG1/IgG2 subclass ratio 10 vs. 12 at T0

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.027 [90]
Method	Regression, Linear

Notes:

[90] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	MenC-PS IgG1/IgG2 subclass ratio 10 vs. 15 at T0

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [91]
Method	Regression, Linear

Notes:

[91] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	MenC-PS IgG1/IgG2 subclass ratio 12 vs. 15 at T0

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.522 [92]
Method	Regression, Linear

Notes:

[92] - P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: Ratio MenC-PS specific IgG1/IgG2 antibodies at T1

End point title	Ratio MenC-PS specific IgG1/IgG2 antibodies at T1

End point description:

Ratio of the Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 1 (IgG1) and Immunoglobulin G Subclass 2 (IgG2) at T1.

End point type	Secondary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	90	85	
Units: Ratio IgG1/IgG2				
number (confidence interval 95%)	11.30 (9.44 to 13.51)	7.59 (6.40 to 9.00)	5.54 (4.31 to 7.10)	

Statistical analyses

Statistical analysis title	MenC-PS IgG1/IgG2 subclass ration 10 vs. 12 at T1

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.255 [93]
Method	Regression, Linear

Notes:

[93] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	MenC-PS IgG1/IgG2 subclass ration 10 vs. 15 at T1

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.054 [94]
Method	Regression, Linear

Notes:

[94] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	MenC-PS IgG1/IgG2 subclass ration 12 vs. 15 at T1

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.276 [95]
Method	Regression, Linear

Notes:

[95] - P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: Ratio MenC-PS specific IgG1/IgG2 antibodies at T2

End point title	Ratio MenC-PS specific IgG1/IgG2 antibodies at T2

End point description:

Ratio of the Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 1 (IgG1) and Immunoglobulin G Subclass 2 (IgG2) at T2.

End point type	Secondary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	89	83	
Units: Ratio IgG1/IgG2				
number (confidence interval 95%)	10.36 (8.36 to 12.84)	6.87 (5.61 to 8.42)	4.94 (3.73 to 6.55)	

Statistical analyses

Statistical analysis title	MenC-PS IgG1/IgG2 subclass ratio 10 vs. 12 at T2

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds

Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.969 [96]
Method	Regression, Linear

Notes:

[96] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	MenC-PS IgG1/IgG2 subclass ratio 10 vs. 15 at T2

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.156 [97]
Method	Regression, Linear

Notes:

[97] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	MenC-PS IgG1/IgG2 subclass ratio 12 vs. 15 at T2

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.297 [98]
Method	Regression, Linear

Notes:

[98] - P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: Mean MenC-PS IgG avidity index age 10

End point title	Mean MenC-PS IgG avidity index age 10

End point description:

Meningococcal Serogroup C Polysaccharide Specific Immunoglobulin G (IgG) Avidity Indices (AI). Mean avidity indices per age group prior to (T0) and 1 month (T1) and 1 year (T2) after the MenC conjugate booster. Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included in the analyses (44 10-year-olds, 49 12-year-olds and 60 15-year-olds). Serum samples were diluted to a concentration of 25 ng/ml. Avidity index = (amount of IgG still bound after treatment with 0.5 M NH4SCN/amount of IgG with PBS) x 100.

End point type	Secondary

End point timeframe:

T0, T1, T2 and T3 of age group 10 years old.

End point values	Age group 10 at T0	Age group 10 at T1	Age group 10 at T2	Age group 10 at T3
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	44[99]	43[100]	42[101]	22[102]
Units: Avidity Index				
arithmetic mean (confidence interval 95%)	45.77 (41.20 to 50.33)	43.04 (38.32 to 47.75)	44.54 (40.94 to 48.13)	43.33 (35.93 to 50.73)

Notes:

[99] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[100] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[101] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[102] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.

Statistical analyses

Statistical analysis title	Avidity index age 10 T0 vs. T1
Statistical analysis description:	
Paired sample t-test avidity index age group 10 year old for T0 and T1.	
Comparison groups	Age group 10 at T0 v Age group 10 at T1
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3127
Method	paired sample t-test

Statistical analysis title	Avidity index age 10 T0 vs. T2
Statistical analysis description:	
Paired sample t-test avidity index age group 10 year old for T0 and T2.	
Comparison groups	Age group 10 at T0 v Age group 10 at T2
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3975
Method	paired sample t-test

Statistical analysis title	Avidity index age 10 T1 vs. T2
Statistical analysis description:	
Paired sample t-test avidity index age group 10 year old for T1 and T2.	
Comparison groups	Age group 10 at T2 v Age group 10 at T1

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6349
Method	paired sample t-test

Statistical analysis title	Avidity index age 10 T2 vs. T3

Statistical analysis description:

Paired sample t-test avidity index age group 10 year old for T2 and T3.

Comparison groups	Age group 10 at T2 v Age group 10 at T3
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.9924
Method	paired sample t-test

Secondary: Mean MenC-PS IgG avidity index age 12

End point title	Mean MenC-PS IgG avidity index age 12

End point description:

Meningococcal Serogroup C Polysaccharide Specific Immunoglobulin G (IgG) Avidity Indices (AI). Mean avidity indices per age group prior to (T0) and 1 month (T1) and 1 year (T2) after the MenC conjugate booster. Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included in the analyses (44 10-year-olds, 49 12-year-olds and 60 15-year-olds). Serum samples were diluted to a concentration of 25 ng/ml. Avidity index = (amount of IgG still bound after treatment with 0.5 M NH4SCN/amount of IgG with PBS) x 100.

End point type	Secondary

End point timeframe:

T0, T1, T2 and T3 of age group 12 years old.

End point values	Age group 12 at T0	Age group 12 at T1	Age group 12 at T2	Age group 12 at T3
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	49[103]	48[104]	48[105]	32[106]
Units: Avidity Index				
arithmetic mean (confidence interval 95%)	47.22 (43.16 to 51.27)	47.28 (43.29 to 51.26)	48.43 (45.15 to 51.72)	48.65 (42.33 to 54.96)

Notes:

[103] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[104] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[105] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[106] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.

Statistical analyses

Statistical analysis title	Avidity index age 12 T0 vs. T1
Statistical analysis description: Paired sample t-test avidity index age group 12 year old for T0 and T1.	
Comparison groups	Age group 12 at T0 v Age group 12 at T1
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.9792
Method	paired sample t-test

Statistical analysis title	Avidity index age 12 T0 vs. T2
Statistical analysis description: Paired sample t-test avidity index age group 12 year old for T0 and T2.	
Comparison groups	Age group 12 at T0 v Age group 12 at T2
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6209 [107]
Method	paired sample t-test
Notes: [107] - not significant	

Statistical analysis title	Avidity index age 12 T1 vs. T2
Statistical analysis description: Paired sample t-test avidity index age group 12 year old for T1 and T2.	
Comparison groups	Age group 12 at T2 v Age group 12 at T1
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5851
Method	paired sample t-test

Statistical analysis title	Avidity index age 12 T2 vs. T3
Statistical analysis description: Paired sample t-test avidity index age group 12 year old for T2 and T3.	
Comparison groups	Age group 12 at T2 v Age group 12 at T3
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5762
Method	paired sample t-test

Secondary: Mean MenC-PS IgG avidity index age 15

End point title	Mean MenC-PS IgG avidity index age 15

End point description:

Meningococcal Serogroup C Polysaccharide Specific Immunoglobulin G (IgG) Avidity Indices (AI). Mean avidity indices per age group prior to (T0) and 1 month (T1) and 1 year (T2) after the MenC conjugate booster. Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included in the analyses (44 10-year-olds, 49 12-year-olds and 60 15-year-olds). Serum samples were diluted to a concentration of 25 ng/ml. Avidity index = (amount of IgG still bound after treatment with 0.5 M NH4SCN/amount of IgG with PBS) x 100.

End point type	Secondary

End point timeframe:

T0, T1, T2 and T3 of age group 15 years old.

End point values	Age group 15 at T0	Age group 15 at T1	Age group 15 at T2	Age group 15 at T3
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	60[108]	60[109]	59[110]	25[111]
Units: Avidity index				
arithmetic mean (confidence interval 95%)	41.67 (37.06 to 46.28)	50.76 (46.83 to 54.96)	46.79 (43.53 to 50.05)	46.08 (39.39 to 52.78)

Notes:

[108] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[109] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[110] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[111] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.

Statistical analyses

Statistical analysis title	Avidity index age 15 T0 vs. T1

Statistical analysis description:

Paired sample t-test avidity index age group 15 year old for T0 and T1.

Comparison groups	Age group 15 at T0 v Age group 15 at T1
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0027
Method	paired sample t-test

Statistical analysis title	Avidity index age 15 T0 vs. T2

Statistical analysis description:

Paired sample t-test avidity index age group 15 year old for T0 and T2.

Comparison groups	Age group 15 at T0 v Age group 15 at T2

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.044
Method	paired sample t-test

Statistical analysis title	Avidity index age 15 T1 vs. T2
Statistical analysis description:	
Paired sample t-test avidity index age group 15 year old for T1 and T2.	
Comparison groups	Age group 15 at T2 v Age group 15 at T1
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0006
Method	paired sample t-test

Statistical analysis title	Avidity index age 15 T2 vs. T3
Statistical analysis description:	
Paired sample t-test avidity index age group 15 year old for T2 and T3.	
Comparison groups	Age group 15 at T2 v Age group 15 at T3
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0029
Method	paired sample t-test

Secondary: GMC of Tetanus Toxoid specific IgG at T0	
End point title	GMC of Tetanus Toxoid specific IgG at T0
End point description:	
Geometric Mean Concentrations (GMCs) of Tetanus Toxoid (TT) Specific Immunoglobulin G (IgG) prior to (T0) the Meningococcal Serogroup C Tetanus Toxoid Conjugate Booster.	
End point type	Secondary
End point timeframe:	
T0	

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	91	86	
Units: ug/mL				
geometric mean (confidence interval 95%)	5.1 (4.3 to 6.0)	1.6 (1.3 to 1.9)	0.7 (0.6 to 0.8)	

Statistical analyses

Statistical analysis title	GMT TT IgG levels 10 vs. 12 at T0

Statistical analysis description:

Differences between age groups in GMC of TT-specific IgG were determined with linear regression analyses, adjusting for concentrations at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [112]
Method	Regression, Linear

Notes:

[112] - * P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMT TT IgG levels 10 vs. 15 at T0

Statistical analysis description:

Differences between age groups in GMC of TT-specific IgG were determined with linear regression analyses, adjusting for concentrations at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [113]
Method	Regression, Linear

Notes:

[113] - * P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMT TT IgG levels 12 vs.15 at T0

Statistical analysis description:

Differences between age groups in GMC of TT-specific IgG were determined with linear regression analyses, adjusting for concentrations at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [114]
Method	Regression, Linear

Notes:

[114] - * P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC of Tetanus Toxoid specific IgG at T1

End point title	GMC of Tetanus Toxoid specific IgG at T1

End point description:

Geometric Mean Concentrations (GMCs) of Tetanus Toxoid (TT) Specific Immunoglobulin G (IgG) 1 Month (T1) after the Meningococcal Serogroup C Tetanus Toxoid Conjugate Booster.

End point type	Secondary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	90	85	
Units: ug/mL				
geometric mean (confidence interval 95%)	7.4 (6.5 to 8.5)	4.4 (3.4 to 5.1)	2.9 (2.4 to 3.5)	

Statistical analyses

Statistical analysis title	GMC TT IgG levels 10 vs. 12 at T1

Statistical analysis description:

Differences between age groups in GMC of TT-specific IgG were determined with linear regression analyses, adjusting for concentrations at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.069 [115]
Method	Regression, Linear

Notes:

[115] - * P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC TT IgG levels 10 vs. 15 at T1

Statistical analysis description:

Differences between age groups in GMC of TT-specific IgG were determined with linear regression analyses, adjusting for concentrations at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.213 [116]
Method	Regression, Linear

Notes:

[116] - * P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC TT IgG levels 12 vs. 15 at T1

Statistical analysis description:

Differences between age groups in GMC of TT-specific IgG were determined with linear regression analyses, adjusting for concentrations at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 1 [117]
Method	Regression, Linear

Notes:

[117] - * P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC of Tetanus Toxoid specific IgG at T2

End point title	GMC of Tetanus Toxoid specific IgG at T2

End point description:

Geometric Mean Concentrations (GMCs) of Tetanus Toxoid (TT) Specific Immunoglobulin G (IgG) 1 Year (T2) after the Meningococcal Serogroup C Tetanus Toxoid Conjugate Booster.

End point type	Secondary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	89	83	
Units: ug/mL				
geometric mean (confidence interval 95%)	3.6 (3.1 to 4.2)	1.9 (1.6 to 2.2)	1.1 (1.0 to 1.4)	

Statistical analyses

Statistical analysis title	GMC TT IgG levels 10 vs. 12 at T2

Statistical analysis description:

Differences between age groups in GMC of TT-specific IgG were determined with linear regression analyses, adjusting for concentrations at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds

Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.006 [118]
Method	Regression, Linear

Notes:

[118] - * P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC TT IgG levels 10 vs. 15 at T2

Statistical analysis description:

Differences between age groups in GMC of TT-specific IgG were determined with linear regression analyses, adjusting for concentrations at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.153 [119]
Method	Regression, Linear

Notes:

[119] - * P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC TT IgG levels 12 vs. 15 at T2

Statistical analysis description:

Differences between age groups in GMC of TT-specific IgG were determined with linear regression analyses, adjusting for concentrations at T0.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.186 [120]
Method	Regression, Linear

Notes:

[120] - * P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: Ratio of GMC TT IgG levels T1/T0

End point title	Ratio of GMC TT IgG levels T1/T0

End point description:

Ratio of the Geometric Mean Concentrations (GMCs) of Tetanus Toxoid (TT) Specific IgG prior to (T0) and 1 month (T1) after the Menongococcal Serogroup C tetanus Toxoid Conjugate Booster.

End point type	Secondary

End point timeframe:

T1 versus T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	90	85	
Units: GCM ratio T1/T0				
number (confidence interval 95%)	1.49 (1.34 to 1.64)	2.75 (2.42 to 3.13)	4.26 (3.59 to 5.05)	

Statistical analyses

Statistical analysis title	Ratio of GMC TT IgG levels T1/T0 10 vs. 12 years

Statistical analysis description:

GMC ratios indicate the level of increase (T1/T0) of Tetanus Toxiod specific IgG between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [121]
Method	t-test, 2-sided

Notes:

[121] - * P-values were adjusted for three comparisons with Bonfe

Statistical analysis title	Ratio of GMC TT IgG levels T1/T0 10 vs. 15 years

Statistical analysis description:

GMC ratios indicate the level of increase (T1/T0) of Tetanus Toxiod specific IgG between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [122]
Method	t-test, 2-sided

Notes:

[122] - * P-values were adjusted for three comparisons with Bonfe

Statistical analysis title	Ratio of GMC TT IgG levels T1/T0 12 vs. 15 years

Statistical analysis description:

GMC ratios indicate the level of increase (T1/T0) of Tetanus Toxiod specific IgG between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [123]
Method	t-test, 2-sided

Notes:

[123] - * P-values were adjusted for three comparisons with Bonfe

Secondary: Ratio of GMC TT IgG levels T1/T2

End point title	Ratio of GMC TT IgG levels T1/T2

End point description:

Ratio of the Geometric Mean Concentrations (GMCs) of Tetanus Toxoid (TT) Specific IgG 1 month (T1) and 1 year (T2) after the Menongococcal Serogroup C tetanus Toxoid Conjugate Booster.

End point type	Secondary

End point timeframe:

T1 versus T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	89	83	
Units: GMC ratio T1/T2				
number (confidence interval 95%)	2.03 (1.89 to 2.18)	2.34 (2.14 to 2.55)	2.50 (2.27 to 2.75)	

Statistical analyses

Statistical analysis title	Ratio of GMC TT IgG levels T1/T2 10 vs. 12 years

Statistical analysis description:

GMC ratios indicate the level of decrease (T1/T2) of Tetanus Toxoid (TT) specific IgG between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.048 [124]
Method	t-test, 2-sided

Notes:

[124] - * P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	Ratio of GMC TT IgG levels T1/T2 10 vs. 15 years

Statistical analysis description:

GMC ratios indicate the level of decrease (T1/T2) of Tetanus Toxoid (TT) specific IgG between time points. Differences in GMC ratios between groups were determined with independent sample t-tests.
* P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds

Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.001 [125]
Method	t-test, 2-sided

Notes:

[125] - * P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	Ratio of GMC TT IgG levels T1/T2 12 vs. 15 years

Statistical analysis description:

GMC ratios indicate the level of decrease (T1/T2) of Tetanus Toxoid (TT) specific IgG between time points. Differences in GMC ratios between groups were determined with independent sample t-tests. * P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.921 [126]
Method	t-test, 2-sided

Notes:

[126] - * P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: Mean MenC-PS IgG avidity index T0

End point title	Mean MenC-PS IgG avidity index T0

End point description:

Meningococcal Serogroup C Polysaccharide Specific Immunoglobulin G (IgG) Avidity Indices (AI). Mean avidity indices per age group prior to (T0) the MenC conjugate booster. Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included in the analyses (44 10-year-olds, 49 12-year-olds and 60 15-year-olds). Serum samples were diluted to a concentration of 25 ng/ml. Avidity index = (amount of IgG still bound after treatment with 0.5 M NH4SCN/amount of IgG with PBS) x 100.

End point type	Secondary

End point timeframe:

T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44[127]	49[128]	60[129]	
Units: Avidity Index				
arithmetic mean (confidence interval 95%)	45.77 (41.20 to 50.33)	47.22 (43.16 to 51.27)	41.67 (37.06 to 46.28)	

Notes:

[127] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[128] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[129] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.

Statistical analyses

Statistical analysis title	Avidity index T0 10 vs. 12 years old
Statistical analysis description: T-test on the mean avidity index at T0 for age groups 10 and 12 years old.	
Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6342
Method	t-test, 2-sided

Statistical analysis title	Avidity index T0 10 vs. 15 years old
Statistical analysis description: T-test on the mean avidity index at T0 for age groups 10 and 15 years old.	
Comparison groups	15 year olds v 10 year olds
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.2076
Method	t-test, 2-sided

Statistical analysis title	Avidity index T0 12 vs. 15 years old
Statistical analysis description: T-test on the mean avidity index at T0 for age groups 12 and 15 years old.	
Comparison groups	12 year olds v 15 year olds
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1564
Method	t-test, 2-sided

Secondary: Mean MenC-PS IgG avidity index T1

End point title	Mean MenC-PS IgG avidity index T1
End point description: Meningococcal Serogroup C Polysaccharide Specific Immunoglobulin G (IgG) Avidity Indices (AI). Mean avidity indices per age group 1 month after the MenC conjugate booster (T1). Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included in the analyses. Serum samples were diluted to a concentration of 25 ng/ml. Avidity index = (amount of IgG still bound after treatment with 0.5 M NH4SCN/amount of IgG with PBS) x 100.	
End point type	Secondary
End point timeframe: T1	

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43[130]	48[131]	60[132]	
Units: Avidity Index				
arithmetic mean (confidence interval 95%)	43.04 (38.32 to 47.75)	47.28 (43.29 to 51.26)	50.76 (46.83 to 54.96)	

Notes:

[130] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[131] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[132] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.

Statistical analyses

Statistical analysis title	Avidity index T1 10 vs. 12 years old

Statistical analysis description:

T-test of mean avidity index at T1 for groups 10 and 12 years old.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1701
Method	t-test, 2-sided

Statistical analysis title	Avidity index T1 10 vs. 15 years old

Statistical analysis description:

T-test of mean avidity index at T1 for groups 10 and 15 years old.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0131
Method	t-test, 2-sided

Statistical analysis title	Avidity index T1 12 vs. 15 years old

Statistical analysis description:

T-test of mean avidity index at T1 for groups 12 and 15 years old.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.2148
Method	t-test, 2-sided

Secondary: Mean MenC-PS IgG avidity index T2

End point title	Mean MenC-PS IgG avidity index T2

End point description:

Meningococcal Serogroup C Polysaccharide Specific Immunoglobulin G (IgG) Avidity Indices (AI). Mean avidity indices per age group 1 year after the MenC conjugate booster (T2). Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included in the analyses. Serum samples were diluted to a concentration of 25 ng/ml. Avidity index = (amount of IgG still bound after treatment with 0.5 M NH4SCN/amount of IgG with PBS) x 100.

End point type	Secondary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42[133]	48[134]	59[135]	
Units: Avidity Index				
arithmetic mean (confidence interval 95%)	44.54 (40.94 to 48.13)	48.43 (45.15 to 51.72)	46.79 (43.53 to 50.05)	

Notes:

[133] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[134] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.
[135] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.

Statistical analyses

Statistical analysis title	Avidity index T2 10 vs. 12 years old

Statistical analysis description:

T-test of mean avidity index at T2 for groups 10 and 12 years old.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1105
Method	t-test, 2-sided

Statistical analysis title	Avidity index T2 10 vs. 15 years old

Statistical analysis description:

T-test of mean avidity index at T2 for groups 10 and 15 years old.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3533
Method	t-test, 2-sided

Statistical analysis title	Avidity index T2 12 vs. 15 years old

Statistical analysis description:

T-test of mean avidity index at T2 for groups 12 and 15 years old.

Comparison groups	12 year olds v 15 year olds
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.4775
Method	t-test, 2-sided

Secondary: Mean MenC-PS IgG avidity index T3

End point title	Mean MenC-PS IgG avidity index T3

End point description:

Meningococcal Serogroup C Polysaccharide Specific Immunoglobulin G (IgG) Avidity Indices (AI). Mean avidity indices per age group 3 years after the MenC conjugate booster (T3). Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included in the analyses. Serum samples were diluted to a concentration of 25 ng/ml. Avidity index = (amount of IgG still bound after treatment with 0.5 M NH4SCN/amount of IgG with PBS) x 100.

End point type	Secondary

End point timeframe:

T3

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22[136]	32[137]	25[138]	
Units: Avidity Index				
arithmetic mean (confidence interval 95%)	43.33 (35.93 to 50.73)	48.65 (42.33 to 54.96)	46.08 (39.39 to 52.78)	

Notes:

[136] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.

[137] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.

[138] - Only serum samples from participants with an IgG concentration of >=0.25 mg/ml at T0 were included.

Statistical analyses

Statistical analysis title	Avidity index T3 10 vs. 12 years old

Statistical analysis description:

T-test of mean avidity index at T3 for age groups 10 and 12 years old.

Comparison groups	10 year olds v 12 year olds

Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.2658
Method	t-test, 2-sided

Statistical analysis title	Avidity index T3 10 vs. 15 years old
Statistical analysis description:	
T-test of mean avidity index at T3 for age groups 10 and 15 years old.	
Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5705
Method	t-test, 2-sided

Statistical analysis title	Avidity index T3 12 vs. 15 years old
Statistical analysis description:	
T-test of mean avidity index at T3 for age groups 12 and 15 years old.	
Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5701
Method	t-test, 2-sided

Secondary: GMC MenC-PS specific IgG antibodies at T3	
End point title	GMC MenC-PS specific IgG antibodies at T3
End point description:	
Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G (IgG) 3 years (T3) after the MenC Conjugate Booster.	
End point type	Secondary
End point timeframe:	
T3	

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	75	58	
Units: ug/mL				
geometric mean (confidence interval 95%)	6.4 (5.3 to 7.7)	14 (11 to 17)	19 (16 to 23)	

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgG 10 vs. 12 at T3

Statistical analysis description:

Differences between age groups in GMC MenC-PS IgG at T3 were determined with linear regression analyses, adjusting for titers and concentrations before the booster vaccination.
All P-values were adjusted for three comparisons with the Bonferroni correction.

Comparison groups	12 year olds v 10 year olds
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [139]
Method	Regression, Linear

Notes:

[139] - All P-values were adjusted for three comparisons with the Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG 10 vs. 15 at T3

Statistical analysis description:

Differences between age groups in GMC MenC-PS IgG at T3 were determined with linear regression analyses, adjusting for titers and concentrations before the booster vaccination.
All P-values were adjusted for three comparisons with the Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [140]
Method	Regression, Linear

Notes:

[140] - All P-values were adjusted for three comparisons with the Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG 12 vs. 15 at T3

Statistical analysis description:

Differences between age groups in GMC MenC-PS IgG at T3 were determined with linear regression analyses, adjusting for titers and concentrations before the booster vaccination.
All P-values were adjusted for three comparisons with the Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.267 [141]
Method	Regression, Linear

Notes:

[141] - All P-values were adjusted for three comparisons with the Bonferroni correction.

Secondary: GMC of Tetanus Toxoid specific IgG at T3

End point title	GMC of Tetanus Toxoid specific IgG at T3

End point description:

Geometric Mean Concentrations (GMCs) of Tetanus Toxoid (TT) Specific Immunoglobulin G (IgG) 3 years (T3) after the Meningococcal Serogroup C Tetanus Toxoid Conjugate Booster.

End point type	Secondary

End point timeframe:

T3

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	75	58	
Units: ug/mL				
geometric mean (confidence interval 95%)	1.37 (1.2 to 1.6)	0.87 (0.7 to 1.1)	0.60 (0.5 to 0.8)	

Statistical analyses

Statistical analysis title	GMC Tetanus Toxoid specific IgG 10 vs. 12 at T3

Statistical analysis description:

Differences in Geometric Mean Concentrations (GMCs) of Tetanus Toxoid (TT) Specific Immunoglobulin G (IgG) 3 years (T3) after the Meningococcal Serogroup C Tetanus Toxoid Conjugate Booster were determined with linear regression, adjusting for concentrations before the booster vaccination. All P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [142]
Method	Regression, Linear

Notes:

[142] - All P-values were adjusted for three comparisons with the Bonferroni correction.

Statistical analysis title	GMC Tetanus Toxoid specific IgG 10 vs. 15 at T3

Statistical analysis description:

Differences in Geometric Mean Concentrations (GMCs) of Tetanus Toxoid (TT) Specific Immunoglobulin G (IgG) 3 years (T3) after the Meningococcal Serogroup C Tetanus Toxoid Conjugate Booster were determined with linear regression, adjusting for concentrations before the booster vaccination. All P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds

Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.001 [143]
Method	Regression, Linear

Notes:

[143] - All P-values were adjusted for three comparisons with the Bonferroni correction.

Statistical analysis title	GMC Tetanus Toxoid specific IgG 12 vs. 15 at T3

Statistical analysis description:

Differences in Geometric Mean Concentrations (GMCs) of Tetanus Toxoid (TT) Specific Immunoglobulin G (IgG) 3 years (T3) after the Meningococcal Serogroup C Tetanus Toxoid Conjugate Booster were determined with linear regression, adjusting for concentrations before the booster vaccination. All P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [144]
Method	Regression, Linear

Notes:

[144] - All P-values were adjusted for three comparisons with the Bonferroni correction.

Secondary: GMC MenC-PS specific IgG1 antibodies at T3

End point title	GMC MenC-PS specific IgG1 antibodies at T3

End point description:

Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 1 (IgG1) 3 years (T3) after booster vaccination.

End point type	Secondary

End point timeframe:

T3

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	75	58	
Units: ug/mL				
geometric mean (confidence interval 95%)	9.42 (7.97 to 11.15)	18.20 (14.96 to 22.14)	21.47 (18.28 to 25.21)	

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgG1 10 vs. 12 at T3

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds

Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [145]
Method	Regression, Linear

Notes:

[145] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG1 10 vs. 15 at T3

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [146]
Method	Regression, Linear

Notes:

[146] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG1 12 vs. 15 at T3

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 1 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.354 [147]
Method	Regression, Linear

Notes:

[147] - P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: GMC MenC-PS specific IgG2 antibodies at T3

End point title	GMC MenC-PS specific IgG2 antibodies at T3

End point description:

Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 2 (IgG2) 3 years (T3) after booster vaccination.

End point type	Secondary

End point timeframe:

T3

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	75	58	
Units: ug/mL				
geometric mean (confidence interval 95%)	0.79 (0.60 to 1.03)	2.06 (1.60 to 2.65)	3.66 (2.55 to 5.26)	

Statistical analyses

Statistical analysis title	GMC MenC-PS specific IgG2 10 vs. 12 at T3

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [148]
Method	Regression, Linear

Notes:

[148] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG2 10 vs. 15 at T3

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001 [149]
Method	Regression, Linear

Notes:

[149] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	GMC MenC-PS specific IgG2 12 vs. 15 at T3

Statistical analysis description:

Differences between age groups in GMC of MenC-PS specific IgG subclass 2 were determined with linear regression analyses, adjusting for concentrations and ratios at T0.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.297 [150]
Method	Regression, Linear

Notes:

[150] - P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: Ratio MenC-PS specific IgG1/IgG2 antibodies at T3

End point title	Ratio MenC-PS specific IgG1/IgG2 antibodies at T3

End point description:

Ratio of the Geometric Mean Concentrations (GMCs) of Meningococcal Serogroup C Polysaccharide (MenC-PS) Specific Immunoglobulin G Subclass 1 (IgG1) and Immunoglobulin G Subclass 2 (IgG2) at T3.

End point type	Secondary

End point timeframe:

T3

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	75	58	
Units: Ratio IgG1/IgG2				
number (confidence interval 95%)	11.4 (8.9 to 14.6)	8.8 (7.1 to 11.0)	5.9 (4.1 to 8.3)	

Statistical analyses

Statistical analysis title	Ratio MenC-PS IgG1/IgG levels 10 vs. 12 at T3

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with independent sample t-test.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.447 [151]
Method	independent sample t-test

Notes:

[151] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	Ratio MenC-PS IgG1/IgG levels 10 vs. 15 at T3

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with independent sample t-test.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	10 year olds v 15 year olds

Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.003 [152]
Method	independent sample t-test

Notes:

[152] - P-values were adjusted for three comparisons with Bonferroni correction.

Statistical analysis title	Ratio MenC-PS IgG1/IgG levels 12 vs. 15 at T3

Statistical analysis description:

Differences between age groups in MenC-PS specific IgG1 / IgG2 subclass ratio were determined with independent sample t-test.
P-values were adjusted for three comparisons with Bonferroni correction.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.06 [153]
Method	independent sample t-test

Notes:

[153] - P-values were adjusted for three comparisons with Bonferroni correction.

Secondary: Decay of SBA titer below 8 (50% predicted interval)

End point title	Decay of SBA titer below 8 (50% predicted interval)

End point description:

Predicted time after the meningococcal serogroup C conjugated to tetanus toxoid (MenC-TT) booster vaccination to fall below an rSBA titer of 8 for the three age groups estimated by the bi-exponential decay model. Calculated median duration of protection (50% predicted interval).

End point type	Secondary

End point timeframe:

T0 - T3

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88[154]	89[155]	85[156]	
Units: years				
number (not applicable)	16.3	45.9	270	

Notes:

[154] - Samples from T0 to T3 were used.

[155] - Samples from T0 to T3 were used.

[156] - Samples from T0 to T3 were used.

Statistical analyses

No statistical analyses for this end point

Secondary: Decay of SBA titer below 8 (5% predicted interval)

End point title	Decay of SBA titer below 8 (5% predicted interval)

End point description:

Predicted time after the meningococcal serogroup C conjugated to tetanus toxoid (MenC-TT) booster vaccination to fall below an rSBA titer of 8 for the three age groups estimated by the bi-exponential decay model. The estimated minimal duration of protection after this booster vaccination (5% predicted interval).

End point type	Secondary

End point timeframe:

T0-T3

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88[157]	89[158]	85[159]	
Units: years				
number (not applicable)	8.7	16.3	29.0	

Notes:

[157] - Samples from T0 to T3 were used.

[158] - Samples from T0 to T3 were used.

[159] - Samples from T0 to T3 were used.

Statistical analyses

No statistical analyses for this end point

Secondary: Decay of SBA titer below 128 (50% predicted interval)

End point title	Decay of SBA titer below 128 (50% predicted interval)

End point description:

Predicted time after the meningococcal serogroup C conjugated to tetanus toxoid (MenC-TT) booster vaccination to fall below an rSBA titer of 128 for the three age groups estimated by the bi-exponential decay model. Calculated median duration of protection (50% predicted interval).

End point type	Secondary

End point timeframe:

T0-T3

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88[160]	89[161]	85[162]	
Units: years				
number (not applicable)	7.7	24.4	145	

Notes:

[160] - Samples from T0 to T3 were used.

[161] - Samples from T0 to T3 were used.

[162] - Samples from T0 to T3 were used.

Statistical analyses

No statistical analyses for this end point

Secondary: Decay of SBA titer below 128 (5% predicted interval)

End point title	Decay of SBA titer below 128 (5% predicted interval)

End point description:

Predicted time after the meningococcal serogroup C conjugated to tetanus toxoid (MenC-TT) booster vaccination to fall below an rSBA titer of 128 for the three age groups estimated by the bi-exponential decay model. The estimated minimal duration of protection after this booster vaccination (5% predicted interval).

End point type	Secondary

End point timeframe:

T0-T3

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88[163]	89[164]	85[165]	
Units: years				
number (not applicable)	3.4	8.2	16.3	

Notes:

[163] - Samples from T0 to T3 were used.

[164] - Samples from T0 to T3 were used.

[165] - Samples from T0 to T3 were used.

Statistical analyses

No statistical analyses for this end point

Secondary: Men-C PS specific IgA memory B-cell responses at T0

End point title	Men-C PS specific IgA memory B-cell responses at T0

End point description:

Frequency of circulating MenC-PS-specific IgA memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells

End point type	Secondary

End point timeframe:

T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	10	9	
Units: Men-C IgA memory B cells				
geometric mean (confidence interval 95%)	0.06 (0.003 to 1.07)	0.09 (0.01 to 0.65)	0.06 (0.007 to 0.48)	

Statistical analyses

Statistical analysis title	Men-C PS IgA memory B cells 10 vs. 12 at T0

Statistical analysis description:

Mann-Whitney U test on circulating MenC-PS-specific IgA memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.7602
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C PS IgA memory B cells 10 vs. 15 at T0

Statistical analysis description:

Mann-Whitney U test on circulating MenC-PS-specific IgA memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.9999
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C PS IgA memory B cells 12 vs. 15 at T0

Statistical analysis description:

Mann-Whitney U test on circulating MenC-PS-specific IgA memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.7942
Method	Wilcoxon (Mann-Whitney)

Secondary: Men-C PS specific IgA memory B-cell responses at T1

End point title	Men-C PS specific IgA memory B-cell responses at T1

End point description:

Frequency of circulating MenC-PS-specific IgA memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells

End point type	Secondary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	11	8	
Units: MenC IgA memory B cells				
geometric mean (confidence interval 95%)	3.27 (0.22 to 49.23)	43.55 (27.83 to 68.15)	32.41 (12.68 to 82.87)	

Statistical analyses

Statistical analysis title	Men-C PS IgA memory B cells 10 vs. 12 at T1

Statistical analysis description:

Mann-Whitney U test on circulating MenC-PS-specific IgA memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0165
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C PS IgA memory B cells 10 vs. 15 at T1

Statistical analysis description:

Mann-Whitney U test on circulating MenC-PS-specific IgA memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0401
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C PS IgA memory B cells 12 vs. 15 at T1

Statistical analysis description:

Mann-Whitney U test on circulating MenC-PS-specific IgA memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.

Comparison groups	15 year olds v 12 year olds

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5304
Method	Wilcoxon (Mann-Whitney)

Secondary: Men-C PS specific IgA memory B-cell responses at T2

End point title	Men-C PS specific IgA memory B-cell responses at T2

End point description:

Frequency of circulating MenC-PS-specific IgA memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells

End point type	Secondary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	11	11	
Units: MenC IgA memory B cells				
geometric mean (confidence interval 95%)	0.29 (0.006 to 13.41)	2.00 (0.33 to 12.19)	2.81 (0.65 to 12.18)	

Statistical analyses

Statistical analysis title	Men-C PS IgA memory B cells 10 vs. 12 at T2

Statistical analysis description:

Mann-Whitney U test on circulating MenC-PS-specific IgA memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0847
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C PS IgA memory B cells 10 vs. 15 at T2

Statistical analysis description:

Mann-Whitney U test on circulating MenC-PS-specific IgA memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 15 year olds

Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1346
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Men-C PS IgA memory B cells 12 vs. 15 at T2

Statistical analysis description:

Mann-Whitney U test on circulating MenC-PS-specific IgA memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of MenC-specific memory B cells per 100,000 B cells.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.96
Method	Wilcoxon (Mann-Whitney)

Secondary: Tetanus Toxoid specific IgG memory B-cell responses at T0

End point title	Tetanus Toxoid specific IgG memory B-cell responses at T0

End point description:

Frequency of circulating Tetanus Toxoid specific IgG memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of TT memory B cells per 100,000 B cells

End point type	Secondary

End point timeframe:

T0

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	13	14	
Units: TT IgG memory B cells				
geometric mean (confidence interval 95%)	10.29 (3.81 to 27.81)	5.53 (1.53 to 20.01)	1.29 (0.26 to 6.42)	

Statistical analyses

Statistical analysis title	Tetanus Toxoid IgG memory B cells 10 vs. 12 at T2

Statistical analysis description:

Mann-Whitney U test on circulating Tetanus Toxoid specific IgG memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of TT-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 12 year olds

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1938
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Tetanus Toxoid IgG memory B cells 10 vs. 15 at T0

Statistical analysis description:

Mann-Whitney U test on circulating Tetanus Toxoid specific IgG memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of TT-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0007
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Tetanus Toxoid IgG memory B cells 12 vs. 15 at T0

Statistical analysis description:

Mann-Whitney U test on circulating Tetanus Toxoid specific IgG memory B cells prior to (T0) the MenC conjugate booster vaccination. Geometric mean number of TT-specific memory B cells per 100,000 B cells.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0865
Method	Wilcoxon (Mann-Whitney)

Secondary: Tetanus Toxoid specific IgG memory B-cell responses at T1

End point title	Tetanus Toxoid specific IgG memory B-cell responses at T1

End point description:

Frequency of circulating Tetanus Toxoid specific IgG memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of TT memory B cells per 100,000 B cells

End point type	Secondary

End point timeframe:

T1

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	14	17	
Units: Tetanus toxoid IgG memory B cells				
geometric mean (confidence interval 95%)	17.09 (11.47 to 25.48)	21.78 (12.62 to 37.59)	7.53 (1.99 to 28.52)	

Statistical analyses

Statistical analysis title	Tetanus Toxoid IgG memory B cells 10 vs. 12 at T1

Statistical analysis description:

Mann-Whitney U test on circulating Tetanus Toxoid specific IgG memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of TT-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3141
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Tetanus Toxoid IgG memory B cells 10 vs 15 at T1

Statistical analysis description:

Mann-Whitney U test on circulating Tetanus Toxoid specific IgG memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of TT-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 15 year olds
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6656
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Tetanus Toxoid IgG memory B cells 12 vs. 15 at T1

Statistical analysis description:

Mann-Whitney U test on circulating Tetanus Toxoid specific IgG memory B cells 1 month (T1) after the MenC conjugate booster vaccination. Geometric mean number of TT-specific memory B cells per 100,000 B cells.

Comparison groups	15 year olds v 12 year olds

Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1701
Method	Wilcoxon (Mann-Whitney)

Secondary: Tetanus Toxoid specific IgG memory B-cell responses at T2

End point title	Tetanus Toxoid specific IgG memory B-cell responses at T2

End point description:

Frequency of circulating Tetanus Toxoid specific IgG memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of TT memory B cells per 100,000 B cells

End point type	Secondary

End point timeframe:

T2

End point values	10 year olds	12 year olds	15 year olds	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	13	16	
Units: Tetanus Toxoid IgG memory B cells				
geometric mean (confidence interval 95%)	3.80 (1.07 to 13.50)	6.44 (1.91 to 21.75)	2.68 (0.68 to 10.50)	

Statistical analyses

Statistical analysis title	Tetanus Toxoid IgG memory B cells 10 vs. 12 at T2

Statistical analysis description:

Mann-Whitney U test on circulating Tetanus Toxoid specific IgG memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of TT-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 12 year olds
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5701
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Tetanus Toxoid IgG memory B cells 10 vs. 15 at T2

Statistical analysis description:

Mann-Whitney U test on circulating Tetanus Toxoid specific IgG memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of TT-specific memory B cells per 100,000 B cells.

Comparison groups	10 year olds v 15 year olds

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5507
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Tetanus Toxoid IgG memory B cells 12 vs. 15 at T2

Statistical analysis description:

Mann-Whitney U test on circulating Tetanus Toxoid specific IgG memory B cells 1 year (T2) after the MenC conjugate booster vaccination. Geometric mean number of TT-specific memory B cells per 100,000 B cells.

Comparison groups	15 year olds v 12 year olds
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3566
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) are defined as any undesirable experience occurring to a participant during the study, whether or not considered related to the vaccine, the vaccination or the venapuncture.

Adverse event reporting additional description:

There were no SAEs and SUSARs.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Self reported Adverse event

Reporting group description:

All adverse events reported spontaneously by the participant, his/her parent(s) or observed by the principal investiga¬tor or her staff .

Serious adverse events	Self reported Adverse event		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 268 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	Self reported Adverse event		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 268 (0.37%)		
Injury, poisoning and procedural complications			
Immunisation reaction	Additional description: one subject had multiple reactions; headache, dizziness, and a feeling of swelling and pain in the throat. And atypical vasovagal reaction after venipuncture and vaccination/ mild allergic reaction after vaccination.		
subjects affected / exposed	1 / 268 (0.37%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 268 (0.37%)		
occurrences (all)	1		
Dizziness			

subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all)	1 / 268 (0.37%) 1 1 / 268 (0.37%) 1		
Immune system disorders Allergic reaction to excipient subjects affected / exposed occurrences (all)	 1 / 268 (0.37%) 1		
Respiratory, thoracic and mediastinal disorders Pharyngeal swelling subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 1 / 268 (0.37%) 1 1 / 268 (0.37%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 June 2014	For adequate protection against Meningococcal C (MenC), sufficient circulating antibodies are required. The first results of the TIM study show that all 10-, 12- and 15-year-olds in the study still have more than enough antibodies 1 year after the study vaccination (booster). However, the rate of decline of the circulating antibodies seems to be the least rapid in the 15-year-olds. We want to further monitor the (differences between the age groups in) the rate of decline of MenC-specific antibodies after the study vaccination and therefore are going to take blood and saliva 3 years after the study vaccination.

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.

Missing data:
* Memory T cells were not measured (all time points)
* Memory B cell analysis is missing for T3
* IgA in serum and saliva are missing for T3

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24963638

http://www.ncbi.nlm.nih.gov/pubmed/26100925

http://www.ncbi.nlm.nih.gov/pubmed/26458006

http://www.ncbi.nlm.nih.gov/pubmed/27817957