Clinical trial results:
A Phase IIIB, Open Label, Multi-Center Extension study of V72_28 to assess antibody persistence, and the safety and tolerability of a booster dose after the completion of the vaccination course in study V72_28.

Summary

EudraCT number	2012-000657-30
Trial protocol	HU ES
Global end of trial date	17 November 2015

Results information

Result version number	v1 (current)
This version publication date	01 December 2016
First version publication date	01 December 2016

Trial information

Trial identification

Sponsor protocol code	V72_28E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01894919
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics
Sponsor organisation address	Via Fiorentina 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 September 2015
Global end of trial reached?	Yes
Global end of trial date	17 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the antibody persistence 24 to 36 months after the completion of the vaccination course, in subjects who participated in the
V72_28 (2010-021528-81) study in Groups I to IV.

Protection of trial subjects:

This clinical study was designed, implemented and reported in accordance with the International conference of Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice, with applicable local regulations, Novartis codes on protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki (European Council 2001, US Code of Federal Regulations, ICH 1997).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 June 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 562
Country: Number of subjects enrolled	Hungary: 289
Worldwide total number of subjects	851
EEA total number of subjects	851

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)	815
Adolescents (12-17 years)	36
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 9 study sites in Hungary and 8 study sites in Spain.

Pre-assignment

Screening details:

All enrolled subjects were included in the study.

Period 1

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

Blinding implementation details:

The trial was designed as an open-label study. Subjects were assigned to one of the vaccination group/subgroup based on the group specific inclusion criteria, using a standard web-randomization procedure.

Arms

Are arms mutually exclusive?	Yes
Arm title	2H3H511_V

Arm description:

In the parent study V72_28, subjects had received three primary doses and one booster dose of Bexsero® vaccine, at 2.5, 3.5, 5 months of age, and at 11 months of age, respectively. The subjects in this group received a fifth dose of Bexsero® vaccine in the present study.

Arm type	Experimental
Investigational medicinal product name	Bexsero®
Investigational medicinal product code	rMenB+OMV NZ
Other name	Meningococcal Recombinant serogroup B with Outer Membrane Vesicles (OMV) Vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL

Arm title	2H3H511_NV

Arm description:

In the parent study V72_28, subjects had received three primary doses and one booster dose of Bexsero® vaccine, at 2.5, 3.5, 5 months of age, and at 11 months of age, respectively. These subjects were evaluated only for persistence.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	3H5_11_V

Arm description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 3.5, 5, and 11 months of age, respectively. These subjects received a fourth dose of Bexsero® vaccine in the present study.

Arm type	Experimental

Investigational medicinal product name	Bexsero®
Investigational medicinal product code	rMenB+OMV NZ
Other name	Meningococcal Recombinant serogroup B with Outer Membrane Vesicles (OMV) Vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL

Arm title	3H5_11_NV

Arm description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 3.5, 5, and 11 months of age, respectively. These subjects were evaluated only for persistence.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	68_11_V

Arm description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 6, 8, and 11 months of age, respectively. These subjects received a fourth dose of Bexsero® vaccine in the present study.

Arm type	Experimental
Investigational medicinal product name	Bexsero®
Investigational medicinal product code	rMenB+OMV NZ
Other name	Meningococcal Recombinant serogroup B with Outer Membrane Vesicles (OMV) Vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL

Arm title	68_11_NV

Arm description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 6, 8, and 11 months of age, respectively. These subjects were evaluated only for persistence.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	02_2_5_V

Arm description:

In the parent study V72_28, subjects had received two catch-up doses of Bexsero® vaccine, two months apart. These subjects received a third dose of Bexsero® vaccine in the present study.

Arm type	Experimental
Investigational medicinal product name	Bexsero®
Investigational medicinal product code	rMenB+OMV NZ
Other name	Meningococcal Recombinant serogroup B with Outer Membrane Vesicles (OMV) Vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL

Arm title	02_2_5_NV

Arm description:

In the parent study V72_28, subjects received two catch-up doses of Bexsero® vaccine, two months apart. These subjects were evaluated only for persistence.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	02_6_10_V

Arm description:

In the parent study V72_28, subjects had received two catch-up doses of Bexsero® vaccine, two months apart. These subjects received a third dose of Bexsero® vaccine in the present study.

Arm type	Experimental
Investigational medicinal product name	Bexsero®
Investigational medicinal product code	rMenB+OMV NZ
Other name	Meningococcal Recombinant serogroup B with Outer Membrane Vesicles (OMV) Vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL

Arm title	02_6_10_NV

Arm description:

In the parent study V72_28, subjects had received two catch-up doses of Bexsero® vaccine, two months apart. These subjects were evaluated only for persistence.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	NAIVE_123

Arm description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Arm type	Experimental
Investigational medicinal product name	Bexsero®
Investigational medicinal product code	rMenB+OMV NZ
Other name	Meningococcal Recombinant serogroup B with Outer Membrane Vesicles (OMV) Vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL

Arm title	NAIVE_4A

Arm description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Arm type	Experimental
Investigational medicinal product name	Bexsero®
Investigational medicinal product code	rMenB+OMV NZ
Other name	Meningococcal Recombinant serogroup B with Outer Membrane Vesicles (OMV) Vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL

Arm title	NAIVE_4B

Arm description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Arm type	Experimental

Investigational medicinal product name	Bexsero®
Investigational medicinal product code	rMenB+OMV NZ
Other name	Meningococcal Recombinant serogroup B with Outer Membrane Vesicles (OMV) Vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL

Number of subjects in period 1	2H3H511_V	2H3H511_NV	3H5_11_V
Started	98	47	89
Completed	96	47	89
Not completed	2	0	0
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	-	-	-
Unspecified	1	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	3H5_11_NV	68_11_V	68_11_NV
Started	43	81	39
Completed	43	78	39
Not completed	0	3	0
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	-	-	-
Unspecified	-	-	-
Lost to follow-up	-	2	-

Number of subjects in period 1	02_2_5_V	02_2_5_NV	02_6_10_V
Started	32	36	91
Completed	32	36	91
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Unspecified	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	02_6_10_NV	NAIVE_123	NAIVE_4A
Started	90	100	55
Completed	89	98	55
Not completed	1	2	0
Consent withdrawn by subject	1	1	-
Adverse event, non-fatal	-	1	-

Unspecified	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	NAIVE_4B
Started	50
Completed	50
Not completed	0
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Unspecified	-
Lost to follow-up	-

Baseline characteristics

Reporting groups

Reporting group title	2H3H511_V

Reporting group description:

In the parent study V72_28, subjects had received three primary doses and one booster dose of Bexsero® vaccine, at 2.5, 3.5, 5 months of age, and at 11 months of age, respectively. The subjects in this group received a fifth dose of Bexsero® vaccine in the present study.

Reporting group title	2H3H511_NV

Reporting group description:

In the parent study V72_28, subjects had received three primary doses and one booster dose of Bexsero® vaccine, at 2.5, 3.5, 5 months of age, and at 11 months of age, respectively. These subjects were evaluated only for persistence.

Reporting group title	3H5_11_V

Reporting group description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 3.5, 5, and 11 months of age, respectively. These subjects received a fourth dose of Bexsero® vaccine in the present study.

Reporting group title	3H5_11_NV

Reporting group description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 3.5, 5, and 11 months of age, respectively. These subjects were evaluated only for persistence.

Reporting group title	68_11_V

Reporting group description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 6, 8, and 11 months of age, respectively. These subjects received a fourth dose of Bexsero® vaccine in the present study.

Reporting group title	68_11_NV

Reporting group description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 6, 8, and 11 months of age, respectively. These subjects were evaluated only for persistence.

Reporting group title	02_2_5_V

Reporting group description:

In the parent study V72_28, subjects had received two catch-up doses of Bexsero® vaccine, two months apart. These subjects received a third dose of Bexsero® vaccine in the present study.

Reporting group title	02_2_5_NV

Reporting group description:

In the parent study V72_28, subjects received two catch-up doses of Bexsero® vaccine, two months apart. These subjects were evaluated only for persistence.

Reporting group title	02_6_10_V

Reporting group description:

In the parent study V72_28, subjects had received two catch-up doses of Bexsero® vaccine, two months apart. These subjects received a third dose of Bexsero® vaccine in the present study.

Reporting group title	02_6_10_NV

Reporting group description:

In the parent study V72_28, subjects had received two catch-up doses of Bexsero® vaccine, two months apart. These subjects were evaluated only for persistence.

Reporting group title	NAIVE_123

Reporting group description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Reporting group title	NAIVE_4A

Reporting group description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Reporting group title	NAIVE_4B

Reporting group description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Reporting group values	2H3H511_V	2H3H511_NV	3H5_11_V
Number of subjects	98	47	89
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)	98	47	89
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	3.1	3	3.1
standard deviation	± 0.2	± 0.18	± 0.23
Gender categorical Units: Subjects			
Female	44	27	48
Male	54	20	41

Reporting group values	3H5_11_NV	68_11_V	68_11_NV
Number of subjects	43	81	39
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)	43	81	39
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	3.1	3.2	3.2
standard deviation	± 0.22	± 0.29	± 0.26

Gender categorical Units: Subjects			
Female	22	35	23
Male	21	46	16

Reporting group values	02_2_5_V	02_2_5_NV	02_6_10_V
Number of subjects	32	36	91
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)	32	36	74
Adolescents (12-17 years)	0	0	17
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	6.5	6.7	10.4
standard deviation	± 1.15	± 1.16	± 1.43
Gender categorical Units: Subjects			
Female	19	15	44
Male	13	21	47

Reporting group values	02_6_10_NV	NAIVE_123	NAIVE_4A
Number of subjects	90	100	55
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)	73	100	55
Adolescents (12-17 years)	17	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	10.4	3.4	5.8
standard deviation	± 1.44	± 0.29	± 1.12
Gender categorical Units: Subjects			
Female	46	46	26
Male	44	54	29

Reporting group values	NAIVE_4B	Total	
Number of subjects	50	851	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	48	815	
Adolescents (12-17 years)	2	36	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	9.7		
standard deviation	± 1.38	-	
Gender categorical Units: Subjects			
Female	27	422	
Male	23	429	

Subject analysis sets

Subject analysis set title	2H3H511
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Combined 2H3H511_V group + 2H3H511_NV group - subjects who received three primary doses and one booster dose of Bexsero® vaccine, at 2.5, 3.5, 5, and 11 months of age, respectively, in the parent study V72_28.

Subject analysis set title	3H5_11
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Combined 3H5_11_V group + 3H5_11_NV group - subjects who received two primary doses and one booster dose of Bexsero® vaccine, at 3.5, 5, and 11 months of age, respectively, in the parent study V72_28.

Subject analysis set title	68_11
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Combined 68_11_V group + 68_11_NV group - subjects who received two primary doses and one booster dose of Bexsero® vaccine, at 6, 8, and 11 months of age, respectively, in the parent study V72_28.

Subject analysis set title	02_2_5
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Combined 02_2_5_V group + 02_2_5_NV group - subjects who received two catch-up doses of Bexsero® vaccine two months apart, at 2 and 5 years of age, respectively, in the parent study V72_28.

Subject analysis set title	02_6_10
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Combined 02_6_10_V group + 02_6_10_NV group - subjects who received two catch-up doses of Bexsero® vaccine two months apart, at 6 and 10 years of age, respectively, in the parent study

Reporting group values	2H3H511	3H5_11	68_11
Number of subjects	140	131	119
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)	140	131	119
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	3	3.1	3.2
standard deviation	± 0.19	± 0.23	± 0.28
Gender categorical			
Units: Subjects			
Female	67	70	58
Male	73	61	61

Reporting group values	02_2_5	02_6_10	
Number of subjects	68	179	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	68	146	
Adolescents (12-17 years)	0	33	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	6.6	10.4	
standard deviation	± 1.15	± 1.43	
Gender categorical			
Units: Subjects			
Female	34	89	
Male	34	90	

End points

End points reporting groups

Reporting group title	2H3H511_V

Reporting group description:

In the parent study V72_28, subjects had received three primary doses and one booster dose of Bexsero® vaccine, at 2.5, 3.5, 5 months of age, and at 11 months of age, respectively. The subjects in this group received a fifth dose of Bexsero® vaccine in the present study.

Reporting group title	2H3H511_NV

Reporting group description:

In the parent study V72_28, subjects had received three primary doses and one booster dose of Bexsero® vaccine, at 2.5, 3.5, 5 months of age, and at 11 months of age, respectively. These subjects were evaluated only for persistence.

Reporting group title	3H5_11_V

Reporting group description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 3.5, 5, and 11 months of age, respectively. These subjects received a fourth dose of Bexsero® vaccine in the present study.

Reporting group title	3H5_11_NV

Reporting group description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 3.5, 5, and 11 months of age, respectively. These subjects were evaluated only for persistence.

Reporting group title	68_11_V

Reporting group description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 6, 8, and 11 months of age, respectively. These subjects received a fourth dose of Bexsero® vaccine in the present study.

Reporting group title	68_11_NV

Reporting group description:

In the parent study V72_28, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 6, 8, and 11 months of age, respectively. These subjects were evaluated only for persistence.

Reporting group title	02_2_5_V

Reporting group description:

In the parent study V72_28, subjects had received two catch-up doses of Bexsero® vaccine, two months apart. These subjects received a third dose of Bexsero® vaccine in the present study.

Reporting group title	02_2_5_NV

Reporting group description:

In the parent study V72_28, subjects received two catch-up doses of Bexsero® vaccine, two months apart. These subjects were evaluated only for persistence.

Reporting group title	02_6_10_V

Reporting group description:

In the parent study V72_28, subjects had received two catch-up doses of Bexsero® vaccine, two months apart. These subjects received a third dose of Bexsero® vaccine in the present study.

Reporting group title	02_6_10_NV

Reporting group description:

In the parent study V72_28, subjects had received two catch-up doses of Bexsero® vaccine, two months apart. These subjects were evaluated only for persistence.

Reporting group title	NAIVE_123

Reporting group description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Reporting group title	NAIVE_4A

Reporting group description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Reporting group title	NAIVE_4B

Reporting group description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Subject analysis set title	2H3H511
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Combined 2H3H511_V group + 2H3H511_NV group - subjects who received three primary doses and one booster dose of Bexsero® vaccine, at 2.5, 3.5, 5, and 11 months of age, respectively, in the parent study V72_28.

Subject analysis set title	3H5_11
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Combined 3H5_11_V group + 3H5_11_NV group - subjects who received two primary doses and one booster dose of Bexsero® vaccine, at 3.5, 5, and 11 months of age, respectively, in the parent study V72_28.

Subject analysis set title	68_11
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Combined 68_11_V group + 68_11_NV group - subjects who received two primary doses and one booster dose of Bexsero® vaccine, at 6, 8, and 11 months of age, respectively, in the parent study V72_28.

Subject analysis set title	02_2_5
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Combined 02_2_5_V group + 02_2_5_NV group - subjects who received two catch-up doses of Bexsero® vaccine two months apart, at 2 and 5 years of age, respectively, in the parent study V72_28.

Subject analysis set title	02_6_10
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Combined 02_6_10_V group + 02_6_10_NV group - subjects who received two catch-up doses of Bexsero® vaccine two months apart, at 6 and 10 years of age, respectively, in the parent study V72_28.

Primary: 1. Percentage of subjects with human serum bactericidal activity titers (hSBA) ≥ 4 or ≥ 5 against Neisseria meningitidis (N. meningitidis) serogroup B strains

End point title	1. Percentage of subjects with human serum bactericidal activity titers (hSBA) ≥ 4 or ≥ 5 against Neisseria meningitidis (N. meningitidis) serogroup B strains[1][2]

End point description:

The antibody persistence in subjects, 24 to 36 months after completion of Bexsero® vaccination course in the parent study according to different schedules, is presented in terms of the percentage of subjects in each vaccine group, with hSBA titers ≥ 4 for what concerns the H44/76, 5/99 and NZ98/254 strains, and hSBA titers ≥ 5 for M10713 strain, alongside with the corresponding antibody responses in age-matched vaccine-naïve subjects at Baseline.
The functional bactericidal antibodies directed against serogroup B meningococcal were assessed by the Serum Bactericidal Assay (SBA) using human serum as the source of exogenous complement (hSBA).
The analysis was performed on the Full analysis set (FAS)-persistence population, which included all subjects in the Enrolled Set who provided an evaluable serum sample at Visit 1.

End point type	Primary

End point timeframe:

24 or 36 months after booster dose in the parent study; Baseline for vaccine-naïve subjects

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	NAIVE_123	NAIVE_4A	NAIVE_4B	2H3H511
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	100	55	50	140
Units: Percentage				
number (confidence interval 95%)				
H44/76 (N=100;55;50;140;131;119;67;178)	38 (28.5 to 48.3)	27 (16.1 to 41)	20 (10 to 33.7)	51 (42.8 to 60)
5/99 (N=100;55;50;140;131;119;67;179)	3 (0.6 to 8.5)	4 (0.44 to 12.5)	8 (2.2 to 19.2)	84 (77.2 to 89.9)
NZ98/254 (N=100;55;50;140;131;119;68;179)	2 (0.24 to 7)	7 (2 to 17.6)	6 (1.3 to 16.5)	45 (36.6 to 53.6)
M10713 (N=93;53;49;127;111;109;65;173)	37 (26.8 to 47.2)	38 (24.8 to 52.1)	55 (40.2 to 69.3)	31 (22.8 to 39.5)

End point values	3H5_11	68_11	02_2_5	02_6_10
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	131	119	68	179
Units: Percentage				
number (confidence interval 95%)				
H44/76 (N=100;55;50;140;131;119;67;178)	53 (43.8 to 61.5)	61 (52 to 70.1)	52 (39.7 to 64.6)	58 (50.3 to 65.2)
5/99 (N=100;55;50;140;131;119;67;179)	88 (80.9 to 92.9)	93 (87.2 to 97.1)	79 (67.4 to 88.1)	85 (79.4 to 90.3)
NZ98/254 (N=100;55;50;140;131;119;68;179)	38 (29.8 to 47.1)	56 (46.9 to 65.4)	29 (19 to 41.7)	50 (42.2 to 57.3)
M10713 (N=93;53;49;127;111;109;65;173)	36 (27.1 to 45.7)	39 (29.4 to 48.3)	34 (22.6 to 46.6)	61 (53 to 68)

Statistical analyses

No statistical analyses for this end point

Primary: 2. Percentage of subjects with hSBA titers ≥ 8 against N.meningitidis serogroup B strains

End point title	2. Percentage of subjects with hSBA titers ≥ 8 against N.meningitidis serogroup B strains[3][4]

End point description:

The antibody persistence in subjects, 24 to 36 months after completion of Bexsero® vaccination course in the parent study according to different schedules, is presented in terms of the percentage of subjects in each vaccine group with hSBA titers ≥ 8, alongside with the corresponding antibody responses in age-matched vaccine-naïve subjects at Baseline.

The analysis was performed on the FAS-Antibody persistence population, which included all subjects in the Enrolled Set who provided an evaluable serum sample at Visit 1.

End point type	Primary

End point timeframe:

24-36 months after booster dose in the parent study; Baseline for vaccine-naïve subjects

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	NAIVE_123	NAIVE_4A	NAIVE_4B	2H3H511
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	100	55	50	140
Units: Percentage				
number (confidence interval 95%)				
H44/76 (N=100;55;50;140;131;119;67;178)	18 (11 to 26.9)	16 (7.8 to 28.8)	10 (3.3 to 21.8)	28 (20.6 to 36.1)
5/99 (N=100;55;50;140;131;119;67;179)	2 (0.24 to 7)	4 (0.44 to 12.5)	6 (1.3 to 16.5)	80 (72.4 to 86.3)
NZ98/254 (N=100;55;50;140;131;119;68;179)	0 (0 to 3.6)	2 (0.05 to 9.7)	0 (0 to 7.1)	21 (14.9 to 29.2)
M10713 (N=93;53;49;127;111;109;65;173)	26 (17.3 to 35.9)	36 (23.1 to 50.2)	49 (34.4 to 63.7)	24 (16.5 to 32)

End point values	3H5_11	68_11	02_2_5	02_6_10
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	131	119	68	179
Units: Percentage				
number (confidence interval 95%)				
H44/76 (N=100;55;50;140;131;119;67;178)	26 (18.7 to 34.3)	32 (23.7 to 41.1)	24 (14.3 to 35.9)	34 (26.8 to 41.2)
5/99 (N=100;55;50;140;131;119;67;179)	82 (74.8 to 88.5)	89 (82 to 94.1)	73 (60.9 to 83.2)	66 (59.1 to 73.3)
NZ98/254 (N=100;55;50;140;131;119;68;179)	18 (12.1 to 26)	29 (20.7 to 37.6)	15 (7.3 to 25.4)	28 (21.5 to 35.1)
M10713 (N=93;53;49;127;111;109;65;173)	22 (14.4 to 30.4)	28 (20.2 to 37.9)	31 (19.9 to 43.4)	54 (46 to 61.4)

Statistical analyses

No statistical analyses for this end point

Primary: 3. The hSBA geometric mean titers (GMTs) against N.meningitidis serogroup B strains

End point title	3. The hSBA geometric mean titers (GMTs) against N.

	meningitidis serogroup B strains[5][6]

End point description:

The hSBA antibody titers in subjects, 24 to 36 months after completion of Bexsero® vaccination course according to different schedules in the parent study, are presented in terms of vaccine-group-specific GMTs, alongside with the corresponding antibody responses in age-matched vaccine-naïve subjects at Baseline.
The analysis was performed on the FAS-Antibody persistence population, which included all subjects in the Enrolled Set who provided an evaluable serum sample at Visit 1.

End point type	Primary

End point timeframe:

24-36 months after booster dose in the parent study; Baseline for vaccine-naïve subjects

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.
[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	NAIVE_123	NAIVE_4A	NAIVE_4B	2H3H511
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	100	55	50	140
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (N=100;55;50;140;131;119;67;178)	2.79 (2.25 to 3.45)	2.33 (1.77 to 3.07)	1.93 (1.39 to 2.68)	4.17 (3.4 to 5.13)
5/99 (N=100;55;50;140;131;119;67;179)	1.15 (1.03 to 1.29)	1.2 (0.96 to 1.51)	1.38 (1.1 to 1.73)	44 (32 to 60)
NZ98/254 (N=100;55;50;140;131;119;68;179)	1.14 (1.06 to 1.22)	1.37 (1.17 to 1.61)	1.22 (1.06 to 1.41)	3.48 (2.78 to 4.36)
M10713 (N=93;53;49;127;111;109;65;173)	3.3 (2.52 to 4.32)	4.26 (2.61 to 6.97)	6.95 (4.18 to 12)	2.77 (2.06 to 3.71)

End point values	3H5_11	68_11	02_2_5	02_6_10
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	131	119	68	179
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (N=100;55;50;140;131;119;67;178)	4.48 (3.6 to 5.57)	5.62 (4.48 to 7.04)	3.97 (2.99 to 5.28)	5.75 (4.78 to 6.91)
5/99 (N=100;55;50;140;131;119;67;179)	52 (37 to 72)	83 (58 to 117)	21 (14 to 33)	21 (16 to 28)
NZ98/254 (N=100;55;50;140;131;119;68;179)	2.98 (2.35 to 3.78)	4.86 (3.8 to 6.22)	2.81 (2.07 to 3.82)	4.57 (3.74 to 5.59)
M10713 (N=93;53;49;127;111;109;65;173)	3.03 (2.2 to 4.16)	3.17 (2.3 to 4.38)	3.53 (2.38 to 5.25)	7.82 (6.04 to 10)

Statistical analyses

No statistical analyses for this end point

Primary: 4. The geometric mean ratio (GMR) of hSBA GMTs against N. meningitidis serogroup B strains

End point title	4. The geometric mean ratio (GMR) of hSBA GMTs against N. meningitidis serogroup B strains[7]

End point description:

The within-subjects GMR of GMTs at 24 to 36 months versus one month after completion of Bexsero® vaccination course according to different schedules vaccination in the parent study are reported.
The analysis was performed on the FAS-Antibody persistence population, which included all subjects in the Enrolled Set who provided an evaluable serum sample at Visit 1.

End point type	Primary

End point timeframe:

Day 1 in the present study over one month after the completion of the vaccination course in the parent study

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	2H3H511	3H5_11	68_11	02_2_5
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	137	130	118	68
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 (N=137;129;118;67;173)	0.029 (0.023 to 0.036)	0.022 (0.017 to 0.028)	0.03 (0.023 to 0.038)	0.028 (0.021 to 0.038)
5/99 (N=136;130;118;66;176)	0.023 (0.017 to 0.03)	0.031 (0.023 to 0.041)	0.054 (0.04 to 0.073)	0.045 (0.031 to 0.066)
NZ98/254 (N=136;129;116;68;174)	0.059 (0.047 to 0.074)	0.038 (0.03 to 0.048)	0.07 (0.055 to 0.09)	0.061 (0.044 to 0.083)
M10713 (N=105;84;78;61;160)	0.19 (0.13 to 0.28)	0.16 (0.11 to 0.25)	0.19 (0.12 to 0.29)	0.17 (0.11 to 0.28)

End point values	02_6_10			
Subject group type	Subject analysis set			
Number of subjects analysed	176			
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 (N=137;129;118;67;173)	0.042 (0.035 to 0.052)			
5/99 (N=136;130;118;66;176)	0.049 (0.038 to 0.063)			
NZ98/254 (N=136;129;116;68;174)	0.095 (0.077 to 0.12)			
M10713 (N=105;84;78;61;160)	0.24 (0.17 to 0.32)			

Statistical analyses

No statistical analyses for this end point

Primary: 5. The GMR of hSBA GMTs against N. meningitidis serogroup B strains

End point title	5. The GMR of hSBA GMTs against N. meningitidis serogroup B strains[8]

End point description:

The within-subjects GMR of GMTs, at 24 to 36 months versus Visit 1 in the vaccination course according to different schedules vaccination in the parent study, are reported.
The analysis was performed on the FAS-Antibody persistence population, which included all subjects in the Enrolled Set who provided an evaluable serum sample at Visit 1.

End point type	Primary

End point timeframe:

Day 1 in the present study over Visit 1 in the vaccination course of the parent study

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	02_2_5	02_6_10		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67	177		
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 (N=67;177)	1.88 (1.32 to 2.69)	2.94 (2.33 to 3.71)		
5/99 (N=67;177)	20 (12 to 32)	14 (10 to 20)		
NZ98/254 (N=67;177)	2.48 (1.76 to 3.49)	3.06 (2.44 to 3.83)		
M10713 (N=56;163)	0.89 (0.49 to 1.61)	0.94 (0.64 to 1.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Number of subjects (35 months to 7 years of age) reporting solicited local and systemic adverse events (AEs)

End point title	6. Number of subjects (35 months to 7 years of age) reporting solicited local and systemic adverse events (AEs)[9]

End point description:

The number of subjects (35 months to 7 years of age) with solicited local and systemic AEs after receiving the Bexsero® booster vaccine in the present study.
The analysis was performed on the Solicited safety set, which included all subjects in the Exposed Set

with solicited adverse event data.

End point type	Secondary

End point timeframe:

From Day 1 (6 hr) through Day 7 after vaccination

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	2H3H511_V	3H5_11_V	68_11_V	02_2_5_V
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	89	80	32
Units: Subjects				
Any local AEs	87	81	73	31
Erythema	60	63	42	22
Induration	48	48	33	15
Swelling	49	50	37	20
Tenderness	84	80	71	31
Any systemic AEs	66	63	54	18
Change in eating habits	31	32	30	5
Diarrhea	4	8	5	0
Irritability	54	52	46	9
Persistent Crying	31	24	25	4
Rash	13	1	3	5
Sleepiness	28	23	26	5
Vomiting	5	5	2	1
Fever (>38.0° C)	17	18	11	2
Medically-Attended Fever	1	0	2	0
Prevention of Pain and/or Fever	23	14	15	1
Treatment of Pain and/or Fever	38	39	41	13

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Number of newly recruited subjects (aged 35 months to 7 years) reporting solicited local and systemic AEs

End point title	7. Number of newly recruited subjects (aged 35 months to 7 years) reporting solicited local and systemic AEs[10]

End point description:

The number of newly recruited subjects (aged 35 months to 7 years) reporting solicited local and systemic adverse events after receiving two catch-up doses of Bexsero® vaccine in the present study. The analysis was performed on the Solicited safety set, which included all subjects in the Exposed Set with solicited adverse event data.

End point type	Secondary

End point timeframe:

From Day 1 (6 hr) through Day 7 after each vaccination

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	NAIVE_123	NAIVE_4A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	55		
Units: Subjects				
Any local AEs (1st vacc.) (N=100;55)	88	55		
Erythema (1st vacc.) (N=100;55)	54	28		
Induration (1st vacc.) (N=100;55)	38	17		
Swelling (1st vacc.) (N=100;55)	40	24		
Tenderness (1st vacc.) (N=100;55)	87	55		
Any systemic AEs (1st vacc.) (N=100;55)	64	24		
Change in Eating Habits (1st vacc.) (N=100;55)	31	5		
Diarrhea (1st vacc.) (N=100;55)	4	3		
Irritability (1st vacc.) (N=100;55)	40	16		
Persistent Crying (1st vacc.) (N=100;55)	15	4		
Rash (1st vacc.) (N=100;55)	5	3		
Sleepiness (1st vacc.) (N=100;55)	18	9		
Vomiting (1st vacc.) (N=100;55)	7	2		
Fever (>38.0° C) (1st vacc.) (N=100;55)	15	2		
Medically-Attended Fever (1st vacc.) (N=100;55)	1	0		
Prevention of Pain/Fever (1st vacc.) (N=100;55)	18	3		
Treatment of Pain/Fever (1st vacc.) (N=99;55)	41	22		
Any local AEs (2nd vacc.) (N=99;55)	79	51		
Erythema (2nd vacc.) (N=99;55)	44	32		
Induration (2nd vacc.) (N=99;55)	29	22		
Swelling (2nd vacc.) (N=99;55)	32	25		
Tenderness (2nd vacc.) (N=99;55)	77	51		
Any systemic AEs (2nd vacc.) (N=99;55)	46	18		
Change in Eating Habits (2nd vacc.) (N=99;55)	15	9		
Diarrhea (2nd vacc.) (N=99;55)	2	3		
Irritability (2nd vacc.) (N=99;55)	25	11		
Persistent Crying (2nd vacc.) (N=99;55)	13	6		
Rash (2nd vacc.) (N=99;55)	2	1		
Sleepiness (2nd vacc.) (N=99;55)	12	5		
Vomiting (2nd vacc.) (N=99;55)	4	2		
Fever (>38.0° C) (2nd vacc.) (N=99;55)	12	3		
Medically-Attended Fever (2nd vacc.) (N=99;55)	0	1		
Prevention of Pain/Fever (2nd vacc.) (N=99;55)	21	4		

Treatment of Pain/Fever (2nd vacc.) (N=99;55)	30	13		

Statistical analyses

No statistical analyses for this end point

Secondary: 8. Number of subjects (8 to 12 years of age) reporting solicited local and systemic AEs

End point title	8. Number of subjects (8 to 12 years of age) reporting solicited local and systemic AEs[11]

End point description:

The number of subjects (8 to 12 years of age) with solicited local and systemic adverse events after receiving a booster dose of Bexsero® vaccine in the present study.
The analysis was performed on the Solicited safety set, which included all subjects in the Exposed Set with solicited adverse event data.

End point type	Secondary

End point timeframe:

From Day 1 (6 hr) through Day 7 after vaccination

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	02_6_10_V			
Subject group type	Reporting group			
Number of subjects analysed	91			
Units: Subjects				
Any local AEs (N=91)	85			
Erythema (N=91)	57			
Induration (N=91)	44			
Swelling (N=91)	52			
Pain (N=90)	84			
Any systemic AEs (N=91)	57			
Arthralgia (N=90)	18			
Chills (N=90)	23			
Headache (N=90)	27			
Malaise (N=90)	35			
Myalgia (N=90)	24			
Nausea (N=90)	12			
Rash (N=90)	10			
Fever (>38.0° C) (N=91)	10			
Medically-Attended Fever (N=91)	0			
Prevention of Pain and/or Fever (N=90)	12			
Treatment of Pain and/or Fever (N=91)	47			

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Number of newly recruited naïve subjects (aged 8 to 12 years of age) reporting solicited local and systemic AEs

End point title	9. Number of newly recruited naïve subjects (aged 8 to 12 years of age) reporting solicited local and systemic AEs[12]

End point description:

The number of newly recruited naïve subjects (aged 8 to 12 years of age) reporting solicited local and systemic AEs after receiving two catch-up doses of Bexsero® vaccine in the present study.
The analysis was performed on the Solicited safety set, which included all subjects in the Exposed Set with solicited adverse event data.

End point type	Secondary

End point timeframe:

From Day 1 (6 hr) through Day 7 after each vaccination

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	NAIVE_4B			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: Subjects				
Any local AEs (1st vacc.) (N=50)	49			
Erythema (1st vacc.) (N=50)	31			
Induration (1st vacc.) (N=50)	19			
Swelling (1st vacc.) (N=50)	29			
Pain (1st vacc.) (N=49)	47			
Any systemic AEs (1st vacc.) (N=50)	24			
Arthralgia (1st vacc.) (N=49)	6			
Chills (1st vacc.) (N=49)	4			
Headache (1st vacc.) (N=49)	15			
Malaise (1st vacc.) (N=49)	7			
Myalgia (1st vacc.) (N=49)	12			
Nausea (1st vacc.) (N=49)	5			
Rash (1st vacc.) (N=50)	1			
Fever (>38.0° C) (1st vacc.) (N=50)	3			
Medically-Attended Fever (1st vacc.) (N=50)	0			
Prevention of Pain and/or Fever (1st vacc.) (N=50)	2			
Treatment of Pain and/or Fever (1st vacc.) (N=50)	21			

Any local AEs (2nd vacc.) (N=50)	43			
Erythema (2nd vacc.) (N=50)	21			
Induration (2nd vacc.) (N=50)	17			
Swelling (2nd vacc.) (N=50)	21			
Pain (2nd vacc.) (N=50)	41			
Any systemic AEs (2nd vacc.) (N=50)	25			
Arthralgia (2nd vacc.) (N=50)	3			
Chills (2nd vacc.) (N=50)	5			
Headache (2nd vacc.) (N=50)	10			
Malaise (2nd vacc.) (N=50)	13			
Myalgia (2nd vacc.) (N=50)	8			
Nausea (2nd vacc.) (N=50)	4			
Rash (2nd vacc.) (N=50)	3			
Fever (>38.0° C) (2nd vacc.) (N=50)	1			
Medically-Attended Fever (2nd vacc.) (N=50)	0			
Prevention of Pain and/or Fever (2nd vacc.) (N=50)	3			
Treatment of Pain and/or Fever (2nd vacc.) (N=50)	12			

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Percentage of subjects with hSBA titers ≥ 4 or ≥ 5 against N.meningitidis serogroup B strains

End point title	10. Percentage of subjects with hSBA titers ≥ 4 or ≥ 5 against N.meningitidis serogroup B strains[13]

End point description:

The percentage of subjects with hSBA titers ≥ 4 against H44/76, 5/99 and NZ98/254 strains, and with hSBA titers ≥ 5 against M10713 strain, after receiving the Bexsero® booster vaccination in the present study (24 to 36 months after completion of vaccination course according to different schedules in the parent study), alongside with the corresponding response after the first dose of Bexsero® vaccine in age-matched vaccine-naïve subjects.
The analysis was performed on the FAS-Booster response population, which included all subjects in the Enrolled Set who received a study vaccination, provided an evaluable serum sample at Visit 2 (one month after the booster dose administration) and received all scheduled vaccinations in the parent study V72_28 (excluding naïve groups).

End point type	Secondary

End point timeframe:

At 24-36 months - Visit 1 (pre-vacc.) and one month after booster vaccination - Day 31 (post-vacc.)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	2H3H511_V	3H5_11_V	68_11_V	02_2_5_V
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	86	76	32
Units: Percentage				
number (confidence interval 95%)				
H44/76 (pre-vacc.) (N=92;86;75;31;91;96;55;50)	48 (37.3 to 58.5)	51 (40.1 to 62.1)	64 (52.1 to 74.8)	39 (21.8 to 57.8)
H44/76 (post-vacc.) (N=96;86;75;32;91;96;55;50)	99 (94.3 to 99.97)	100 (95.8 to 100)	100 (95.2 to 100)	97 (83.8 to 99.92)
5/99 (pre-vacc.) (N=92;87;76;31;91;96;55;50)	84 (74.5 to 90.6)	91 (82.7 to 95.9)	95 (87.1 to 98.5)	74 (55.4 to 88.1)
5/99 (post-vacc.) (N=96;87;76;32;91;96;55;50)	99 (94.3 to 99.97)	99 (93.8 to 99.97)	97 (90.8 to 99.68)	100 (89.1 to 100)
NZ98/254 (pre-vacc.) (N=92;86;75;32;91;96;54;50)	45 (34.2 to 55.3)	42 (31.3 to 53)	52 (40.2 to 63.7)	25 (11.5 to 43.4)
NZ98/254 (post-vacc.) (N=96;86;75;32;91;96;54;50)	99 (94.3 to 99.97)	100 (95.8 to 100)	100 (95.2 to 100)	100 (89.1 to 100)
M10713 (pre-vacc.) (N=78;68;65;29;87;84;49;46)	36 (25.3 to 47.6)	35 (24.1 to 47.8)	45 (32.3 to 57.5)	21 (8 to 39.7)
M10713 (post-vacc.) (N=88;79;67;30;89;88;51;47)	70 (59.8 to 79.7)	81 (70.6 to 89)	97 (89.6 to 99.64)	93 (77.9 to 99.2)

End point values	02_6_10_V	NAIVE_123	NAIVE_4A	NAIVE_4B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	91	96	55	50
Units: Percentage				
number (confidence interval 95%)				
H44/76 (pre-vacc.) (N=92;86;75;31;91;96;55;50)	59 (48.5 to 69.5)	39 (28.8 to 49)	27 (16.1 to 41)	20 (10 to 33.7)
H44/76 (post-vacc.) (N=96;86;75;32;91;96;55;50)	99 (94 to 99.97)	95 (88.3 to 98.3)	91 (80 to 97)	80 (66.3 to 90)
5/99 (pre-vacc.) (N=92;87;76;31;91;96;55;50)	86 (76.8 to 92.2)	3 (0.6 to 8.9)	4 (0.44 to 12.5)	8 (2.2 to 19.2)
5/99 (post-vacc.) (N=96;87;76;32;91;96;55;50)	100 (96 to 100)	88 (79.2 to 93.4)	93 (82.4 to 98)	80 (66.3 to 90)
NZ98/254 (pre-vacc.) (N=92;86;75;32;91;96;54;50)	47 (36.7 to 58)	2 (0.25 to 7.3)	7 (2.1 to 17.9)	6 (1.3 to 16.5)
NZ98/254 (post-vacc.) (N=96;86;75;32;91;96;54;50)	100 (96 to 100)	78 (68.5 to 85.9)	85 (72.9 to 93.4)	70 (55.4 to 82.1)
M10713 (pre-vacc.) (N=78;68;65;29;87;84;49;46)	63 (52.2 to 73.3)	39 (28.8 to 50.5)	41 (27 to 55.8)	59 (43.2 to 73)
M10713 (post-vacc.) (N=88;79;67;30;89;88;51;47)	96 (88.9 to 98.8)	47 (35.9 to 57.5)	59 (44.2 to 72.4)	60 (44.3 to 73.6)

Statistical analyses

No statistical analyses for this end point

Secondary: 11. Percentage of subjects with hSBA titers ≥ 8 against N.meningitidis serogroup B strains

End point title	11. Percentage of subjects with hSBA titers ≥ 8 against N.meningitidis serogroup B strains[14]

End point description:

The percentage of subjects with hSBA titers ≥ 8, after receiving Bexsero® booster vaccination in the present study (24 to 36 months after completion of vaccination course according to different schedules in the parent study), alongside with the corresponding response after the first dose of Bexsero® vaccine in age-matched vaccine-naïve subjects.
The analysis was performed on the FAS-Booster response population, which included all subjects in the Enrolled Set who received a study vaccination, provided an evaluable serum sample at Visit 2 (one month after the booster dose administration) and received all scheduled vaccinations in the parent study V72_28 (excluding naïve groups).

End point type	Secondary

End point timeframe:

At 24-36 months - Visit 1 (pre-vacc.) and one month after booster vaccination - Day 31 (post-vacc.)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	2H3H511_V	3H5_11_V	68_11_V	02_2_5_V
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	87	76	32
Units: Percentage				
number (confidence interval 95%)				
H44/76 (pre-vacc.) (N=92;86;75;31;91;96;55;50)	26 (17.5 to 36.3)	31 (21.8 to 42.3)	33 (22.9 to 45.2)	19 (7.5 to 37.5)
H44/76 (post-vacc.) (N=96;86;75;32;91;96;55;50)	97 (91.1 to 99.4)	98 (91.9 to 99.72)	99 (92.8 to 99.97)	97 (83.8 to 99.92)
5/99 (pre-vacc.) (N=92;87;76;31;91;96;55;50)	79 (69.6 to 87.1)	85 (75.8 to 91.8)	91 (81.9 to 96.2)	71 (52 to 85.8)
5/99 (post-vacc.) (N=96;87;76;32;91;96;55;50)	99 (94.3 to 99.97)	99 (93.8 to 99.97)	97 (90.8 to 99.68)	100 (89.1 to 100)
NZ98/254 (pre-vacc.) (N=92;86;75;32;91;96;54;50)	22 (13.8 to 31.6)	19 (11 to 28.4)	28 (18.2 to 39.6)	13 (3.5 to 29)
NZ98/54 (post-vacc.) (N=96;86;75;32;91;96;54;50)	97 (91.1 to 99.4)	98 (91.9 to 99.72)	100 (95.2 to 100)	97 (83.8 to 99.92)
M10713 (pre-vacc.) (N=78;68;65;29;87;84;49;46)	28 (18.6 to 39.5)	22 (12.9 to 33.8)	34 (22.6 to 46.6)	17 (5.8 to 35.8)
M10713 (post-vacc.) (N=88;79;67;30;89;88;51;47)	64 (52.7 to 73.6)	71 (59.6 to 80.6)	94 (85.4 to 98.3)	90 (73.5 to 97.9)

End point values	02_6_10_V	NAIVE_123	NAIVE_4A	NAIVE_4B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	91	96	55	50
Units: Percentage				
number (confidence interval 95%)				
H44/76 (pre-vacc.) (N=92;86;75;31;91;96;55;50)	30 (20.5 to 40.2)	18 (10.7 to 26.8)	16 (7.8 to 28.8)	10 (3.3 to 21.8)
H44/76 (post-vacc.) (N=96;86;75;32;91;96;55;50)	97 (90.7 to 99.3)	68 (57.4 to 76.9)	71 (57.1 to 82.4)	60 (45.2 to 73.6)
5/99 (pre-vacc.) (N=92;87;76;31;91;96;55;50)	68 (57.5 to 77.5)	2 (0.25 to 7.3)	4 (0.44 to 12.5)	6 (1.3 to 16.5)
5/99 (post-vacc.) (N=96;87;76;32;91;96;55;50)	100 (96 to 100)	77 (67.4 to 85)	78 (65 to 88.2)	60 (45.2 to 73.6)

NZ98/254 (pre-vacc.) (N=92;86;75;32;91;96;54;50)	26 (17.7 to 36.7)	0 (0 to 3.8)	2 (0.05 to 9.9)	0 (0 to 7.1)
NZ98/54 (post-vacc.) (N=96;86;75;32;91;96;54;50)	97 (90.7 to 99.3)	34 (25 to 44.8)	54 (39.6 to 67.4)	40 (26.4 to 54.8)
M10713 (pre-vacc.) (N=78;68;65;29;87;84;49;46)	55 (44.1 to 65.9)	27 (18.2 to 38.2)	39 (25.2 to 53.8)	52 (36.9 to 67.1)
M10713 (post-vacc.) (N=88;79;67;30;89;88;51;47)	92 (84.5 to 96.8)	34 (24.3 to 45)	51 (36.6 to 65.2)	57 (42.2 to 71.7)

Statistical analyses

No statistical analyses for this end point

Secondary: 12. Percentage of subjects with four-fold rise in hSBA titers against N.meningitidis serogroup B strains

End point title	12. Percentage of subjects with four-fold rise in hSBA titers against N.meningitidis serogroup B strains[15]

End point description:

The percentage of subjects with a four-fold rise in hSBA titers after receiving Bexsero® booster vaccination in the present study to pre-vaccination (24 to 36 months after completion of vaccination course according to different schedules in the parent study), alongside with the corresponding response after the first dose of Bexsero® vaccine in age-matched vaccine-naïve subjects.
The analysis was performed on the FAS-Booster response population, which included all subjects in the Enrolled Set who received a study vaccination, provided an evaluable serum sample at Visit 2 (one month after the booster dose administration) and received all scheduled vaccinations in the parent study V72_28 (excluding naïve groups).

End point type	Secondary

End point timeframe:

One month after booster vaccination (Day 31) over Visit 1 of the present study (PRE)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	2H3H511_V	3H5_11_V	68_11_V	02_2_5_V
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92	87	76	32
Units: Percentage				
number (confidence interval 95%)				
H44/76 (Day 31/PRE) (N=92;86;75;31;91;96;55;50)	95 (87.8 to 98.2)	95 (88.5 to 98.7)	97 (90.7 to 99.68)	94 (78.6 to 99.2)
5/99 (Day 31/PRE) (N=92;87;76;31;91;96;55;50)	98 (92.4 to 99.74)	98 (91.9 to 99.72)	95 (87.1 to 98.5)	100 (88.8 to 100)
NZ98/254 (Day 31/PRE) (N=92;86;75;32;91;96;54;50)	92 (84.9 to 96.9)	95 (88.5 to 98.7)	93 (85.1 to 97.8)	94 (79.2 to 99.2)
M10713 (Day 31/PRE) (N=78;68;65;29;87;84;49;46)	41 (30 to 52.7)	50 (37.6 to 62.4)	68 (54.9 to 78.8)	72 (52.8 to 87.3)

End point values	02_6_10_V	NAIVE_123	NAIVE_4A	NAIVE_4B

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	91	96	55	50
Units: Percentage				
number (confidence interval 95%)				
H44/76 (Day 31/PRE) (N=92;86;75;31;91;96;55;50)	97 (90.7 to 99.3)	43 (32.7 to 53.2)	53 (38.8 to 66.3)	46 (31.8 to 60.7)
5/99 (Day 31/PRE) (N=92;87;76;31;91;96;55;50)	98 (92.3 to 99.73)	77 (67.4 to 85)	76 (63 to 86.8)	60 (45.2 to 73.6)
NZ98/254 (Day 31/PRE) (N=92;86;75;32;91;96;54;50)	86 (76.8 to 92.2)	34 (25 to 44.8)	54 (39.6 to 67.4)	40 (26.4 to 54.8)
M10713 (Day 31/PRE) (N=78;68;65;29;87;84;49;46)	53 (41.9 to 63.7)	11 (5 to 19.4)	20 (10.2 to 34.3)	13 (4.9 to 26.3)

Statistical analyses

No statistical analyses for this end point

Secondary: 13. The hSBA antibody titers against N.meningitidis serogroup B strains

End point title	13. The hSBA antibody titers against N.meningitidis serogroup B strains[16]

End point description:

The hSBA antibody titers in subjects, after receiving Bexsero® booster vaccination in the present study (24 to 36 months after completion of vaccination course according to different schedules in the parent study), alongside with the corresponding response in terms of GMTs, after the first dose of Bexsero® vaccine in age-matched vaccine-naïve subjects.
The analysis was performed on the FAS-Booster response population, which included all subjects in the Enrolled Set who received a study vaccination, provided an evaluable serum sample at Visit 2 (one month after the booster dose administration) and received all scheduled vaccinations in the parent study V72_28 (excluding naïve groups).

End point type	Secondary

End point timeframe:

Pre-booster or pre-first dose - Visit 1 (pre-vacc.) and one month post-booster or post-first dose - Day 31 (post-vacc.)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	2H3H511_V	3H5_11_V	68_11_V	02_2_5_V
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	87	76	32
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (pre-vacc.) (N=92;86;75;31;91;96;55;50)	3.91 (3.01 to 5.08)	4.84 (3.66 to 6.41)	6.21 (4.65 to 8.31)	3.14 (2.08 to 4.75)
H44/76 (post-vacc.) (N=96;86;75;32;91;96;55;50)	158 (116 to 215)	205 (147 to 287)	288 (204 to 408)	155 (95 to 252)
5/99 (pre-vacc.) (N=92;87;76;31;91;96;55;50)	39 (26 to 58)	53 (35 to 82)	89 (57 to 139)	19 (9.92 to 35)
5/99 (post-vacc.) (N=96;87;76;32;91;96;55;50)	2908 (2059 to 4107)	3593 (2474 to 5218)	3677 (2495 to 5419)	3205 (1860 to 5526)

NZ98/254 (pre-vacc.) (N=92;86;75;32;91;96;54;50)	3.41 (2.57 to 4.54)	3.17 (2.34 to 4.31)	4.86 (3.54 to 6.67)	2.99 (1.92 to 4.65)
NZ98/254 (post-vacc.) (N=96;86;75;32;91;96;54;50)	92 (70 to 122)	91 (68 to 123)	133 (97 to 181)	71 (46 to 110)
M10713 (pre-vacc.) (N=78;68;65;29;87;84;49;46)	3.05 (2.08 to 4.46)	3.1 (2.05 to 4.68)	3.58 (2.35 to 5.45)	2.31 (1.29 to 4.13)
M10713 (post-vacc.) (N=88;79;67;30;89;88;51;47)	13 (9.15 to 18)	18 (13 to 26)	40 (27 to 59)	32 (19 to 54)

End point values	02_6_10_V	NAIVE_123	NAIVE_4A	NAIVE_4B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	91	96	55	50
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (pre-vacc.) (N=92;86;75;31;91;96;55;50)	6.15 (4.77 to 7.93)	2.82 (2.26 to 3.5)	2.33 (1.77 to 3.07)	1.93 (1.39 to 2.68)
H44/76 (post-vacc.) (N=96;86;75;32;91;96;55;50)	258 (190 to 349)	14 (11 to 17)	16 (12 to 23)	13 (8.67 to 20)
5/99 (pre-vacc.) (N=92;87;76;31;91;96;55;50)	22 (15 to 32)	1.15 (1.02 to 1.29)	1.2 (0.96 to 1.51)	1.38 (1.1 to 1.73)
5/99 (post-vacc.) (N=96;87;76;32;91;96;55;50)	2921 (2079 to 4104)	38 (28 to 54)	27 (18 to 40)	20 (12 to 33)
NZ98/254 (pre-vacc.) (N=92;86;75;32;91;96;54;50)	4.49 (3.4 to 5.92)	1.14 (1.06 to 1.23)	1.35 (1.15 to 1.59)	1.22 (1.06 to 1.41)
NZ98/254 (post-vacc.) (N=96;86;75;32;91;96;54;50)	82 (63 to 108)	6.94 (5.6 to 8.59)	13 (8.88 to 19)	8.56 (5.51 to 13)
M10713 (pre-vacc.) (N=78;68;65;29;87;84;49;46)	7.83 (5.52 to 11)	3.53 (2.64 to 4.71)	4.8 (2.86 to 8.06)	7.7 (4.55 to 13)
M10713 (post-vacc.) (N=88;79;67;30;89;88;51;47)	53 (38 to 73)	4.92 (3.39 to 7.13)	9.44 (5.84 to 15)	12 (6.61 to 21)

Statistical analyses

No statistical analyses for this end point

Secondary: 14. The GMR of hSBA titers against N.meningitidis serogroup B strains

End point title	14. The GMR of hSBA titers against N.meningitidis serogroup B strains[17]

End point description:

The within-subjects GMR of hSBA antibody titers (one month post booster vaccination versus pre-vaccination) after Bexsero® booster vaccination in the present study (24 to 36 months after completion of vaccination course according to different schedules in the parent study), alongside with the within-subject GMR for the first dose of Bexsero® vaccination of age-matched vaccine-naïve subjects.
The analysis was performed on the FAS-Booster response population, which included all subjects in the Enrolled Set who received a study vaccination, provided an evaluable serum sample at Visit 2 (one month after the booster dose administration) and received all scheduled vaccinations in the parent study V72_28 (excluding naïve groups).

End point type	Secondary

End point timeframe:

Day 1 (PRE) and Day 31

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	2H3H511_V	3H5_11_V	68_11_V	02_2_5_V
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92	87	76	32
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 (Day 31/PRE) (N=92;86;75;31;91;96;55;50)	41 (30 to 55)	43 (31 to 59)	46 (33 to 65)	50 (31 to 80)
5/99 (Day 31/PRE) (N=92;87;76;31;91;96;55;50)	75 (54 to 104)	67 (47 to 96)	41 (29 to 60)	160 (95 to 270)
NZ98/254 (Day 31/PRE) (N=92;86;75;32;91;96;54;50)	28 (20 to 38)	29 (21 to 41)	27 (19 to 39)	24 (15 to 40)
M10713 (Day 31/PRE) (N=78;68;65;29;87;84;49;46)	4.07 (2.8 to 5.91)	5.65 (3.77 to 8.47)	11 (7.15 to 16)	13 (7.29 to 23)

End point values	02_6_10_V	NAIVE_123	NAIVE_4A	NAIVE_4B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	91	96	55	50
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 (Day 31/PRE) (N=92;86;75;31;91;96;55;50)	42 (31 to 56)	4.81 (3.81 to 6.07)	7.08 (5.07 to 9.88)	6.87 (4.62 to 10)
5/99 (Day 31/PRE) (N=92;87;76;31;91;96;55;50)	135 (98 to 186)	34 (24 to 46)	22 (15 to 34)	14 (9.11 to 23)
NZ98/254 (Day 31/PRE) (N=92;86;75;32;91;96;54;50)	18 (13 to 25)	6.07 (4.97 to 7.41)	9.58 (6.8 to 13)	7.01 (4.54 to 11)
M10713 (Day 31/PRE) (N=78;68;65;29;87;84;49;46)	6.85 (4.86 to 9.66)	1.38 (1.01 to 1.88)	2.06 (1.36 to 3.12)	1.55 (1.1 to 2.18)

Statistical analyses

No statistical analyses for this end point

Secondary: 15. Percentage of subjects with hSBA titers ≥ 4 or ≥ 5 against N.meningitidis serogroup B strains

End point title	15. Percentage of subjects with hSBA titers ≥ 4 or ≥ 5 against N.meningitidis serogroup B strains[18]

End point description:

The percentage of vaccine-naïve subjects with hSBA titers ≥ 4 against H44/76, 5/99 and NZ98/254 strains, and ≥ 5 against M10713 strain, one month after receiving two catch-up doses of Bexsero® booster vaccination in the present study.

The analysis was performed on the FAS-Two-dose Catch-up population, which included all subjects in the Enrolled Set who received at least one study vaccination and provided evaluable serum samples

whose assay results were available on at least one post-baseline visit (Visit 1 or Visit 2).

End point type	Secondary

End point timeframe:

At Baseline and one month post-second vaccination (Day 61)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	NAIVE_123	NAIVE_4A	NAIVE_4B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	54	49	
Units: Percentage				
number (confidence interval 95%)				
H44/76 (baseline) (N=98;54;49)	38 (28.2 to 48.1)	26 (15 to 39.7)	20 (10.2 to 34.3)	
H44/76 (Day 61) (N=98;54;49)	100 (96.3 to 100)	98 (90.1 to 99.95)	100 (92.7 to 100)	
5/99 (baseline) (N=98;54;49)	3 (0.6 to 8.7)	4 (0.45 to 12.7)	6 (1.3 to 16.9)	
5/99 (Day 61) (N=98;54;49)	100 (96.3 to 100)	100 (93.4 to 100)	100 (92.7 to 100)	
NZ98/254 (baseline) (N=98;54;48)	2 (0.25 to 7.2)	7 (2.1 to 17.9)	6 (1.3 to 17.2)	
NZ98/254 (Day 61) (N=98;54;48)	100 (96.3 to 100)	100 (93.4 to 100)	100 (92.6 to 100)	
M10713 (baseline) (N=87;50;49)	34 (24.6 to 45.4)	40 (26.4 to 54.8)	55 (40.2 to 69.3)	
M10713 (Day 61) (N=91;52;49)	75 (64.5 to 83.3)	69 (54.9 to 81.3)	76 (61.1 to 86.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: 16. Percentage of subjects with hSBA titers ≥ 8 against N.meningitidis serogroup B strains

End point title	16. Percentage of subjects with hSBA titers ≥ 8 against N.meningitidis serogroup B strains[19]

End point description:

The percentage of vaccine-naïve subjects with hSBA titers ≥ 8 against N.meningitidis serogroup B strains, one month after receiving two catch-up doses of Bexsero® booster vaccination in the present study, is reported.
The analysis was performed on the FAS-Two-dose catch-up population, which included all subjects in the Enrolled Set who received at least one study vaccination and provided evaluable serum samples whose assay results were available on at least one post-baseline visit (Visit 1 or Visit 2).

End point type	Secondary

End point timeframe:

At Baseline and one month post-second vaccination (Day 61)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	NAIVE_123	NAIVE_4A	NAIVE_4B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	54	49	
Units: Percentage				
number (confidence interval 95%)				
H44/76 (baseline) (N=98;54;49)	17 (10.4 to 26.3)	15 (6.6 to 27.1)	10 (3.4 to 22.2)	
H44/76 (Day 61) (N=98;54;49)	99 (94.4 to 99.97)	96 (87.3 to 99.55)	98 (89.1 to 99.95)	
5/99 (baseline) (N=98;54;49)	2 (0.25 to 7.2)	4 (0.45 to 12.7)	4 (0.5 to 14)	
5/99 (Day 61) (N=98;54;49)	100 (96.3 to 100)	100 (93.4 to 100)	98 (89.1 to 99.95)	
NZ98/254 (baseline) (N=98;54;48)	0 (0 to 3.7)	2 (0.05 to 9.9)	0 (0 to 7.4)	
NZ98/254 (Day 61) (N=98;54;48)	96 (89.9 to 98.9)	93 (82.1 to 97.9)	94 (82.8 to 98.7)	
M10713 (baseline) (N=87;50;49)	25 (16.6 to 35.7)	38 (24.7 to 52.8)	49 (34.4 to 63.7)	
M10713 (Day 61) (N=91;52;49)	65 (54.1 to 74.6)	63 (49 to 76.4)	69 (54.6 to 81.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: 17. Percentage of subjects with four-fold rise in hSBA titers against N.meningitidis serogroup B strains

End point title	17. Percentage of subjects with four-fold rise in hSBA titers against N.meningitidis serogroup B strains[20]

End point description:

The percentage of naïve subjects with a four-fold rise in hSBA titers against N.meningitidis serogroup B strains from baseline, one month after receiving two catch-up doses of Bexsero® booster vaccination, in comparison to pre-vaccination in the present study, is reported.
The analysis was performed on the FAS-Two-dose catch-up population, which included all subjects in the Enrolled Set who received at least one study vaccination and provided evaluable serum samples whose assay results were available on at least one post-baseline visit (Visit 1 or Visit 2).

End point type	Secondary

End point timeframe:

One month post second vaccination (Day 61)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	NAIVE_123	NAIVE_4A	NAIVE_4B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	54	49	
Units: Percentage				
number (confidence interval 95%)				
H44/76 (N=98;54;49)	94 (87.1 to 97.7)	89 (77.4 to 95.8)	94 (83.1 to 98.7)	
5/99 (N=98;54;49)	100 (96.3 to 100)	100 (93.4 to 100)	98 (89.1 to 99.95)	
NZ98/254 (N=98;54;48)	94 (87.1 to 97.7)	91 (79.7 to 96.9)	94 (82.8 to 98.7)	
M10713 (N=87;50;49)	37 (26.7 to 47.8)	28 (16.2 to 42.5)	22 (11.8 to 36.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: 18. The hSBA antibody titers in naïve subjects against N.meningitidis serogroup B strains

End point title	18. The hSBA antibody titers in naïve subjects against N.meningitidis serogroup B strains[21]

End point description:

The hSBA antibody titers in naïve subjects, after receiving two catch-up doses of Bexsero® vaccination in this study, are reported in terms of GMTs.
The analysis was performed on the FAS-Two-dose catch-up population, which included all subjects in the Enrolled Set who received at least one study vaccination and provided evaluable serum samples whose assay results were available on at least one post-baseline visit (Visit 1 or Visit 2).

End point type	Secondary

End point timeframe:

At Baseline and one month post-second vaccination (Day 61)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	NAIVE_123	NAIVE_4A	NAIVE_4B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	54	49	
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (baseline) (N=98;54;49)	2.3 (1.75 to 3.01)	2.15 (1.55 to 3)	1.56 (1.11 to 2.2)	
H44/76 (Day 61) (N=98;54;49)	107 (84 to 135)	74 (56 to 99)	63 (47 to 85)	
5/99 (baseline) (N=98;54;49)	1.13 (0.94 to 1.36)	1.13 (0.9 to 1.41)	1.31 (1.04 to 1.65)	
5/99 (Day 61) (N=98;54;49)	631 (503 to 792)	421 (319 to 555)	317 (238 to 423)	
NZ98/254 (baseline) (N=98;54;48)	1.11 (0.98 to 1.26)	1.34 (1.15 to 1.56)	1.2 (1.02 to 1.4)	

NZ98/254 (Day 61) (N=98;54;48)	34 (27 to 42)	37 (28 to 49)	34 (26 to 46)	
M10713 (baseline) (N=87;50;49)	2.9 (1.94 to 4.34)	4.12 (2.54 to 6.69)	6.4 (3.91 to 10)	
M10713 (Day 61) (N=91;52;49)	12 (7.57 to 18)	11 (6.87 to 19)	14 (8.34 to 24)	

Statistical analyses

No statistical analyses for this end point

Secondary: 19. The GMRs of hSBA titers after two catch-up doses of Bexsero® vaccination versus hSBA titers at baseline

End point title	19. The GMRs of hSBA titers after two catch-up doses of Bexsero® vaccination versus hSBA titers at baseline[22]

End point description:

The within-subject GMRs of hSBA titers at one month after receiving the second catch-up dose to hSBA titers at baseline, for naïve subjects who received two catch-up doses of Bexsero® vaccination in this study, are reported.
The analysis was performed on the FAS-Two-dose catch-up population, which included all subjects in the Enrolled Set who received at least one study vaccination and provided evaluable serum samples whose assay results were available on at least one post-baseline visit (Visit 1 or Visit 2).

End point type	Secondary

End point timeframe:

Day 1 and Day 61

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	NAIVE_123	NAIVE_4A	NAIVE_4B	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	54	49	
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 (N=98;54;49)	46 (34 to 63)	34 (24 to 50)	41 (27 to 60)	
5/99 (N=98;54;49)	558 (423 to 737)	373 (266 to 524)	242 (171 to 344)	
NZ98/254 (N=98;54;48)	30 (24 to 39)	27 (20 to 37)	29 (21 to 39)	
M10713 (N=87;50;49)	3.86 (2.62 to 5.69)	2.93 (1.84 to 4.67)	2.2 (1.37 to 3.53)	

Statistical analyses

No statistical analyses for this end point

Secondary: 20. Number of subjects reporting unsolicited AEs

End point title	20. Number of subjects reporting unsolicited AEs[23]

End point description:

The number of subjects reporting unsolicited AEs, after receiving Bexsero® booster vaccination (24 to 36 months after completion of vaccination course according to different schedules in the parent study) or two catch-up schedule of Bexsero® vaccine, is reported.
An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. 'Any' was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. 'Possibly or Probably Related' = AE assessed by the investigator as related to the vaccination.
The analysis was performed on the Unsolicited safety set, which included all subjects in the Exposed Set with unsolicited AE data.

End point type	Secondary

End point timeframe:

From Day 1 throughout Day 7 after any vaccination (Any AEs) and throughout the entire study period for all other AEs

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	2H3H511_V	3H5_11_V	68_11_V	02_2_5_V
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	89	78	32
Units: Subjects				
Any AEs	26	19	26	9
Possibly or Probably Related AEs	9	7	10	6
AEs leading to Premature Withdrawal	0	0	0	0

End point values	02_6_10_V	NAIVE_123	NAIVE_4A	NAIVE_4B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	91	100	55	50
Units: Subjects				
Any AEs	14	43	25	12
Possibly or Probably Related AEs	11	12	10	6
AEs leading to Premature Withdrawal	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: 21. Number of subjects reporting Serious Adverse Events (SAEs)

End point title	21. Number of subjects reporting Serious Adverse Events (SAEs)[24]

End point description:

The number of subjects reporting SAEs, after receiving Bexsero® booster vaccination (24 to 36 months after completion of vaccination course according to different schedules in the parent study) or two catch-up schedule of Bexsero® vaccine, is reported.

SAEs assessed include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.
The analysis was performed on the Unsolicited safety set, which included all subjects in the Exposed Set with unsolicited AE data.

End point type	Secondary

End point timeframe:

Throughout the entire study period

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	2H3H511_V	3H5_11_V	68_11_V	02_2_5_V
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	89	78	32
Units: Subjects				
Any SAEs	0	0	0	0
Possibly or probably related SAEs	0	0	0	0

End point values	02_6_10_V	NAIVE_123	NAIVE_4A	NAIVE_4B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	91	100	55	50
Units: Subjects				
Any SAEs	0	0	0	0
Possibly or probably related SAEs	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited and unsolicited AEs were collected from Day 1 (30 minutes) throughout Day 7; SAEs, medically-attended AEs and AEs leading to premature withdrawal were collected throughout the entire study period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	2H3H511_V

Reporting group description:

In the parent study, subjects had received three primary doses and one booster dose of Bexsero® vaccine, at 2.5, 3.5, 5 months of age, and at 11 months of age, respectively. The subjects in this group received a fifth dose of Bexsero® vaccine in the present study.

Reporting group title	3H5_11_V

Reporting group description:

In the parent study, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 3.5, 5 and 11 months of age, respectively. These subjects received a fourth dose of Bexsero® vaccine in the present study.

Reporting group title	68_11_V

Reporting group description:

In the parent study, subjects had received two primary doses and one booster dose of Bexsero® vaccine, at 6, 8, and 11 months of age, respectively. These subjects received a fourth dose of Bexsero® vaccine in the present study.

Reporting group title	02_2_5_V

Reporting group description:

In the parent study, subjects had received two catch-up doses of Bexsero® vaccine, two months apart. These subjects received a third dose of Bexsero® vaccine in the present study.

Reporting group title	02_6_10_V

Reporting group description:

In the parent study, subjects had received two catch-up doses of Bexsero® vaccine, two months apart. These subjects received a third dose of Bexsero® vaccine in the present study.

Reporting group title	NAIVE_123

Reporting group description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Reporting group title	NAIVE_4A

Reporting group description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Reporting group title	NAIVE_4B

Reporting group description:

Newly recruited naïve subjects who received two catch-up doses of Bexsero® vaccine, one month apart, in the present study.

Serious adverse events	2H3H511_V	3H5_11_V	68_11_V
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 97 (0.00%)	0 / 89 (0.00%)	0 / 80 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	02_2_5_V	02_6_10_V	NAIVE_123
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	0 / 91 (0.00%)	0 / 100 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	NAIVE_4A	NAIVE_4B	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 55 (0.00%)	0 / 50 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	2H3H511_V	3H5_11_V	68_11_V
Total subjects affected by non-serious adverse events			
subjects affected / exposed	91 / 97 (93.81%)	84 / 89 (94.38%)	75 / 80 (93.75%)
Nervous system disorders			
Headache			
subjects affected / exposed[1]	0 / 96 (0.00%)	0 / 89 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed[2]	28 / 96 (29.17%)	23 / 89 (25.84%)	26 / 78 (33.33%)
occurrences (all)	29	25	26
General disorders and administration site conditions			
Chills			
subjects affected / exposed[3]	0 / 96 (0.00%)	0 / 89 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Crying			

subjects affected / exposed[4]	31 / 96 (32.29%)	24 / 89 (26.97%)	25 / 78 (32.05%)
occurrences (all)	32	26	26
Injection site erythema			
subjects affected / exposed[5]	61 / 96 (63.54%)	63 / 89 (70.79%)	42 / 78 (53.85%)
occurrences (all)	62	65	43
Injection site induration			
subjects affected / exposed[6]	48 / 96 (50.00%)	48 / 89 (53.93%)	33 / 78 (42.31%)
occurrences (all)	53	52	38
Injection site pain			
subjects affected / exposed[7]	84 / 96 (87.50%)	80 / 89 (89.89%)	71 / 78 (91.03%)
occurrences (all)	89	81	76
Injection site swelling			
subjects affected / exposed[8]	49 / 96 (51.04%)	50 / 89 (56.18%)	37 / 78 (47.44%)
occurrences (all)	51	52	40
Malaise			
subjects affected / exposed[9]	0 / 96 (0.00%)	0 / 89 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed[10]	17 / 96 (17.71%)	18 / 89 (20.22%)	12 / 78 (15.38%)
occurrences (all)	18	19	13
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed[11]	4 / 96 (4.17%)	8 / 89 (8.99%)	5 / 78 (6.41%)
occurrences (all)	5	9	5
Nausea			
subjects affected / exposed[12]	0 / 96 (0.00%)	0 / 89 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed[13]	5 / 96 (5.21%)	6 / 89 (6.74%)	2 / 78 (2.56%)
occurrences (all)	7	6	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed[14]	1 / 96 (1.04%)	0 / 89 (0.00%)	1 / 78 (1.28%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed[15]	13 / 96 (13.54%)	1 / 89 (1.12%)	3 / 78 (3.85%)
occurrences (all)	14	1	4
Psychiatric disorders			
Eating disorder			
subjects affected / exposed[16]	31 / 96 (32.29%)	32 / 89 (35.96%)	30 / 78 (38.46%)
occurrences (all)	32	35	33
Irritability			
subjects affected / exposed[17]	54 / 96 (56.25%)	52 / 89 (58.43%)	46 / 78 (58.97%)
occurrences (all)	54	61	49
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed[18]	0 / 96 (0.00%)	0 / 89 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed[19]	0 / 96 (0.00%)	0 / 89 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Pharyngitis			
subjects affected / exposed[20]	3 / 96 (3.13%)	2 / 89 (2.25%)	1 / 78 (1.28%)
occurrences (all)	3	2	1
Tonsillitis			
subjects affected / exposed[21]	1 / 96 (1.04%)	1 / 89 (1.12%)	2 / 78 (2.56%)
occurrences (all)	1	1	2

Non-serious adverse events	02_2_5_V	02_6_10_V	NAIVE_123
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 32 (96.88%)	86 / 91 (94.51%)	97 / 100 (97.00%)
Nervous system disorders			
Headache			
subjects affected / exposed[1]	0 / 32 (0.00%)	27 / 91 (29.67%)	0 / 100 (0.00%)
occurrences (all)	0	28	0
Somnolence			
subjects affected / exposed[2]	5 / 32 (15.63%)	0 / 91 (0.00%)	23 / 100 (23.00%)
occurrences (all)	5	0	31
General disorders and administration site conditions			

Chills			
subjects affected / exposed[3]	0 / 32 (0.00%)	23 / 91 (25.27%)	0 / 100 (0.00%)
occurrences (all)	0	23	0
Crying			
subjects affected / exposed[4]	4 / 32 (12.50%)	0 / 91 (0.00%)	23 / 100 (23.00%)
occurrences (all)	4	0	30
Injection site erythema			
subjects affected / exposed[5]	22 / 32 (68.75%)	57 / 91 (62.64%)	65 / 100 (65.00%)
occurrences (all)	23	64	101
Injection site induration			
subjects affected / exposed[6]	15 / 32 (46.88%)	44 / 91 (48.35%)	48 / 100 (48.00%)
occurrences (all)	17	50	76
Injection site pain			
subjects affected / exposed[7]	31 / 32 (96.88%)	84 / 91 (92.31%)	94 / 100 (94.00%)
occurrences (all)	32	89	170
Injection site swelling			
subjects affected / exposed[8]	20 / 32 (62.50%)	52 / 91 (57.14%)	51 / 100 (51.00%)
occurrences (all)	21	59	75
Malaise			
subjects affected / exposed[9]	0 / 32 (0.00%)	35 / 91 (38.46%)	0 / 100 (0.00%)
occurrences (all)	0	36	0
Pyrexia			
subjects affected / exposed[10]	2 / 32 (6.25%)	10 / 91 (10.99%)	25 / 100 (25.00%)
occurrences (all)	2	10	28
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed[11]	0 / 32 (0.00%)	0 / 91 (0.00%)	7 / 100 (7.00%)
occurrences (all)	0	0	7
Nausea			
subjects affected / exposed[12]	0 / 32 (0.00%)	12 / 91 (13.19%)	0 / 100 (0.00%)
occurrences (all)	0	12	0
Vomiting			
subjects affected / exposed[13]	1 / 32 (3.13%)	0 / 91 (0.00%)	10 / 100 (10.00%)
occurrences (all)	1	0	12
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed[14]	2 / 32 (6.25%)	0 / 91 (0.00%)	2 / 100 (2.00%)
occurrences (all)	3	0	2
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed[15]	5 / 32 (15.63%)	10 / 91 (10.99%)	8 / 100 (8.00%)
occurrences (all)	5	10	8
Psychiatric disorders			
Eating disorder			
subjects affected / exposed[16]	5 / 32 (15.63%)	0 / 91 (0.00%)	36 / 100 (36.00%)
occurrences (all)	5	0	49
Irritability			
subjects affected / exposed[17]	9 / 32 (28.13%)	0 / 91 (0.00%)	48 / 100 (48.00%)
occurrences (all)	9	0	66
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed[18]	0 / 32 (0.00%)	18 / 91 (19.78%)	0 / 100 (0.00%)
occurrences (all)	0	18	0
Myalgia			
subjects affected / exposed[19]	0 / 32 (0.00%)	24 / 91 (26.37%)	0 / 100 (0.00%)
occurrences (all)	0	24	0
Infections and infestations			
Pharyngitis			
subjects affected / exposed[20]	0 / 32 (0.00%)	0 / 91 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Tonsillitis			
subjects affected / exposed[21]	0 / 32 (0.00%)	0 / 91 (0.00%)	6 / 100 (6.00%)
occurrences (all)	0	0	7

Non-serious adverse events	NAIVE_4A	NAIVE_4B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 55 (100.00%)	50 / 50 (100.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed[1]	1 / 55 (1.82%)	20 / 50 (40.00%)	
occurrences (all)	1	27	
Somnolence			

subjects affected / exposed[2]	10 / 55 (18.18%)	0 / 50 (0.00%)	
occurrences (all)	14	0	
General disorders and administration site conditions			
Chills			
subjects affected / exposed[3]	0 / 55 (0.00%)	7 / 50 (14.00%)	
occurrences (all)	0	9	
Crying			
subjects affected / exposed[4]	8 / 55 (14.55%)	0 / 50 (0.00%)	
occurrences (all)	10	0	
Injection site erythema			
subjects affected / exposed[5]	38 / 55 (69.09%)	37 / 50 (74.00%)	
occurrences (all)	63	54	
Injection site induration			
subjects affected / exposed[6]	28 / 55 (50.91%)	25 / 50 (50.00%)	
occurrences (all)	45	42	
Injection site pain			
subjects affected / exposed[7]	55 / 55 (100.00%)	48 / 50 (96.00%)	
occurrences (all)	109	89	
Injection site swelling			
subjects affected / exposed[8]	36 / 55 (65.45%)	34 / 50 (68.00%)	
occurrences (all)	54	54	
Malaise			
subjects affected / exposed[9]	0 / 55 (0.00%)	16 / 50 (32.00%)	
occurrences (all)	0	20	
Pyrexia			
subjects affected / exposed[10]	5 / 55 (9.09%)	4 / 50 (8.00%)	
occurrences (all)	6	5	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed[11]	6 / 55 (10.91%)	0 / 50 (0.00%)	
occurrences (all)	7	0	
Nausea			
subjects affected / exposed[12]	0 / 55 (0.00%)	8 / 50 (16.00%)	
occurrences (all)	0	9	
Vomiting			

subjects affected / exposed[13]	5 / 55 (9.09%)	0 / 50 (0.00%)	
occurrences (all)	5	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed[14]	0 / 55 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed[15]	4 / 55 (7.27%)	4 / 50 (8.00%)	
occurrences (all)	4	5	
Psychiatric disorders			
Eating disorder			
subjects affected / exposed[16]	13 / 55 (23.64%)	0 / 50 (0.00%)	
occurrences (all)	14	0	
Irritability			
subjects affected / exposed[17]	19 / 55 (34.55%)	1 / 50 (2.00%)	
occurrences (all)	27	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed[18]	0 / 55 (0.00%)	8 / 50 (16.00%)	
occurrences (all)	0	9	
Myalgia			
subjects affected / exposed[19]	0 / 55 (0.00%)	15 / 50 (30.00%)	
occurrences (all)	0	20	
Infections and infestations			
Pharyngitis			
subjects affected / exposed[20]	3 / 55 (5.45%)	0 / 50 (0.00%)	
occurrences (all)	3	0	
Tonsillitis			
subjects affected / exposed[21]	4 / 55 (7.27%)	1 / 50 (2.00%)	
occurrences (all)	4	1	

Notes:

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

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 January 2013	Changes have been implemented prior to the first protocol Submission, in order to better clarify the reminder calls intervals and next visit date after vaccination, to specify that Fever is defined as temperature ≥ 38ºC, to remove the collection of Ethnicity as a demographic data, to remove the reference to unblinding and to specify that medically attended Fever symptoms are collected during the 7 days after vaccination.
14 October 2013	The protocol has been amended to better clarify that the immune response following the MenB vaccination will be assessed by the percentage of subjects achieving hSBA titer of at least 4, and also to better clarify that, for the Serum Bactericidal Assays (SBA), using human serum as the source of exogenous complement (hSBA), performed at the Novartis Vaccines Clinical Serology Laboratory (Marburg, Germany), a cut-off of 5 is used to take account of the assay validation, while for hSBA not performed at the Novartis Vaccines Clinical Serology Laboratory (Marburg, Germany), a cut-off of 4 is used. This amendment also provides the opportunity to better clarify the description of response variables for the statistical plan, to better define study description and to harmonize primary and secondary endpoints with revised study objectives. The list of abbreviation has also been updated and minor editorial changes have been implemented.
28 November 2013	The protocol has been amended to define End of study in compliance with the Novartis Quality Manual and the Corporate Data Disclosure Policy.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported