



Clinical trial results:

A phase IIIB, randomized, controlled, observer-blind study to evaluate safety and immunogenicity of GSK's meningococcal ABCWY vaccine when administered in healthy adolescents and adults, previously primed with meningococcal ACWY vaccine

Summary

EudraCT number	2019-004982-42
Trial protocol	Outside EU/EEA
Global end of trial date	03 May 2023

Results information

Result version number	v1 (current)
This version publication date	13 April 2024
First version publication date	13 April 2024

Trial information

Trial identification

Sponsor protocol code	213171
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut, 89, Rixensart, Belgium, 1330
Public contact	GSK Response Center, GSK Response Center, 044 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 044 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2023
Global end of trial reached?	Yes
Global end of trial date	03 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

-To demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4 fold rise¹ in hSBA titers against N. meningitidis serogroups A, C, W, and Y, at 1 month after the second MenABCWY vaccination (0,6-months) and 1 month after the MenACWY vaccination (single dose).

-To demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4 fold rise¹ in hSBA titers against N. meningitidis serogroups A, C, W, and Y, at 1 month after the first MenABCWY vaccination (0,6-months) and 1 month after the MenACWY vaccination (single dose).

-To evaluate the safety and reactogenicity of the MenABCWY and MenACWY vaccines.

Protection of trial subjects:

The participants were observed closely for at least 30 minutes after the administration of the vaccine(s)/product. Appropriate medical treatment was readily available during the observation period in case of anaphylaxis and/or syncope.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 May 2021
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	Argentina: 232
Country: Number of subjects enrolled	Australia: 237
Country: Number of subjects enrolled	Canada: 49
Country: Number of subjects enrolled	United States: 729
Worldwide total number of subjects	1247
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
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Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	891
Adults (18-64 years)	356
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of 1250 participants enrolled, 3 participants did not receive vaccination as they did not meet the eligibility criteria, therefore only 1247 participants were included in the Exposed Set and started the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind ^[1]
Roles blinded	Data analyst, Assessor

Blinding implementation details:

This was an Observer-blind study. Recipients & study evaluators were unaware of vaccine administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	ABCWY Group

Arm description:

Participants received 2 doses of the MenABCWY vaccine on Day 1 and Day 181 (0,6-month schedule) and 1 dose of placebo on Day 211.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of placebo on Day 211.

Investigational medicinal product name	Meningococcal Group B Vaccine
Investigational medicinal product code	rMenB+OMV NZ
Other name	Bexsero
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of MenB vaccine on Day 181 and Day 211.

Investigational medicinal product name	Combined Meningococcal Groups A, B, C, W and Y vaccine
Investigational medicinal product code	MenABCWY
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of the MenABCWY vaccine on Day 1 and Day 181 (0,6-month schedule).

Arm title	ACWY Group
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Arm description:

Participants received 1 dose of MenACWY vaccine on Day 1 and 2 doses of MenB vaccine on Day 181 and Day 211.

Arm type	Active comparator
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Investigational medicinal product name	Meningococcal Groups A, C, W and Y Conjugate Vaccine
Investigational medicinal product code	MenACWY
Other name	Menveo
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of MenACWY vaccine administered intramuscularly on Day 1.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: This was an Observer-blind study. Recipients & study evaluators were unaware of vaccine administered.

Number of subjects in period 1	ABCWY Group	ACWY Group
Started	626	621
Completed	541	542
Not completed	85	79
Consent withdrawn by subject	27	25
Adverse event, non-fatal	5	8
MIGRATED / MOVED FROM THE STUDY AREA	8	8
Lost to follow-up	44	31
UNSPECIFIED	-	2
Protocol deviation	1	5

Baseline characteristics

Reporting groups

Reporting group title	ABCWY Group
Reporting group description:	
Participants received 2 doses of the MenABCWY vaccine on Day 1 and Day 181 (0,6-month schedule) and 1 dose of placebo on Day 211.	
Reporting group title	ACWY Group
Reporting group description:	
Participants received 1 dose of MenACWY vaccine on Day 1 and 2 doses of MenB vaccine on Day 181 and Day 211.	

Reporting group values	ABCWY Group	ACWY Group	Total
Number of subjects	626	621	1247
Age categorical			
Units: Subjects			
Adolescents (12-17 years)	450	441	891
Adults (18-64 years)	176	180	356
Age continuous			
Units: years			
arithmetic mean	17.2	17.2	
standard deviation	± 2.53	± 2.63	-
Sex: Female, Male			
Units: Participants			
Male	283	297	580
Female	343	324	667
Race/Ethnicity, Customized			
Units: Subjects			
Black or African American	94	86	180
American Indian or Alaska Native	1	1	2
Asian	22	33	55
Native Hawaiian or Other Pacific Islander	2	6	8
White	474	464	938
Other UNSPECIFIED	33	31	64

End points

End points reporting groups

Reporting group title	ABCWY Group
Reporting group description: Participants received 2 doses of the MenABCWY vaccine on Day 1 and Day 181 (0,6-month schedule) and 1 dose of placebo on Day 211.	
Reporting group title	ACWY Group
Reporting group description: Participants received 1 dose of MenACWY vaccine on Day 1 and 2 doses of MenB vaccine on Day 181 and Day 211.	

Primary: Percentages of Participants with a 4-fold Rise in human serum bactericidal assay (hSBA) Titers against N. Meningitidis Serogroups A, C, W, and Y at 1 month after the Second MenABCWY Vaccination and the Single MenACWY Vaccination, Relative to Baseline

End point title	Percentages of Participants with a 4-fold Rise in human serum bactericidal assay (hSBA) Titers against N. Meningitidis Serogroups A, C, W, and Y at 1 month after the Second MenABCWY Vaccination and the Single MenACWY Vaccination, Relative to Baseline
End point description: Four-fold rise is defined as: - a post-vaccination hSBA titer equal to or higher than (\geq) 16 for participants with a pre-vaccination hSBA titer <4 ; - a post-vaccination hSBA titer ≥ 4 times the LLOQ for participants with a pre vaccination hSBA titer \geq limit of detection (LOD) but $< \text{LLOQ}$; and - a post-vaccination hSBA titer ≥ 4 times the pre-vaccination titer for participants with a pre-vaccination hSBA titer $\geq \text{LLOQ}$.	
End point type	Primary
End point timeframe: At 1 month after vaccination schedule (i.e., Day 211 for ABCWY group and Day 31 for ACWY group) compared to Day 1 (Baseline)	

End point values	ABCWY Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	546		
Units: Percentage of Participants				
number (confidence interval 95%)				
Meningitis A (N=169,505)	95.3 (90.89 to 97.93)	95.0 (92.78 to 96.77)		
Meningitis C (N=181,546)	94.5 (90.07 to 97.32)	94.0 (91.62 to 95.80)		
Meningitis W (N=181,544)	95.6 (91.48 to 98.07)	93.9 (91.59 to 95.79)		
Meningitis Y (N=180,537)	95.0 (90.72 to 97.69)	94.4 (92.12 to 96.20)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
To demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4-fold rise in hSBA titers against N. meningitidis serogroups A at 1 month after the second MenABCWY vaccination (0,6-months) and 1 month after the MenACWY vaccination (single dose).	
Comparison groups	ABCWY Group v ACWY Group
Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage of participants
Point estimate	0.2
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	-4.38
upper limit	3.5

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
To demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4-fold rise in hSBA titers against N. meningitidis serogroups W at 1 month after the second MenABCWY vaccination (0,6-months) and 1 month after the MenACWY vaccination (single dose).	
Comparison groups	ABCWY Group v ACWY Group
Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage of participants
Point estimate	1.6
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	-2.73
upper limit	4.89

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
To demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4-fold rise in hSBA titers against N. meningitidis serogroups Y at 1 month after the second MenABCWY vaccination (0,6-months) and 1 month after the MenACWY vaccination (single dose).	
Comparison groups	ABCWY Group v ACWY Group

Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage of participants
Point estimate	0.6
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	-3.93
upper limit	3.91

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

To demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4-fold rise in hSBA titers against N. meningitidis serogroups C at 1 month after the second MenABCWY vaccination (0,6-months) and 1 month after the MenACWY vaccination (single dose).

Comparison groups	ABCWY Group v ACWY Group
Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage of participants
Point estimate	0.5
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	-4.14
upper limit	3.98

Primary: Percentages of Participants with a 4-fold Rise in hSBA Titers against N. Meningitidis Serogroups A, C, W, and Y at 1 month after the First MenABCWY Vaccination and the Single MenACWY Vaccination, Relative to Baseline

End point title	Percentages of Participants with a 4-fold Rise in hSBA Titers against N. Meningitidis Serogroups A, C, W, and Y at 1 month after the First MenABCWY Vaccination and the Single MenACWY Vaccination, Relative to Baseline
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End point description:

Four-fold rise is defined as: - a post-vaccination hSBA titer equal to or higher than (\geq) 16 for participants with a pre-vaccination hSBA titer <4 ; - a post-vaccination hSBA titer ≥ 4 times the LLOQ for participants with a pre vaccination hSBA titer \geq limit of detection (LOD) but $< \text{LLOQ}$; and - a post-vaccination hSBA titer ≥ 4 times the pre-vaccination titer for participants with a pre-vaccination hSBA titer $\geq \text{LLOQ}$.

End point type	Primary
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End point timeframe:

At 1 month after the first vaccination (i.e., Day 31) compared to Day 1 (Baseline)

End point values	ABCWY Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	570	546		
Units: Percentage of Participants				
number (confidence interval 95%)				
Meningitis A (N=509, 505)	92.5 (89.90 to 94.66)	95.0 (92.78 to 96.77)		
Meningitis C (N=570, 546)	94.0 (91.76 to 95.83)	94.0 (91.62 to 95.80)		
Meningitis W (N=565,544)	94.3 (92.10 to 96.09)	93.9 (91.59 to 95.79)		
Meningitis Y (N=567,537)	93.7 (91.32 to 95.51)	94.4 (92.12 to 96.20)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
To demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4-fold rise in hSBA titers against N. meningitidis serogroups A at 1 month after the first MenABCWY vaccination (0,6-months) and 1 month after the MenACWY vaccination (single dose).	
Comparison groups	ABCWY Group v ACWY Group
Number of subjects included in analysis	1116
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage of participants
Point estimate	-2.5
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	-5.59
upper limit	0.47

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
To demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4-fold rise in hSBA titers against N. meningitidis serogroups Y at 1 month after the first MenABCWY vaccination (0,6-months) and 1 month after the MenACWY vaccination (single dose).	
Comparison groups	ABCWY Group v ACWY Group
Number of subjects included in analysis	1116
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage of participants
Point estimate	-0.8

Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	-3.62
upper limit	2.09

Statistical analysis title	Statistical analysis 3
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Statistical analysis description:

To demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4-fold rise in hSBA titers against N. meningitidis serogroupsW at 1 month after the first MenABCWY vaccination (0,6-months) and 1 month after the MenACWY vaccination (single dose).

Comparison groups	ABCWY Group v ACWY Group
Number of subjects included in analysis	1116
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage of participants
Point estimate	0.4
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	-2.41
upper limit	3.25

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

To demonstrate the immunological non-inferiority of the MenABCWY vaccine, compared to MenACWY vaccine given to healthy participants, previously primed with a MenACWY vaccine, as measured by the percentages of participants achieving a 4-fold rise in hSBA titers against N. meningitidis serogroups C at 1 month after the first MenABCWY vaccination (0,6-months) and 1 month after the MenACWY vaccination (single dose).

Comparison groups	ABCWY Group v ACWY Group
Number of subjects included in analysis	1116
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage of participants
Point estimate	0.1
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	-2.76
upper limit	2.94

Primary: Number of Participants with solicited administration site events following vaccination at day 1 for ABCWY group and ACWY group

End point title	Number of Participants with solicited administration site events following vaccination at day 1 for ABCWY group and ACWY group ^[1]
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End point description:

Assessed solicited administration site events include injection site pain, erythema, swelling, induration. Any pain = occurrence of the symptom regardless of intensity grade and any erythema, swelling and induration are defined as a symptom with a surface diameter equal to or greater than 25 millimeters.

End point type	Primary
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End point timeframe:

During the 7 days (including day of vaccination) following vaccination at day 1 for ABCWY group and ACWY group

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 analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	ABCWY Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	608	601		
Units: Participants				
Injection site pain (N=608,601)	486	191		
Erythema (N=608,600)	29	9		
Swelling (N=608,600)	26	13		
Induration (N=608,600)	24	14		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with solicited administration site events following vaccination at Day 181 for ABCWY group

End point title	Number of Participants with solicited administration site events following vaccination at Day 181 for ABCWY group ^{[2][3]}
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End point description:

Assessed solicited administration site events include injection site pain, erythema, swelling, induration. Any pain = occurrence of the symptom regardless of intensity grade and any erythema, swelling and induration are defined as a symptom with a surface diameter equal to or greater than 25 millimeters.

End point type	Primary
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End point timeframe:

During the 7 days (including day of vaccination) following vaccination at Day 181 for ABCWY group

Notes:

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

Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[3] - 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: As specified in the Protocol, the analysis assesses the safety and reactogenicity of the MenABCWY vaccines.

End point values	ABCWY Group			
Subject group type	Reporting group			
Number of subjects analysed	507			
Units: Participants				
Injection site pain (N=507)	377			
Erythema (N=505)	31			
Swelling (N=505)	30			
Induration (N=505)	22			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with solicited systemic events following vaccination at day 1 for the ABCWY group and ACWY group

End point title	Number of Participants with solicited systemic events following vaccination at day 1 for the ABCWY group and ACWY group ^[4]
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End point description:

Assessed solicited systemic events include fever [body temperature $\geq 38.0^{\circ}\text{C}$ (celsius) / 100.4°F (Fahrenheit)], nausea, fatigue, myalgia, arthralgia, headache.

End point type	Primary
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End point timeframe:

During the 7 days (including day of vaccination) following vaccination at day 1 for the ABCWY group and ACWY group

Notes:

[4] - 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 analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	ABCWY Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	608	601		
Units: participants				
Fever (N=608,600)	12	7		
Nausea (N=608,600)	88	75		
Fatigue (N=608,600)	244	222		
Myalgia (N=608,600)	90	66		
Arthralgia (N=608,600)	45	49		
Headache (N=608,601)	249	208		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with solicited systemic events following vaccination at day 181 for the ABCWY group

End point title	Number of Participants with solicited systemic events following
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End point description:

Assessed solicited systemic events include fever [body temperature $\geq 38.0^{\circ}\text{C}/100.4^{\circ}\text{F}$], nausea, fatigue, myalgia, arthralgia, headache.

End point type	Primary
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End point timeframe:

During the 7 days (including day of vaccination) following vaccination at day 181 for the ABCWY group

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 analysis of this primary endpoint was descriptive i.e. 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: As specified in the Protocol, the analysis assesses the safety and reactogenicity of the MenABCWY vaccines.

End point values	ABCWY Group			
Subject group type	Reporting group			
Number of subjects analysed	505			
Units: Participants				
Fever (N=505)	9			
Nausea (N=505)	58			
Fatigue (N=505)	167			
Myalgia (N=505)	67			
Arthralgia (N=505)	30			
Headache (N=505)	167			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with any unsolicited adverse events (AEs) (including all serious adverse events [SAEs], AEs leading to withdrawal, AEs of special interest [AESIs] and medically attended AEs)

End point title	Number of Participants with any unsolicited adverse events (AEs) (including all serious adverse events [SAEs], AEs leading to withdrawal, AEs of special interest [AESIs] and medically attended AEs) ^[7]
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End point description:

Unsolicited AE-AE not solicited using an eDiary and spontaneously communicated by a participant/participant's parent(s)/Legally acceptable representative(s) who has signed informed consent. SAEs-events that result in death, life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is congenital anomaly/birth defect in the offspring of a study participant/results in abnormal pregnancy outcomes. AESIs-predefined AEs of scientific and medical concern specific to the product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate, because such an event might warrant further investigation in order to characterize and understand it. An MAE is defined as an unsolicited AE for which the participant received medical attention such as hospitalization, or an emergency room visit, or visit to/by a health care provider.

End point type	Primary
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End point timeframe:

During the 30 days (including day of vaccination) following vaccination at day 1 for ABCWY group and ACWY group

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 analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	ABCWY Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	626	621		
Units: Participants	96	93		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with any unsolicited adverse events (AEs) (including all serious adverse events [SAEs], AEs leading to withdrawal, AEs of special interest [AESIs] and medically attended AEs) following vaccination at day 181 for ABCWY group

End point title	Number of Participants with any unsolicited adverse events (AEs) (including all serious adverse events [SAEs], AEs leading to withdrawal, AEs of special interest [AESIs] and medically attended AEs) following vaccination at day 181 for ABCWY group ^[8] ^[9]
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End point description:

Any AE-untoward medical occurrence in a patient/clinical investigation participant, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product. Unsolicited AE-AE not solicited using an eDiary and spontaneously communicated by a participant/participant's parent(s)/Legally acceptable representative(s) who has signed informed consent. SAEs-events that result in death, life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is congenital anomaly/birth defect in the offspring of a study participant/results in abnormal pregnancy outcomes. AESIs-predefined AEs of scientific and medical concern specific to the product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate, because such an event might warrant further investigation in order to characterize and understand it.

End point type	Primary
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End point timeframe:

During the 30 days (including day of vaccination) following vaccination at day 181 for ABCWY group

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 analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: As specified in the Protocol, the analysis assesses the safety and reactogenicity of the MenABCWY vaccines.

End point values	ABCWY Group			
Subject group type	Reporting group			
Number of subjects analysed	626			
Units: Participants	72			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with SAEs, AEs leading to withdrawal, AESIs and medically attended AEs

End point title	Number of Participants with SAEs, AEs leading to withdrawal, AESIs and medically attended AEs ^[10]
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End point description:

SAEs, AEs leading to withdrawal, AESIs and medically attended AEs were assessed throughout the study period are reported in this outcome measure.

End point type	Primary
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End point timeframe:

From Day 1 to Day 361 (throughout the study period)

Notes:

[10] - 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 analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	ABCWY Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	626	621		
Units: Participants				
SAEs	18	7		
AEs leading to withdrawal	4	6		
AESIs	0	4		
Medically Attended AEs	223	206		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Participants with hSBA titers \geq Lower Limit of Quantitation (LLOQ) against serogroups A, C, W, and Y at day 1, 1 month after the first and second MenABCWY vaccination and after the single MenACWY vaccination

End point title	Percentages of Participants with hSBA titers \geq Lower Limit of Quantitation (LLOQ) against serogroups A, C, W, and Y at day 1, 1 month after the first and second MenABCWY vaccination and after the single MenACWY vaccination
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End point description:

The immune response to MenABCWY vaccine after the first and second dose and single dose of MenACWY vaccine was evaluated by measuring the percentage of participants with hSBA titers \geq LLOQ against each of the serogroups A, C, W and Y.

End point type	Secondary
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End point timeframe:

At Day 1 (pre-vaccination) and 1 month after the vaccination schedule (i.e., Day 31 for ABCWY group [first dose] and ACWY group, Day 211 for ABCWY group [second dose])

End point values	ABCWY Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	609	593		
Units: Percentage of Participants				
number (confidence interval 95%)				
Meningitis A, Day 1 (N=546, 549)	27.7 (23.94 to 31.61)	28.8 (25.02 to 32.77)		
Meningitis A, Day 31 (N=605,585)	98.3 (96.98 to 99.20)	98.1 (96.66 to 99.06)		
Meningitis A, Day 211 (N=213,585)	99.5 (97.41 to 99.99)	98.1 (96.66 to 99.06)		
Meningitis C, Day 1 (N=601,584)	57.7 (53.67 to 61.72)	56.2 (52.03 to 60.23)		
Meningitis C, Day 31 (N=609,593)	98.9 (97.65 to 99.54)	99.0 (97.81 to 99.63)		
Meningitis C, Day 211 (N=211,593)	100.0 (98.27 to 100.00)	99.0 (97.81 to 99.63)		
Meningitis W, Day 1 (N=597,583)	36.3 (32.48 to 40.35)	33.4 (29.62 to 37.44)		
Meningitis W, Day 31 (N=607,592)	98.4 (96.99 to 99.21)	96.8 (95.03 to 98.06)		
Meningitis W, Day 211 (N=212,592)	100.0 (98.28 to 100.00)	96.8 (95.03 to 98.06)		
Meningitis Y, Day 1 (N=600,576)	37.5 (33.61 to 41.51)	34.9 (31.00 to 38.94)		
Meningitis Y, Day 31 (N=606,591)	97.9 (96.36 to 98.85)	97.6 (96.06 to 98.70)		
Meningitis Y, Day 211 (N=210,591)	100.0 (98.26 to 100.00)	97.6 (96.06 to 98.70)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers (GMTs) against serogroups A, C, W, and Y at day 1, 1 month after the first and second MenABCWY vaccination and after the single MenACWY vaccination

End point title	hSBA Geometric Mean Titers (GMTs) against serogroups A, C, W, and Y at day 1, 1 month after the first and second MenABCWY vaccination and after the single MenACWY vaccination
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End point description:

The immune response to MenABCWY after first and second dose and single dose of MenACWY vaccine was evaluated by measuring the human serum bactericidal activity against each of the serogroups A, C, W and Y in terms of GMTs. For each serogroup, the GMTs with their associated 2-sided 95% confidence intervals were calculated.

End point type	Secondary
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End point timeframe:

At Day 1 and 1 month after the vaccination schedule (i.e., Day 31 for ABCWY group [first dose] and ACWY group, Day 211 for ABCWY group [second dose])

End point values	ABCWY Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	609	593		
Units: Titers				
geometric mean (confidence interval 95%)				
Meningitis A, Day 1 (N=546,549)	15.30 (13.07 to 17.92)	16.34 (13.96 to 19.14)		
Meningitis A, Day 31 (N=605,585)	670.78 (594.71 to 756.58)	1282.56 (1135.84 to 1448.23)		
Meningitis A, Day 211 (N=213,585)	645.24 (544.11 to 765.16)	1249.18 (1102.47 to 1415.41)		
Meningitis C, Day 1 (N=601,584)	31.90 (26.63 to 38.23)	29.76 (24.81 to 35.71)		
Meningitis C, Day 31 (N=609,593)	2945.68 (2471.13 to 3511.36)	2552.27 (2138.66 to 3045.87)		
Meningitis C, Day 211 (N=211,593)	2350.14 (1809.69 to 3052.00)	2512.26 (2077.25 to 3038.38)		
Meningitis W, Day 1 (N=592,583)	12.08 (10.31 to 14.15)	11.08 (9.45 to 12.99)		
Meningitis W, Day 31 (N=607, 592)	1899.60 (1638.73 to 2202.00)	1665.64 (1435.57 to 1932.58)		
Meningitis W, Day 211 (N=212,592)	1173.61 (940.25 to 1464.89)	1671.10 (1421.70 to 1964.25)		
Meningitis Y, Day 1 (N=600,576)	12.84 (11.16 to 14.76)	11.86 (10.29 to 13.66)		
Meningitis Y, Day 31 (N=606,591)	1590.71 (1380.78 to 1832.55)	1578.42 (1369.00 to 1819.88)		
Meningitis Y, Day 211 (N=210,591)	1130.54 (916.85 to 1394.04)	1624.85 (1395.48 to 1891.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean ratios (GMRs) against serogroups A, C, W, and Y at 1 month after the first and second MenABCWY vaccination and after the single MenACWY vaccination

End point title	Geometric mean ratios (GMRs) against serogroups A, C, W, and Y at 1 month after the first and second MenABCWY vaccination and after the single MenACWY vaccination
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End point description:

The immune response to MenABCWY vaccine after first and second dose and single dose of MenACWY vaccine are evaluated by measuring the human serum bactericidal activity against each of the serogroups A, C, W and Y, compared to baseline (Day 1) and expressed as GMRs. Within group GMRs was calculated as ratio of GMTs in the post-vaccination timepoint to the pre-vaccination timepoint.

End point type	Secondary
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End point timeframe:

At 1 month after the vaccination schedule (i.e., Day 31 for ABCWY group [first dose] and ACWY group,

End point values	ABCWY Group	ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	583		
Units: Ratio				
geometric mean (confidence interval 95%)				
Meningitis A, Day 31/Baseline(N=539,539)	43.98 (36.92 to 52.40)	76.91 (64.53 to 91.66)		
Meningitis A, Day 211/Baseline(N=196,539)	44.74 (34.67 to 57.74)	77.13 (63.95 to 93.02)		
Meningitis C, Day 31/Baseline(N=597,583)	92.87 (77.13 to 111.83)	86.36 (71.63 to 104.12)		
Meningitis C, Day 211/Baseline(N=205,583)	68.33 (52.19 to 89.46)	78.47 (64.57 to 95.37)		
Meningitis W, Day 1/Baseline(N=591,581)	154.09 (125.80 to 188.73)	150.83 (123.00 to 184.96)		
Meningitis W, Day 211/Baseline(N=207,581)	97.66 (72.52 to 131.52)	162.43 (130.80 to 201.69)		
Meningitis Y, Day 1/Baseline(N=593,573)	124.11 (103.23 to 149.23)	134.66 (111.75 to 162.26)		
Meningitis Y, Day 211/Baseline(N=202,573)	82.45 (62.80 to 108.24)	141.00 (115.70 to 171.84)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Participants with hSBA Titers \geq LLOQ for Each and all Serogroup B indicator Strains at Day 1 and at 1 month after the second dose of MenABCWY vaccination

End point title	Percentages of Participants with hSBA Titers \geq LLOQ for Each and all Serogroup B indicator Strains at Day 1 and at 1 month after the second dose of MenABCWY vaccination ^[11]
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End point description:

The immune response to MenABCWY vaccine after second dose was evaluated by measuring bactericidal activity against each (individual response) and all (composite response) N. meningitidis serogroup B indicator strains (M14459, 96217, M13520 and NZ98/254 for fHbp, NadA, NHBA and PorA P1.4 antigens, respectively).

End point type	Secondary
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End point timeframe:

At Day 1 and at Day 211

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: As specified in the Protocol, the analysis assesses the immune response to the MenABCWY vaccine against N. meningitidis serogroup B indicator strains.

End point values	ABCWY Group			
Subject group type	Reporting group			
Number of subjects analysed	184			
Units: Percentage of Participants				
number (confidence interval 95%)				
fHbp (M14459) Ab, Day 1 (N=184)	8.7 (5.05 to 13.74)			
fHbp (M14459) Ab, Day 211 (N=165)	88.5 (82.60 to 92.92)			
NadA (96217) Ab, Day 1 (N=183)	7.7 (4.25 to 12.50)			
NadA (96217) Ab, Day 211 (N=165)	95.8 (91.45 to 98.28)			
NHBA (M13520) Ab, Day 1 (N=183)	20.2 (14.65 to 26.77)			
NHBA (M13520) Ab, Day 211 (N=164)	96.3 (92.21 to 98.65)			
PorAP1.4 (NZ98/254) Ab, Day 1 (N=184)	2.7 (0.89 to 6.23)			
PorAP1.4 (NZ98/254) Ab, Day 211 (N=164)	75.6 (68.30 to 81.97)			
Composite Response, Day 1 (N=181)	1.1 (0.13 to 3.93)			
Composite Response, Day 211 (N=164)	72.0 (64.41 to 78.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of participants with 4-fold rise in hSBA titers against each N. meningitidis serogroup B indicator strains at 1 month after the second MenABCWY vaccination

End point title	Percentages of participants with 4-fold rise in hSBA titers against each N. meningitidis serogroup B indicator strains at 1 month after the second MenABCWY vaccination ^[12]
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End point description:

The immune response to MenABCWY after second dose is evaluated by measuring bactericidal activity against each of the N. meningitidis serogroup B test strains (M14459, 96217, M13520 and NZ98/254 for fHbp, NadA, NHBA and PorA P1.4 antigens, respectively). compared to baseline (day 1) in terms of 4-fold rise in hSBA titers. For each of the serogroup B indicator strains, the 4-fold rise is defined as: a post-vaccination hSBA titer ≥ 16 for participants with a pre-vaccination hSBA titer < 4 ; a post-vaccination hSBA titer ≥ 4 times the LLOQ for participants with a prevaccination hSBA titer \geq limit of detection (LOD) but $< \text{LLOQ}$; and, a post-vaccination hSBA titer ≥ 4 times the pre-vaccination titer for participants with a pre-vaccination hSBA titer $\geq \text{LLOQ}$.

End point type	Secondary
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End point timeframe:

At Day 211 compared to baseline (Day 1)

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: As specified in the Protocol, the analysis assesses the immune response to the MenABCWY vaccine against N. meningitidis serogroup B indicator strains.

End point values	ABCWY Group			
Subject group type	Reporting group			
Number of subjects analysed	163			
Units: Percentage of Participants				
number (confidence interval 95%)				
fHbp (M14459) Ab (N=163)	68.1 (60.35 to 75.17)			
NadA (96217) Ab (N=162)	90.1 (84.46 to 94.25)			
NHBA (M13520) Ab (N=161)	64.6 (56.68 to 71.96)			
PorAP1.4 (NZ98/254) Ab (N=162)	45.7 (37.84 to 53.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs against each serogroup B indicator strains at day 1 and at 1 month after second MenABCWY vaccination

End point title	GMTs against each serogroup B indicator strains at day 1 and at 1 month after second MenABCWY vaccination ^[13]
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End point description:

The immune response to MenABCWY vaccine after the second dose is evaluated by measuring bactericidal activity against each of the *N. meningitidis* serogroup B indicator strains (M14459, 96217, M13520 and NZ98/254 for fHbp, NadA, NHBA and PorA P1.4 antigens, respectively) in terms of GMTs at baseline (Day 1) and 1 month after second MenABCWY vaccination.

End point type	Secondary
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End point timeframe:

At Day 1 and at Day 211

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: As specified in the Protocol, the analysis assesses the immune response to the MenABCWY vaccine against *N. meningitidis* serogroup B indicator strains.

End point values	ABCWY Group			
Subject group type	Reporting group			
Number of subjects analysed	184			
Units: Titers				
geometric mean (confidence interval 95%)				
fHbp (M14459) Ab, Day 1 (N=184)	2.84 (2.53 to 3.19)			
fHbp (M14459) Ab, Day 211 (N=165)	17.56 (13.52 to 22.80)			
NadA (96217) Ab, Day 1 (N=183)	8.62 (7.39 to 10.06)			
NadA (96217) Ab, Day 211 (N=165)	143.61 (106.71 to 193.26)			
NHBA (M13520) Ab, Day 1 (N=183)	3.28 (2.59 to 4.15)			

NHBA (M13520) Ab, Day 211 (N=164)	24.82 (19.19 to 32.11)			
PorAP1.4 (NZ98/254) Ab, Day 1 (N=184)	3.13 (2.86 to 3.43)			
PorAP1.4 (NZ98/254) Ab, Day 211 (N=164)	11.44 (8.61 to 15.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: GMRs against each serogroup B indicator strains at 1 month after second dose of MenABCWY vaccination

End point title	GMRs against each serogroup B indicator strains at 1 month after second dose of MenABCWY vaccination ^[14]
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End point description:

The immune response to MenABCWY vaccine after second dose is evaluated by measuring the human serum bactericidal activity against each of the *N. meningitidis* serogroup B indicator strains (M14459, 96217, M13520 and NZ98/254 for fHbp, NadA, NHBA and PorA P1.4 antigens, respectively) compared to baseline (Day 1) and expressed as GMRs. Within group GMRs was calculated as ratio of GMTs in the post-vaccination timepoint to the pre-vaccination timepoint.

End point type	Secondary
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End point timeframe:

At Day 211 compared to baseline (Day 1)

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: As specified in the Protocol, the analysis assesses the immune response to the MenABCWY vaccine against *N. meningitidis* serogroup B indicator strains.

End point values	ABCWY Group			
Subject group type	Reporting group			
Number of subjects analysed	163			
Units: Ratio				
geometric mean (confidence interval 95%)				
fHbp (M14459) Ab, Day 211/Baseline (N=163)	6.29 (4.84 to 8.18)			
NadA (96217) Ab, Day 211/Baseline (N=162)	16.67 (12.25 to 22.70)			
NHBA (M13520) Ab, Day 211/Baseline (N=161)	7.69 (6.08 to 9.72)			
PorAP1.4 (NZ98/254) Ab, Day 211/Baseline (N=162)	3.65 (2.76 to 4.83)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs were collected during the 7-day follow-up period after vaccination. Unsolicited AEs were collected during the 30-day follow-up period after vaccination. SAEs were collected from Day 1 up to study end [Day 361]

Assessment type	Systematic
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Dictionary used

Dictionary name	v26.0
Dictionary version	26.0

Reporting groups

Reporting group title	ACWY Group
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Reporting group description:

Participants received 1 dose of MenACWY vaccine on Day 1 and 2 doses of MenB vaccine on Day 181 and Day 211.

Reporting group title	ABCWY Group
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Reporting group description:

Participants received 2 doses of the MenABCWY vaccine on Day 1 and Day 181 (0,6-month schedule) and 1 dose of placebo on Day 211.

Serious adverse events	ACWY Group	ABCWY Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 621 (1.13%)	18 / 626 (2.88%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Gun shot wound			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax traumatic			

subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Wolff-Parkinson-White syndrome congenital			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroschisis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Impaired gastric emptying			

subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Depression			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional self-injury			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Norovirus infection			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal disease			
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	ACWY Group	ABCWY Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	552 / 621 (88.89%)	583 / 626 (93.13%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Infected naevus			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	

Melanocytic naevus subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 1	
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	2 / 621 (0.32%) 2	1 / 626 (0.16%) 1	
Pregnancy, puerperium and perinatal conditions Abortion spontaneous complete subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 1	
General disorders and administration site conditions Administration site pain subjects affected / exposed occurrences (all)	455 / 621 (73.27%) 1949	524 / 626 (83.71%) 2656	
Administration site erythema subjects affected / exposed occurrences (all)	30 / 621 (4.83%) 63	53 / 626 (8.47%) 139	
Administration site induration subjects affected / exposed occurrences (all)	40 / 621 (6.44%) 143	54 / 626 (8.63%) 136	
Injection site bruising subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	0 / 626 (0.00%) 0	
Influenza like illness subjects affected / exposed occurrences (all)	6 / 621 (0.97%) 6	2 / 626 (0.32%) 2	
Fatigue subjects affected / exposed occurrences (all)	293 / 621 (47.18%) 1006	318 / 626 (50.80%) 974	
Facial pain subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 1	
Chills subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	2 / 626 (0.32%) 2	

Chest pain		
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)
occurrences (all)	2	0
Administration site swelling		
subjects affected / exposed	37 / 621 (5.96%)	49 / 626 (7.83%)
occurrences (all)	93	136
Injection site induration		
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)
occurrences (all)	2	1
Non-cardiac chest pain		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	1
Malaise		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Injection site reaction		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Injection site rash		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Injection site pruritus		
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)
occurrences (all)	2	1
Injection site pain		
subjects affected / exposed	5 / 621 (0.81%)	2 / 626 (0.32%)
occurrences (all)	5	2
Injection site nodule		
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)
occurrences (all)	2	0
Injection site mass		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Pain		
subjects affected / exposed	3 / 621 (0.48%)	2 / 626 (0.32%)
occurrences (all)	3	2

Swelling face			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Vaccination site pain			
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)	
occurrences (all)	2	1	
Vaccination site reaction			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Vessel puncture site pain			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	16 / 621 (2.58%)	24 / 626 (3.83%)	
occurrences (all)	33	39	
Immune system disorders			
Allergy to animal			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Drug hypersensitivity			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Hypocomplementaemia			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Mite allergy			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Seasonal allergy			
subjects affected / exposed	0 / 621 (0.00%)	6 / 626 (0.96%)	
occurrences (all)	0	6	
Food allergy			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Social circumstances			

Physical assault subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 1	
Reproductive system and breast disorders			
Cervical dysplasia subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	0 / 626 (0.00%) 0	
Bartholin's cyst subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 2	
Dysmenorrhoea subjects affected / exposed occurrences (all)	3 / 621 (0.48%) 3	4 / 626 (0.64%) 4	
Menstrual disorder subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	0 / 626 (0.00%) 0	
Menstruation irregular subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	2 / 626 (0.32%) 2	
Varicocele subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	2 / 626 (0.32%) 3	
Breast pain subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 1	
Respiratory, thoracic and mediastinal disorders			
Asthma exercise induced subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	0 / 626 (0.00%) 0	
Asthma subjects affected / exposed occurrences (all)	5 / 621 (0.81%) 6	5 / 626 (0.80%) 6	
Asthmatic crisis subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	1 / 626 (0.16%) 1	
Bronchial obstruction			

subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Bronchospasm		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	1
Cough		
subjects affected / exposed	4 / 621 (0.64%)	4 / 626 (0.64%)
occurrences (all)	6	4
Dyspnoea		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	1
Epistaxis		
subjects affected / exposed	2 / 621 (0.32%)	3 / 626 (0.48%)
occurrences (all)	2	3
Nasal congestion		
subjects affected / exposed	5 / 621 (0.81%)	6 / 626 (0.96%)
occurrences (all)	5	7
Nasal polyps		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Nasal septum deviation		
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)
occurrences (all)	0	2
Oropharyngeal pain		
subjects affected / exposed	15 / 621 (2.42%)	10 / 626 (1.60%)
occurrences (all)	15	10
Pneumonitis		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Rhinitis allergic		
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)
occurrences (all)	2	1
Rhinorrhoea		
subjects affected / exposed	3 / 621 (0.48%)	2 / 626 (0.32%)
occurrences (all)	3	2
Sleep apnoea syndrome		

subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Tonsillolith			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Behavioural insomnia of childhood			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Affective disorder			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	8 / 621 (1.29%)	13 / 626 (2.08%)	
occurrences (all)	8	13	
Anxiety disorder			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Attention deficit hyperactivity disorder			
subjects affected / exposed	4 / 621 (0.64%)	5 / 626 (0.80%)	
occurrences (all)	4	5	
Autism spectrum disorder			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Bipolar disorder			
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences (all)	0	2	
Stress			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Depressed mood			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Depression			

subjects affected / exposed	8 / 621 (1.29%)	7 / 626 (1.12%)
occurrences (all)	8	8
Depressive symptom		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Generalised anxiety disorder		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Insomnia		
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)
occurrences (all)	2	1
Intentional self-injury		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Major depression		
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)
occurrences (all)	2	0
Mixed anxiety and depressive disorder		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	1
Obsessive-compulsive disorder		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	1
Panic attack		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Psychotic disorder		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Social anxiety disorder		
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)
occurrences (all)	2	0
Borderline personality disorder		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1

Trichotillomania subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 1	
Investigations			
Antinuclear antibody positive subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	0 / 626 (0.00%) 0	
Weight increased subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	0 / 626 (0.00%) 0	
Weight decreased subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	2 / 626 (0.32%) 2	
SARS-CoV-2 test positive subjects affected / exposed occurrences (all)	4 / 621 (0.64%) 4	0 / 626 (0.00%) 0	
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	3 / 621 (0.48%) 3	2 / 626 (0.32%) 2	
Concussion subjects affected / exposed occurrences (all)	3 / 621 (0.48%) 3	5 / 626 (0.80%) 5	
Bone contusion subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	0 / 626 (0.00%) 0	
Arthropod bite subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	0 / 626 (0.00%) 0	
Ankle fracture subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 1	
Animal bite subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	2 / 626 (0.32%) 2	
Face injury			

subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)
occurrences (all)	0	2
Fall		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	1
Fibula fracture		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Foot fracture		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Fractured coccyx		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Gun shot wound		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Hand fracture		
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)
occurrences (all)	2	1
Immunisation reaction		
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)
occurrences (all)	0	2
Joint dislocation		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	2
Joint injury		
subjects affected / exposed	1 / 621 (0.16%)	4 / 626 (0.64%)
occurrences (all)	1	4
Ligament injury		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Ligament rupture		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Ligament sprain		

subjects affected / exposed	7 / 621 (1.13%)	8 / 626 (1.28%)
occurrences (all)	7	8
Limb injury		
subjects affected / exposed	2 / 621 (0.32%)	3 / 626 (0.48%)
occurrences (all)	2	3
Muscle injury		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Muscle rupture		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Muscle strain		
subjects affected / exposed	1 / 621 (0.16%)	2 / 626 (0.32%)
occurrences (all)	1	2
Nail avulsion		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Tooth fracture		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Tibia fracture		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Thermal burn		
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)
occurrences (all)	2	1
Tendon injury		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Nail injury		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Nasal injury		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Procedural pain		

subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)	
occurrences (all)	2	0	
Radial head dislocation			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Radial nerve injury			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Road traffic accident			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Skin laceration			
subjects affected / exposed	1 / 621 (0.16%)	8 / 626 (1.28%)	
occurrences (all)	1	8	
Soft tissue injury			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Splinter			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
Stab wound			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Torus fracture			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
Tooth injury			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Underdose			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
Traumatic haematoma			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
Congenital, familial and genetic			

disorders			
Hypermobility syndrome			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Phimosi			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences (all)	0	2	
Nervous system disorders			
Headache			
subjects affected / exposed	291 / 621 (46.86%)	323 / 626 (51.60%)	
occurrences (all)	828	878	
Idiopathic intracranial hypertension			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Loss of consciousness			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Migraine			
subjects affected / exposed	3 / 621 (0.48%)	1 / 626 (0.16%)	
occurrences (all)	3	1	
Migraine with aura			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Migraine without aura			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Ophthalmic migraine			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			

subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	0 / 621 (0.00%)	3 / 626 (0.48%)	
occurrences (all)	0	4	
Sensory disturbance			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	3 / 621 (0.48%)	2 / 626 (0.32%)	
occurrences (all)	3	3	
Tension headache			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	7 / 621 (1.13%)	9 / 626 (1.44%)	
occurrences (all)	7	10	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Lymphadenitis			
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences (all)	0	2	
Lymphadenopathy			
subjects affected / exposed	4 / 621 (0.64%)	0 / 626 (0.00%)	
occurrences (all)	5	0	
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)	
occurrences (all)	2	1	
Deafness neurosensory			

subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Ear congestion			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Ear pain			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Ear swelling			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Eustachian tube dysfunction			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Tympanic membrane perforation			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences (all)	0	2	
Eye irritation			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Retinal detachment			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	2	0	
Retinal tear			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	2	0	
Keratitis			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			

subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Coeliac disease		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Irritable bowel syndrome		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Abdominal pain upper		
subjects affected / exposed	4 / 621 (0.64%)	8 / 626 (1.28%)
occurrences (all)	4	8
Abdominal pain lower		
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)
occurrences (all)	0	2
Abdominal pain		
subjects affected / exposed	5 / 621 (0.81%)	3 / 626 (0.48%)
occurrences (all)	5	6
Abdominal hernia		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Abdominal distension		
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)
occurrences (all)	2	0
Constipation		
subjects affected / exposed	6 / 621 (0.97%)	2 / 626 (0.32%)
occurrences (all)	6	2
Crohn's disease		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Diarrhoea		
subjects affected / exposed	5 / 621 (0.81%)	10 / 626 (1.60%)
occurrences (all)	5	11
Food poisoning		
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)
occurrences (all)	2	0
Gastritis		

subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Gastrointestinal disorder		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Gastrooesophageal reflux disease		
subjects affected / exposed	4 / 621 (0.64%)	1 / 626 (0.16%)
occurrences (all)	4	2
Haematochezia		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Haemorrhoids		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Aphthous ulcer		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Tooth impacted		
subjects affected / exposed	2 / 621 (0.32%)	4 / 626 (0.64%)
occurrences (all)	2	4
Stomatitis		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Reflux gastritis		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Odynophagia		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Nausea		
subjects affected / exposed	124 / 621 (19.97%)	132 / 626 (21.09%)
occurrences (all)	256	260
Mouth ulceration		
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)
occurrences (all)	2	0
Malpositioned teeth		

subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	1 / 626 (0.16%) 1	
Toothache subjects affected / exposed occurrences (all)	3 / 621 (0.48%) 3	1 / 626 (0.16%) 1	
Vomiting subjects affected / exposed occurrences (all)	6 / 621 (0.97%) 7	4 / 626 (0.64%) 4	
Uvulitis subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 1	
Ulcerative Colitis subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	0 / 626 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Dermatitis contact subjects affected / exposed occurrences (all)	2 / 621 (0.32%) 2	5 / 626 (0.80%) 5	
Dermatitis atopic subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 1	
Angioedema subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 1	
Alopecia subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	2 / 626 (0.32%) 2	
Acne subjects affected / exposed occurrences (all)	6 / 621 (0.97%) 7	8 / 626 (1.28%) 8	
Eczema subjects affected / exposed occurrences (all)	0 / 621 (0.00%) 0	1 / 626 (0.16%) 1	
Ingrowing nail subjects affected / exposed occurrences (all)	1 / 621 (0.16%) 1	2 / 626 (0.32%) 3	

Night sweats			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Pityriasis rosea			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
Urticaria			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Skin mass			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	2	
Skin hyperpigmentation			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Skin fissures			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Rosacea			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Glycosuria			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Chromaturia			

subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	3 / 621 (0.48%)	1 / 626 (0.16%)	
occurrences (all)	3	1	
Pollakiuria			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Nephrolithiasis			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Joint stiffness			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	5 / 621 (0.81%)	5 / 626 (0.80%)	
occurrences (all)	5	5	
Arthritis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Arthralgia			
subjects affected / exposed	78 / 621 (12.56%)	71 / 626 (11.34%)	
occurrences (all)	148	131	
Ligament laxity			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			

subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	113 / 621 (18.20%)	139 / 626 (22.20%)	
occurrences (all)	247	265	
Neck pain			
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)	
occurrences (all)	2	1	
Pain in extremity			
subjects affected / exposed	2 / 621 (0.32%)	5 / 626 (0.80%)	
occurrences (all)	2	5	
Pain in jaw			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Plantar fasciitis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Scoliosis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Synovial cyst			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
Tendonitis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Tenosynovitis stenosans			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	6 / 621 (0.97%)	3 / 626 (0.48%)	
occurrences (all)	6	3	

Abscess limb		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Atypical pneumonia		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	1
Bacterial vaginosis		
subjects affected / exposed	0 / 621 (0.00%)	3 / 626 (0.48%)
occurrences (all)	0	3
Cervicitis human papilloma virus		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Campylobacter infection		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Cellulitis		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	1
Bronchitis		
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)
occurrences (all)	3	1
Chlamydial infection		
subjects affected / exposed	2 / 621 (0.32%)	5 / 626 (0.80%)
occurrences (all)	3	5
Conjunctivitis		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	1
Conjunctivitis bacterial		
subjects affected / exposed	1 / 621 (0.16%)	3 / 626 (0.48%)
occurrences (all)	1	3
COVID-19		
subjects affected / exposed	97 / 621 (15.62%)	92 / 626 (14.70%)
occurrences (all)	99	97
Fungal foot infection		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0

Ear infection		
subjects affected / exposed	2 / 621 (0.32%)	2 / 626 (0.32%)
occurrences (all)	2	2
Epididymitis		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Escherichia urinary tract infection		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Cystitis		
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)
occurrences (all)	0	3
Gastroenteritis		
subjects affected / exposed	3 / 621 (0.48%)	3 / 626 (0.48%)
occurrences (all)	3	3
Lower respiratory tract infection		
subjects affected / exposed	3 / 621 (0.48%)	0 / 626 (0.00%)
occurrences (all)	3	0
Gastrointestinal viral infection		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Gonorrhoea		
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)
occurrences (all)	0	3
Hand-foot-and-mouth disease		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Helicobacter infection		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Herpeszoster		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Hordeolum		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1

Impetigo		
subjects affected / exposed	1 / 621 (0.16%)	3 / 626 (0.48%)
occurrences (all)	1	3
Infectious mononucleosis		
subjects affected / exposed	2 / 621 (0.32%)	2 / 626 (0.32%)
occurrences (all)	2	2
Influenza		
subjects affected / exposed	7 / 621 (1.13%)	11 / 626 (1.76%)
occurrences (all)	7	11
Laryngitis		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Laryngitis viral		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Localised infection		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	1
Gastroenteritis viral		
subjects affected / exposed	2 / 621 (0.32%)	3 / 626 (0.48%)
occurrences (all)	2	3
Nasopharyngitis		
subjects affected / exposed	6 / 621 (0.97%)	10 / 626 (1.60%)
occurrences (all)	6	11
Pilonidal disease		
subjects affected / exposed	1 / 621 (0.16%)	2 / 626 (0.32%)
occurrences (all)	1	3
Oral herpes		
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)
occurrences (all)	2	0
Orchitis		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Otitis externa		
subjects affected / exposed	3 / 621 (0.48%)	2 / 626 (0.32%)
occurrences (all)	3	2

Otitis media		
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)
occurrences (all)	0	2
Otitis media acute		
subjects affected / exposed	3 / 621 (0.48%)	2 / 626 (0.32%)
occurrences (all)	3	2
Paronychia		
subjects affected / exposed	1 / 621 (0.16%)	2 / 626 (0.32%)
occurrences (all)	1	2
Pelvic inflammatory disease		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Pericoronitis		
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)
occurrences (all)	3	0
Pharyngitis		
subjects affected / exposed	7 / 621 (1.13%)	5 / 626 (0.80%)
occurrences (all)	8	5
Pharyngitis bacterial		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Pharyngitis streptococcal		
subjects affected / exposed	6 / 621 (0.97%)	7 / 626 (1.12%)
occurrences (all)	6	7
Pharyngotonsillitis		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Omphalitis		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Post procedural infection		
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)
occurrences (all)	2	0
Tooth abscess		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1

Rash pustular		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Respiratory tract infection viral		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Rhinitis		
subjects affected / exposed	1 / 621 (0.16%)	3 / 626 (0.48%)
occurrences (all)	1	3
Rhinovirus infection		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Scrotal abscess		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Sinusitis		
subjects affected / exposed	10 / 621 (1.61%)	5 / 626 (0.80%)
occurrences (all)	10	5
Sinusitis bacterial		
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)
occurrences (all)	1	1
Subcutaneous abscess		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Suspected COVID-19		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Tinea infection		
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)
occurrences (all)	0	1
Tinea versicolour		
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)
occurrences (all)	1	0
Tonsillitis		
subjects affected / exposed	2 / 621 (0.32%)	2 / 626 (0.32%)
occurrences (all)	2	2

Pyuria			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Tooth infection			
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)	
occurrences (all)	2	0	
Upper respiratory tract infection			
subjects affected / exposed	8 / 621 (1.29%)	17 / 626 (2.72%)	
occurrences (all)	8	17	
Urinary tract infection			
subjects affected / exposed	7 / 621 (1.13%)	10 / 626 (1.60%)	
occurrences (all)	7	10	
Viral infection			
subjects affected / exposed	4 / 621 (0.64%)	1 / 626 (0.16%)	
occurrences (all)	4	1	
Viral pharyngitis			
subjects affected / exposed	1 / 621 (0.16%)	2 / 626 (0.32%)	
occurrences (all)	1	2	
Viral upper respiratory tract infection			
subjects affected / exposed	9 / 621 (1.45%)	7 / 626 (1.12%)	
occurrences (all)	9	8	
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Trichomoniasis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			

subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
Iron deficiency			
subjects affected / exposed	0 / 621 (0.00%)	4 / 626 (0.64%)	
occurrences (all)	0	4	
Vitamin D deficiency			
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2021	The primary goal of this amendment was to promote one of the secondary endpoints to co-primary, which allowed to evaluate vaccine immunogenicity at 1 month after both the first and the second MenABCWY vaccinations (0,6-months). Also, considering that some of the study interventions are combination products constituted of a device and biologic product (pre-filled syringes), the amended protocol provides instructions for collection of safety information related to the use of medical devices.
01 November 2021	<ol style="list-style-type: none">1. To extend the window for the priming MenACWY vaccination prior to enrollment from 4 to 6 years to at least 4 years. This was to increase the pool of potential participants who may benefit from the intervention.2. To allow for interim analyses of immunological objectives after all participants have completed Visit 4, and of safety objectives after at least 50% of participants have completed Visit 4.3. Other minor changes included the timing for reporting pregnancies and the change of the reference N MenB NHBA strain.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported