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	v2 (current)
This version publication date	15 August 2024
First version publication date	13 April 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	213171

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

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	Assessor, Data analyst

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	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).

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	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.

Arm title	ACWY Group

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

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 (>=) 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 >= limit of detection (LOD) but < LLOQ; and - a post-vaccination hSBA titer >= 4 times the pre-vaccination titer for participants with a pre-vaccination hSBA titer >= 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

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

End point description:

Four-fold rise is defined as: - a post-vaccination hSBA titer equal to or higher than (>=) 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 >= limit of detection (LOD) but < LLOQ; and - a post-vaccination hSBA titer >= 4 times the pre-vaccination titer for participants with a pre-vaccination hSBA titer >= LLOQ.

End point type	Primary

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

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

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]

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

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]

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

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]

End point description:

Assessed solicited systemic events include fever [body temperature >= 38.0°C (celsius) /100.4°F (Fahrenheit)], nausea, fatigue, myalgia, arthralgia, headache.

End point type	Primary

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=608,600)	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

	vaccination at day 181 for the ABCWY group[5][6]

End point description:

Assessed solicited systemic events include fever [body temperature >= 38.0°C/100.4°F], nausea, fatigue, myalgia, arthralgia, headache.

End point type	Primary

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]

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

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]

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

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]

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

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 >= Lower Limit of Quantitation (LLOQ) against serogroups A, C, W, and Y at day 1, 1 month after the first MenABCWY vaccination and after the single MenACWY vaccination

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

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 >= LLOQ against each of the serogroups A, C, W and Y.

End point type	Secondary

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)

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 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 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 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)		

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 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 MenABCWY vaccination and after the single MenACWY vaccination

End point description:

The immune response to MenABCWY after first 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

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)

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 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 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 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)		

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

End point description:

The immune response to MenABCWY vaccine after first 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

End point timeframe:

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

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 C, Day 31/Baseline(N=597,583)	92.87 (77.13 to 111.83)	86.36 (71.63 to 104.12)		
Meningitis W, Day 1/Baseline(N=591,581)	154.09 (125.80 to 188.73)	150.83 (123.00 to 184.96)		

Meningitis Y, Day 1/Baseline(N=593.573)	124.11 (103.23 to 149.23)	134.66 (111.75 to 162.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Participants with hSBA Titers >= 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 >= LLOQ for Each and all Serogroup B indicator Strains at Day 1 and at 1 month after the second dose of MenABCWY vaccination[11]

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

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: 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[12]

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

End point timeframe:

At Day 1 and at Day 211

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	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: 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[13]

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 >= limit of detection (LOD) but < LLOQ; and, a post-vaccination hSBA titer >= 4 times the pre-vaccination titer for participants with a pre-vaccination hSBA titer >= LLOQ.

End point type	Secondary

End point timeframe:

At Day 211 compared to baseline (Day 1)

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	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: 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]

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

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

Secondary: Percentages of Participants with hSBA titers >= Lower Limit of Quantitation (LLOQ) against serogroups A, C, W, and Y at 1 month after the second MenABCWY vaccination

End point title	Percentages of Participants with hSBA titers >= Lower Limit of Quantitation (LLOQ) against serogroups A, C, W, and Y at 1 month after the second MenABCWY vaccination[15]

End point description:

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

End point type	Secondary

End point timeframe:

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

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: 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	609			
Units: Percentage of Participants				
number (confidence interval 95%)				
Meningitis A, Day 211 (N=213)	99.5 (97.41 to 99.99)			
Meningitis C, Day 211 (N=211)	100.0 (98.27 to 100.0)			
Meningitis W, Day 211 (N=212)	100.0 (98.28 to 100.0)			
Meningitis Y, Day 211 (N=210)	100.0 (98.26 to 100.0)			

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 second MenABCWY vaccination

End point title	Geometric mean ratios (GMRs) against serogroups A, C, W, and Y at 1 month after second MenABCWY vaccination[16]

End point description:

The immune response to MenABCWY vaccine after second dose 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

End point timeframe:

At 1 month after the vaccination schedule (i.e., Day 211 for ABCWY group [second dose]) compared to baseline (Day 1)

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: 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	597			
Units: Ratio				
geometric mean (confidence interval 95%)				
Meningitis A, Day 211 (N=196)	44.74 (34.67 to 57.74)			
Meningitis C, Day 211 (N=205)	68.33 (52.19 to 89.46)			
Meningitis W, Day 211 (N=207)	97.66 (72.52 to 131.52)			
Meningitis Y, Day 211 (N=202)	82.45 (62.80 to 108.24)			

Statistical analyses

No statistical analyses for this end point

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

End point title	hSBA Geometric Mean Titers (GMTs) against serogroups A, C, W, and Y at 1 month after the second MenABCWY vaccination[17]

End point description:

The immune response to MenABCWY after second dose 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

End point timeframe:

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

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: 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	609			
Units: Titers				
geometric mean (confidence interval 95%)				
Meningitis A, Day 211 (N=213)	645.24 (544.11 to 765.16)			
Meningitis C, Day 211 (N=211)	2350.14 (1809.69 to 3052.00)			
Meningitis W, Day 211 (N=212)	1173.61 (940.25 to 1464.89)			
Meningitis Y, Day 211 (N=210)	1130.54 (916.85 to 1394.04)			

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

Dictionary used

Dictionary name	v26.0
Dictionary version	26.0

Reporting groups

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 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.

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			
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	
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	
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	
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	
Congenital, familial and genetic disorders			
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	
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	
Nervous system disorders			
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	
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	
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	
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	
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	
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	
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			

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	
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	
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	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)	
occurrences (all)	2	1	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous complete			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Facial pain			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
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	
Administration site pain			
subjects affected / exposed	455 / 621 (73.27%)	524 / 626 (83.71%)	
occurrences (all)	1949	2656	
Administration site induration			
subjects affected / exposed	40 / 621 (6.44%)	54 / 626 (8.63%)	
occurrences (all)	143	136	
Administration site erythema			
subjects affected / exposed	30 / 621 (4.83%)	53 / 626 (8.47%)	
occurrences (all)	63	139	
Chills			
subjects affected / exposed	1 / 621 (0.16%)	2 / 626 (0.32%)	
occurrences (all)	1	2	
Pain			
subjects affected / exposed	3 / 621 (0.48%)	2 / 626 (0.32%)	
occurrences (all)	3	2	

Pyrexia			
subjects affected / exposed	16 / 621 (2.58%)	24 / 626 (3.83%)	
occurrences (all)	33	39	
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	
Fatigue			
subjects affected / exposed	293 / 621 (47.18%)	318 / 626 (50.80%)	
occurrences (all)	1006	974	
Influenza like illness			
subjects affected / exposed	6 / 621 (0.97%)	2 / 626 (0.32%)	
occurrences (all)	6	2	
Injection site bruising			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Injection site induration			
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)	
occurrences (all)	2	1	
Injection site mass			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Injection site nodule			
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)	
occurrences (all)	2	0	
Injection site pain			
subjects affected / exposed	5 / 621 (0.81%)	2 / 626 (0.32%)	
occurrences (all)	5	2	

Injection site pruritus			
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)	
occurrences (all)	2	1	
Injection site rash			
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	
Malaise			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
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	
Food allergy			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
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	
Social circumstances			

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

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

subjects affected / exposed	1 / 621 (0.16%)	8 / 626 (1.28%)	
occurrences (all)	1	8	
Road traffic accident			
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	
Radial head dislocation			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)	
occurrences (all)	2	0	
Nasal injury			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Nail injury			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Nail avulsion			
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	
Muscle rupture			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Muscle injury			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
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	
Tooth injury			
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	
Splinter			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
Soft tissue 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	
Torus fracture			
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	
Congenital, familial and genetic			

disorders			
Phimosis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Hypermobility syndrome			
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			
Migraine without aura			
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	
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	
Ophthalmic migraine			

subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
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	
Paraesthesia			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
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	
Keratitis			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
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	
Gastrointestinal disorders			
Abdominal discomfort			

subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)	
occurrences (all)	2	0	
Abdominal hernia			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	5 / 621 (0.81%)	3 / 626 (0.48%)	
occurrences (all)	5	6	
Abdominal pain lower			
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences (all)	0	2	
Abdominal pain upper			
subjects affected / exposed	4 / 621 (0.64%)	8 / 626 (1.28%)	
occurrences (all)	4	8	
Aphthous ulcer			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Coeliac disease			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	6 / 621 (0.97%)	2 / 626 (0.32%)	
occurrences (all)	6	2	
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	
Irritable bowel syndrome			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Malpositioned teeth			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
Mouth ulceration			
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	124 / 621 (19.97%)	132 / 626 (21.09%)	
occurrences (all)	256	260	
Odynophagia			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Reflux gastritis			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Stomatitis			
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	
Toothache			

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

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	
Rash			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
Pruritus			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Pityriasis rosea			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	2	
Night sweats			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Ingrowing nail			
subjects affected / exposed	1 / 621 (0.16%)	2 / 626 (0.32%)	
occurrences (all)	1	3	
Renal and urinary disorders			
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	
Glycosuria			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Dysuria			
subjects affected / exposed	3 / 621 (0.48%)	1 / 626 (0.16%)	
occurrences (all)	3	1	
Chromaturia			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Synovial cyst			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Scoliosis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Plantar fasciitis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Pain in jaw			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	2 / 621 (0.32%)	5 / 626 (0.80%)	
occurrences (all)	2	5	
Neck pain			
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)	
occurrences (all)	2	1	
Myalgia			

subjects affected / exposed	113 / 621 (18.20%)	139 / 626 (22.20%)	
occurrences (all)	247	265	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences (all)	0	2	
Muscle spasms			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Ligament laxity			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
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	
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 621 (0.16%)	1 / 626 (0.16%)	
occurrences (all)	1	1	
Tenosynovitis stenosans			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Tendonitis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
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	
Acute sinusitis			
subjects affected / exposed	6 / 621 (0.97%)	3 / 626 (0.48%)	
occurrences (all)	6	3	
Bacterial vaginosis			
subjects affected / exposed	0 / 621 (0.00%)	3 / 626 (0.48%)	
occurrences (all)	0	3	
Bronchitis			
subjects affected / exposed	2 / 621 (0.32%)	1 / 626 (0.16%)	
occurrences (all)	3	1	
Cervicitis human papilloma virus			
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	
Campylobacter infection			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
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	
Epididymitis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences (all)	0	3	

Ear infection			
subjects affected / exposed	2 / 621 (0.32%)	2 / 626 (0.32%)	
occurrences (all)	2	2	
COVID-19			
subjects affected / exposed	97 / 621 (15.62%)	92 / 626 (14.70%)	
occurrences (all)	99	97	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Gastroenteritis viral			
subjects affected / exposed	2 / 621 (0.32%)	3 / 626 (0.48%)	
occurrences (all)	2	3	
Gastroenteritis			
subjects affected / exposed	3 / 621 (0.48%)	3 / 626 (0.48%)	
occurrences (all)	3	3	
Fungal foot infection			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	7 / 621 (1.13%)	5 / 626 (0.80%)	
occurrences (all)	8	5	
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	
Lower respiratory tract infection			
subjects affected / exposed	3 / 621 (0.48%)	0 / 626 (0.00%)	
occurrences (all)	3	0	
Nasopharyngitis			
subjects affected / exposed	6 / 621 (0.97%)	10 / 626 (1.60%)	
occurrences (all)	6	11	
Omphalitis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
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	
Gonorrhoea			
subjects affected / exposed	0 / 621 (0.00%)	2 / 626 (0.32%)	
occurrences (all)	0	3	
Pharyngitis bacterial			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	7 / 621 (1.13%)	10 / 626 (1.60%)	
occurrences (all)	7	10	
Pharyngotonsillitis			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Pilonidal disease			
subjects affected / exposed	1 / 621 (0.16%)	2 / 626 (0.32%)	
occurrences (all)	1	3	
Post procedural infection			
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)	
occurrences (all)	2	0	
Pyuria			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	

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	

Tooth abscess			
subjects affected / exposed	0 / 621 (0.00%)	1 / 626 (0.16%)	
occurrences (all)	0	1	
Tooth infection			
subjects affected / exposed	2 / 621 (0.32%)	0 / 626 (0.00%)	
occurrences (all)	2	0	
Trichomoniasis			
subjects affected / exposed	1 / 621 (0.16%)	0 / 626 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	8 / 621 (1.29%)	17 / 626 (2.72%)	
occurrences (all)	8	17	
Pharyngitis streptococcal			
subjects affected / exposed	6 / 621 (0.97%)	7 / 626 (1.12%)	
occurrences (all)	6	7	
Viral infection			
subjects affected / exposed	4 / 621 (0.64%)	1 / 626 (0.16%)	
occurrences (all)	4	1	
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	
Viral pharyngitis			
subjects affected / exposed	1 / 621 (0.16%)	2 / 626 (0.32%)	
occurrences (all)	1	2	
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	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