Clinical trial results:
Immunogenicity and Safety of a Booster Dose of an Investigational Quadrivalent Meningococcal Conjugate Vaccine in Adolescents and Adults

Summary

EudraCT number	2019-004461-41
Trial protocol	Outside EU/EEA
Global end of trial date	14 September 2020

Results information

Result version number	v1 (current)
This version publication date	12 August 2021
First version publication date	12 August 2021

Trial information

Trial identification

Sponsor protocol code	MET59

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04084769
WHO universal trial number (UTN)	U1111-1217-2137

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	Discovery Drive, Swiftwater, PA, United States, 18370-0187
Public contact	Trial Transparency Team, Sanofi Pasteur Inc, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur Inc, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001930-PIP01-16
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 March 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the vaccine seroresponse sufficiency of meningococcal serogroups A, C, Y, and W following the administration of a booster dose of meningococcal Polysaccharide (Serogroups A, C, Y and W) Tetanus Toxoid (MenACYW) Conjugate vaccine in subjects who were first vaccinated with 1 dose of MenACYW Conjugate vaccine or Menveo (meningococcal Group B) vaccine 3-6 years before the booster dose (Groups 1 and 2).

Protection of trial subjects:

Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment were also available on site in case of any immediate allergic reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 September 2019
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	United States: 530
Country: Number of subjects enrolled	Puerto Rico: 40
Worldwide total number of subjects	570
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)	546
Adults (18-64 years)	24

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled from 03-September-2019 to 07-March-2020 at 30 active sites in the United States and Puerto Rico.

Pre-assignment

Screening details:

A total of 570 subjects who received MenACYW Conjugate vaccine or Menveo vaccine in Study MET50 (NCT02199691) or Study MET43 (NCT02842853), or outside of Sanofi Pasteur trials were enrolled in the present study (MET59).

Period 1

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

Blinding implementation details:

Partially-randomised design: all subjects primed with MenACYW Conjugate vaccine who meet the inclusion/exclusion criteria were randomly assigned to Group 1, 3, or 4, while subjects primed with Menveo vaccine were automatically allocated to Group 2 (not randomised).

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: MenACYW Conjugate Vaccine

Arm description:

Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single intramuscular (IM) dose of MenACYW Conjugate vaccine, at Day 0 in the present study (MET59).

Arm type	Experimental
Investigational medicinal product name	Meningococcal polysaccharide (serogroups A, C, Y, and W) tetanus toxoid Conjugate vaccine MenACYW Conjugate vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM, single dose.

Arm title	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)

Arm description:

Subjects who received a single dose of Menveo vaccine in previous study MET50 or outside of Sanofi Pasteur trials, received a single IM dose of MenACYW Conjugate vaccine, at Day 0 in the present study (MET59).

Arm type	Experimental
Investigational medicinal product name	Meningococcal polysaccharide (serogroups A, C, Y, and W) tetanus toxoid Conjugate vaccine MenACYW Conjugate vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM, single dose.

Arm title	Group 3: MenACYW Conjugate vaccine + Trumenba vaccine

Arm description:

Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single IM dose of MenACYW Conjugate vaccine, concomitantly with 1 dose of Trumenba vaccine at Day 0 in the present study (MET59).

Arm type	Experimental
Investigational medicinal product name	Meningococcal polysaccharide (serogroups A, C, Y, and W) tetanus toxoid Conjugate vaccine MenACYW Conjugate vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM, single dose.

Investigational medicinal product name	Meningococcal Group B vaccine (Trumenba®)
Investigational medicinal product code	
Other name	Trumenba®
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM, single dose.

Arm title	Group 4: MenACYW Conjugate vaccine + Bexsero vaccine

Arm description:

Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single IM dose of MenACYW Conjugate vaccine, concomitantly with 1 dose of Bexsero vaccine at Day 0 in the present study (MET59).

Arm type	Experimental
Investigational medicinal product name	Meningococcal polysaccharide (serogroups A, C, Y, and W) tetanus toxoid Conjugate vaccine MenACYW Conjugate vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM, single dose.

Investigational medicinal product name	Meningococcal Group B vaccine (Bexsero®)
Investigational medicinal product code	
Other name	Bexsero®
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM, single dose.

Number of subjects in period 1	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)	Group 3: MenACYW Conjugate vaccine + Trumenba vaccine
Started	191	190	95
Safety Analysis Set (SAfAS)	186 [1]	184 [2]	93 [3]
Full Analysis Set (FAS)	191	190	95

Per-Protocol Analysis Set 1 (PPAS1)	46 [4]	45 [5]	0 [6]
Per-Protocol Analysis Set 2 (PPAS2)	174 [7]	176 [8]	90 [9]
Completed	187	186	95
Not completed	4	4	0
Withdrawal by parent/ guardian	1	-	-
Withdrawal by Subject	-	1	-
Protocol Violation	1	3	-
Lost to follow-up	2	-	-

Number of subjects in period 1	Group 4: MenACYW Conjugate vaccine + Bexsero vaccine
Started	94
Safety Analysis Set (SAfAS)	92
Full Analysis Set (FAS)	94
Per-Protocol Analysis Set 1 (PPAS1)	0 [10]
Per-Protocol Analysis Set 2 (PPAS2)	89 [11]
Completed	92
Not completed	2
Withdrawal by parent/ guardian	1
Withdrawal by Subject	-
Protocol Violation	1
Lost to follow-up	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: SAfAS: Subjects who had received study vaccine in MET59 and had available safety data.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: SAfAS: Subjects who had received study vaccine in MET59 and had available safety data.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: SAfAS: Subjects who had received study vaccine in MET59 and had available safety data.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: PPAS1: Subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result with no relevant protocol deviation; defined for evaluating the immune response of MenACYW vaccine measured by serum bactericidal assay using human complement (hSBA) assessed at Day 06 after vaccination in Group 1 and 2.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: PPAS1: Subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result with no relevant protocol deviation; defined for evaluating the immune response of MenACYW vaccine measured by hSBA assessed at Day 06 after vaccination in Group 1 and 2.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that

completed, minus those who left.

Justification: PPAS1: Subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result with no relevant protocol deviation; defined for evaluating the immune response of MenACYW vaccine measured by hSBA assessed at Day 06 after vaccination in Group 1 and 2.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: PPAS2: Subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result with no relevant protocol deviation; defined for evaluating the immune response of MenACYW vaccine measured by hSBA or serum bactericidal assay using baby rabbit complement (rSBA) assessed at Day 30 after vaccination

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: PPAS2: Subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result with no relevant protocol deviation; defined for evaluating the immune response of MenACYW vaccine measured by hSBA or rSBA assessed at Day 30 after vaccination.

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: PPAS2: Subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result with no relevant protocol deviation; defined for evaluating the immune response of MenACYW vaccine measured by hSBA or rSBA assessed at Day 30 after vaccination.

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: PPAS1: Subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result with no relevant protocol deviation; defined for evaluating the immune response of MenACYW vaccine measured by hSBA assessed at Day 06 after vaccination in Group 1 and 2.

[11] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: PPAS2: Subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result with no relevant protocol deviation; defined for evaluating the immune response of MenACYW vaccine measured by hSBA or rSBA assessed at Day 30 after vaccination.

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: MenACYW Conjugate Vaccine
Reporting group description:	
Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single intramuscular (IM) dose of MenACYW Conjugate vaccine, at Day 0 in the present study (MET59).	
Reporting group title	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)
Reporting group description:	
Subjects who received a single dose of Menveo vaccine in previous study MET50 or outside of Sanofi Pasteur trials, received a single IM dose of MenACYW Conjugate vaccine, at Day 0 in the present study (MET59).	
Reporting group title	Group 3: MenACYW Conjugate vaccine + Trumenba vaccine
Reporting group description:	
Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single IM dose of MenACYW Conjugate vaccine, concomitantly with 1 dose of Trumenba vaccine at Day 0 in the present study (MET59).	
Reporting group title	Group 4: MenACYW Conjugate vaccine + Bexsero vaccine
Reporting group description:	
Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single IM dose of MenACYW Conjugate vaccine, concomitantly with 1 dose of Bexsero vaccine at Day 0 in the present study (MET59).	

Reporting group values	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)	Group 3: MenACYW Conjugate vaccine + Trumenba vaccine
Number of subjects	191	190	95
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	15.4	15.8	15.1
standard deviation	± 1.59	± 1.37	± 1.12
Gender categorical Units: Subjects			
Female	99	85	41
Male	92	105	54
Race Units: Subjects			
Native Hawaiian or Other Pacific Islander	1	0	0
Black or African American	19	16	7
White	163	165	83
More than one race	8	6	5
Unknown or Not Reported	0	3	0

Reporting group values	Group 4: MenACYW Conjugate vaccine + Bexsero vaccine	Total	
Number of subjects	94	570	

Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	15.3		
standard deviation	± 1.34	-	
Gender categorical Units: Subjects			
Female	45	270	
Male	49	300	
Race Units: Subjects			
Native Hawaiian or Other Pacific Islander	1	2	
Black or African American	7	49	
White	86	497	
More than one race	0	19	
Unknown or Not Reported	0	3	

End points

End points reporting groups

Reporting group title	Group 1: MenACYW Conjugate Vaccine

Reporting group description:

Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single intramuscular (IM) dose of MenACYW Conjugate vaccine, at Day 0 in the present study (MET59).

Reporting group title	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)

Reporting group description:

Subjects who received a single dose of Menveo vaccine in previous study MET50 or outside of Sanofi Pasteur trials, received a single IM dose of MenACYW Conjugate vaccine, at Day 0 in the present study (MET59).

Reporting group title	Group 3: MenACYW Conjugate vaccine + Trumenba vaccine

Reporting group description:

Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single IM dose of MenACYW Conjugate vaccine, concomitantly with 1 dose of Trumenba vaccine at Day 0 in the present study (MET59).

Reporting group title	Group 4: MenACYW Conjugate vaccine + Bexsero vaccine

Reporting group description:

Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single IM dose of MenACYW Conjugate vaccine, concomitantly with 1 dose of Bexsero vaccine at Day 0 in the present study (MET59).

Subject analysis set title	Pooled Groups 1, 3 and 4: MenACYW Conjugate Vaccine
Subject analysis set type	Full analysis

Subject analysis set description:

Included all subjects of Groups 1, 3 and 4 who received MenACYW Conjugate vaccine in previous studies MET50 or MET43. Subjects of Group 1 received a single IM dose of MenACYW Conjugate vaccine and Group 3 and 4 subjects received a single IM dose of MenACYW Conjugate vaccine, concomitantly with 1 dose of Trumenba vaccine and Bexsero vaccine at Day 0 in the present study (MET59).

Subject analysis set title	Pooled Groups 3 and 4: MenACYW Conjugate Vaccine
Subject analysis set type	Per protocol

Subject analysis set description:

Included all subjects of Groups 3 and 4 who received MenACYW Conjugate vaccine in previous studies MET50 or MET43. Subjects of Group 3 and 4 subjects received a single IM dose of MenACYW Conjugate vaccine, concomitantly with 1 dose of Trumenba vaccine and Bexsero vaccine at Day 0 in the present study (MET59).

Primary: Percentage of Subjects With Vaccine Seroresponse Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1

End point title	Percentage of Subjects With Vaccine Seroresponse Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1[1][2]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by hSBA. The hSBA vaccine seroresponse was defined as a post-vaccination hSBA titer greater than or equal to (>=) 1:16 for subjects with pre-vaccination hSBA titer less than (<) 1:8, or a >= 4-fold increase in hSBA titer from pre-vaccination to post-vaccination for subjects with pre-vaccination hSBA titer >= 1:8. Immune response was considered sufficient if lower limit of the 1-sided 97.5% CI for percentage of subjects with hSBA seroresponse against serogroups A, C, Y and W was greater than 75%. Analysis was performed on PPAS2 population that included subjects who received 1 dose of study vaccine in MET59 and had a valid post-vaccination serology result with no relevant protocol deviation; defined for evaluating the immune response of MenACYW vaccine measured by hSBA or rSBA assessed at Day 30 after vaccination.

End point type	Primary

End point timeframe:

Day 30 (post-vaccination) in study MET59

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: There was a statistical hypothesis as described in the endpoint description but could not reported due to single arm design.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For this endpoint, data were not planned to be collected and analysed for Groups 3, and 4 as pre-specified in the protocol.

End point values	Group 1: MenACYW Conjugate Vaccine			
Subject group type	Reporting group			
Number of subjects analysed	174			
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	94.8 (90.4 to 97.6)			
Serogroup C	97.1 (93.4 to 99.1)			
Serogroup Y	98.9 (95.9 to 99.9)			
Serogroup W	97.7 (94.2 to 99.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Vaccine Seroresponse Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 2

End point title	Percentage of Subjects With Vaccine Seroresponse Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 2[3][4]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by hSBA. The hSBA vaccine seroresponse was defined as a post-vaccination hSBA titer >=1:16 for subjects with pre-vaccination hSBA titer <1:8, or a >= 4-fold increase in hSBA titer from pre-vaccination to post-vaccination for subjects with pre-vaccination hSBA titer >= 1:8. Immune response was considered sufficient if lower limit of the 1-sided 97.5% CI for percentage of subjects with hSBA seroresponse against serogroups A, C, Y and W was greater than 75%. Analysis was performed on PPAS2 population.

End point type	Primary

End point timeframe:

Day 30 (post-vaccination) in study MET59

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There was a statistical hypothesis as described in the endpoint description but could not reported due to single arm design.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the

baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: For this endpoint, data were not planned to be collected and analysed for Groups 3, and 4 as pre-specified in the protocol.

End point values	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)			
Subject group type	Reporting group			
Number of subjects analysed	176			
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	93.2 (88.4 to 96.4)			
Serogroup C	98.9 (96.0 to 99.9)			
Serogroup Y	100 (97.9 to 100)			
Serogroup W	98.9 (96.0 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Vaccine Seroresponse Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2

End point title	Percentage of Subjects With Vaccine Seroresponse Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2[5]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by hSBA. The hSBA vaccine seroresponse was defined as a post-vaccination hSBA titer >=1:16 for subjects with pre-vaccination hSBA titer <1:8, or a >= 4-fold increase in hSBA titer from pre-vaccination to post-vaccination for subjects with pre-vaccination hSBA titer >= 1:8. Analysis was performed on PPAS1 population that included subjects who received 1 dose of study vaccine in MET59 and had valid serology result with no relevant protocol deviations; defined for evaluating the immune response of MenACYW vaccine measured by hSBA assessed at Day 06 after vaccination in Groups 1 and 2.

End point type	Secondary

End point timeframe:

Day 6 (post-vaccination) in study MET59

Notes:

[5] - 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: For this endpoint, data were not planned to be collected and analysed for Groups 3, and 4 as pre-specified in the protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	45		
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	82.6 (68.6 to 92.2)	77.8 (62.9 to 88.8)		
Serogroup C	89.1 (76.4 to 96.4)	93.3 (81.7 to 98.6)		
Serogroup Y	95.7 (85.2 to 99.5)	91.1 (78.8 to 97.5)		
Serogroup W	97.8 (88.5 to 99.9)	88.9 (75.9 to 96.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Vaccine Seroprotection Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2

End point title	Percentage of Subjects With Vaccine Seroprotection Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2[6]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by hSBA. Seroprotection was defined as hSBA titer >=1:8. Analysis was performed on PPAS1 population.

End point type	Secondary

End point timeframe:

Day 6 (post-vaccination) in study MET59

Notes:

[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: For this endpoint, data were not planned to be collected and analysed for Groups 3, and 4 as pre-specified in the protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	45		
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	91.3 (79.2 to 97.6)	95.6 (84.9 to 99.5)		

Serogroup C	100 (92.3 to 100)	97.8 (88.2 to 99.9)		
Serogroup Y	97.8 (88.5 to 99.9)	100 (92.1 to 100)		
Serogroup W	100 (92.3 to 100)	100 (92.1 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Antibodies Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2

End point title	Geometric Mean Titers (GMTs) of Antibodies Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2[7]

End point description:

GMTs of antibodies against meningococcal serogroups A, C, Y, and W were measured by hSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on PPAS1 population.

End point type	Secondary

End point timeframe:

Day 6 (post-vaccination) in study MET59

Notes:

[7] - 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: For this endpoint, data were not planned to be collected and analysed for Groups 3, and 4 as pre-specified in the protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	45		
Units: titers				
geometric mean (confidence interval 95%)				
Serogroup A	289 (133 to 625)	161 (93.0 to 280)		
Serogroup C	3799 (2504 to 5763)	919 (500 to 1690)		
Serogroup Y	1658 (973 to 2826)	800 (467 to 1371)		
Serogroup W	1928 (1187 to 3131)	708 (463 to 1082)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Vaccine Seroresponse Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2

End point title	Percentage of Subjects With Vaccine Seroresponse Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2[8]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by hSBA. The hSBA vaccine seroresponse was defined as a post-vaccination hSBA titer >=1:16 for subjects with pre-vaccination hSBA titer <1:8, or a >= 4-fold increase in hSBA titer from pre-vaccination to post-vaccination for subjects with pre-vaccination hSBA titer >= 1:8. Analysis was performed on PPAS2 population.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination) in study MET59

Notes:

[8] - 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: For this endpoint, data were not planned to be collected and analysed for Groups 3, and 4 as pre-specified in the protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	176		
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	94.8 (90.4 to 97.6)	93.2 (88.4 to 96.4)		
Serogroup C	97.1 (93.4 to 99.1)	98.9 (96.0 to 99.9)		
Serogroup Y	98.9 (95.9 to 99.9)	100 (97.9 to 100)		
Serogroup W	97.7 (94.2 to 99.4)	98.9 (96.0 to 99.9)		

Statistical analyses

Statistical analysis title	Serogroup A
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)

Number of subjects included in analysis	350
Analysis specification	Pre-specified
Analysis type	other[9]
Parameter estimate	Difference in percentage
Point estimate	1.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.58
upper limit	6.95

Notes:

[9] - 95% Confidence Interval (CI) of the difference in percentage was calculated from the Wilson Score method without continuity correction.

Statistical analysis title	Serogroup C
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)
Number of subjects included in analysis	350
Analysis specification	Pre-specified
Analysis type	other[10]
Parameter estimate	Difference in percentage
Point estimate	-1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.5
upper limit	1.6

Notes:

[10] - 95% CI of the difference in percentage was calculated from the Wilson Score Method without continuity correction.

Statistical analysis title	Serogroup Y
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)
Number of subjects included in analysis	350
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	Difference in percentage
Point estimate	-1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.09
upper limit	1.14

Notes:

[11] - 95% CI of the difference in percentage was calculated from the Wilson Score Method without continuity correction.

Statistical analysis title	Serogroup W
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)

Number of subjects included in analysis	350
Analysis specification	Pre-specified
Analysis type	other[12]
Parameter estimate	Difference in percentage
Point estimate	-1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.72
upper limit	2.07

Notes:

[12] - 95% CI of the difference in percentage was calculated from the Wilson Score Method without continuity correction.

Secondary: Percentage of Subjects With Vaccine Seroprotection Against Meningococcal Serogroups A, C, Y, and W at Day 0 and at Day 30 Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2

End point title	Percentage of Subjects With Vaccine Seroprotection Against Meningococcal Serogroups A, C, Y, and W at Day 0 and at Day 30 Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2[13]

End point description:

Antibody titers against meningococcal serogroups A, C, W, and Y were measured by hSBA. Seroprotection were defined as hSBA titer >=1:8. Analysis was performed on PPAS2 population.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 (post-vaccination) in study MET59

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: For this endpoint, data were not planned to be collected and analysed for Groups 3, and 4 as pre-specified in the protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	176		
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A: Day 0	71.3 (63.9 to 77.9)	71.0 (63.7 to 77.6)		
Serogroup A: Day 30	99.4 (96.8 to 100)	99.4 (96.9 to 100)		
Serogroup C: Day 0	87.9 (82.1 to 92.4)	50.6 (42.9 to 58.2)		
Serogroup C: Day 30	100 (97.9 to 100)	100 (97.9 to 100)		
Serogroup Y: Day 0	79.9 (73.2 to 85.6)	52.8 (45.2 to 60.4)		
Serogroup Y: Day 30	100 (97.9 to 100)	100 (97.9 to 100)		
Serogroup W: Day 0	86.2 (80.2 to 91.0)	77.8 (71.0 to 83.7)		

Serogroup W: Day 30	100 (97.9 to 100)	100 (97.9 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs of Antibodies Against Meningococcal Serogroups A, C, Y, and W at Day 0 and at Day 30 Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2

End point title	GMTs of Antibodies Against Meningococcal Serogroups A, C, Y, and W at Day 0 and at Day 30 Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1 and 2[14]

End point description:

GMTs of antibodies against meningococcal serogroups A, C, W, and Y were measured by hSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on PPAS2 population.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 (post-vaccination) in study MET59

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: For this endpoint, data were not planned to be collected and analysed for Groups 3, and 4 as pre-specified in the protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	176		
Units: titers				
geometric mean (confidence interval 95%)				
Serogroup A: Day 0	11.7 (9.89 to 13.8)	11.5 (9.72 to 13.7)		
Serogroup A: Day 30	502 (388 to 649)	399 (318 to 502)		
Serogroup C: Day 0	36.6 (28.8 to 46.7)	10.2 (8.03 to 13.0)		
Serogroup C: Day 30	3708 (3146 to 4369)	2533 (2076 to 3091)		
Serogroup Y: Day 0	20.5 (16.6 to 25.2)	8.35 (6.70 to 10.4)		
Serogroup Y: Day 30	2308 (1925 to 2767)	3036 (2547 to 3620)		
Serogroup W: Day 0	27.0 (22.0 to 33.1)	14.8 (12.2 to 18.1)		
Serogroup W: Day 30	2290 (1934 to 2711)	2574 (2178 to 3041)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Vaccine Seroprotection Against Meningococcal Serogroups A, C, Y, and W at Day 0

End point title	Percentage of Subjects With Vaccine Seroprotection Against Meningococcal Serogroups A, C, Y, and W at Day 0

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by hSBA. Seroprotection was defined as hSBA titer >=1:8. Analysis was performed on full analysis set which included all subjects who had a valid pre-vaccination serology result. Here, 'n'=subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) in study MET59

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)	Group 3: MenACYW Conjugate vaccine + Trumenba vaccine	Group 4: MenACYW Conjugate vaccine + Bexsero vaccine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	191	190	95	94
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A (n=191,190,95,93)	72.3 (65.3 to 78.5)	71.1 (64.0 to 77.4)	73.7 (63.6 to 82.2)	73.1 (62.9 to 81.8)
Serogroup C (n=191,190,95,94)	86.9 (81.3 to 91.3)	52.6 (45.3 to 59.9)	86.3 (77.7 to 92.5)	85.1 (76.3 to 91.6)
Serogroup Y (n=191,190,94,94)	79.1 (72.6 to 84.6)	55.3 (47.9 to 62.5)	88.3 (80.0 to 94.0)	80.9 (71.4 to 88.2)
Serogroup W (n=191,190,95,93)	86.9 (81.3 to 91.3)	77.9 (71.3 to 83.6)	90.5 (82.8 to 95.6)	91.4 (83.8 to 96.2)

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs of Antibodies Against Meningococcal Serogroups A, C, Y, and W at Day 0

End point title	GMTs of Antibodies Against Meningococcal Serogroups A, C, Y, and W at Day 0

End point description:

GMTs of antibodies against meningococcal serogroups A, C, Y, and W were measured by hSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on full analysis set which included all subjects who had a valid pre-vaccination serology results. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) in study MET59

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)	Group 3: MenACYW Conjugate vaccine + Trumenba vaccine	Group 4: MenACYW Conjugate vaccine + Bexsero vaccine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	191	190	95	94
Units: titers				
geometric mean (confidence interval 95%)				
Serogroup A (n=191,190,95,93)	12.3 (10.5 to 14.5)	12.2 (10.2 to 14.6)	12.8 (10.0 to 16.3)	12.7 (9.70 to 16.6)
Serogroup C (n=191,190,95,94)	34.5 (27.4 to 43.6)	11.9 (9.17 to 15.3)	38.4 (27.3 to 54.0)	43.3 (29.8 to 63.0)
Serogroup Y (n=191,190,94,94)	19.8 (16.2 to 24.2)	9.19 (7.39 to 11.4)	26.0 (19.6 to 34.5)	22.0 (16.1 to 30.0)
Serogroup W (n=191,190,95,93)	27.4 (22.4 to 33.4)	15.1 (12.5 to 18.3)	28.1 (21.8 to 36.2)	32.7 (24.5 to 43.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Vaccine Seroprotection Against Meningococcal Serogroups A, C, Y, and W at Day 0 and 30 Days Post-Vaccination in Study MET50 or MET43

End point title	Percentage of Subjects Achieving Vaccine Seroprotection Against Meningococcal Serogroups A, C, Y, and W at Day 0 and 30 Days Post-Vaccination in Study MET50 or MET43[15]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by hSBA. Seroprotection was defined as hSBA titer >=1:8. Analysis was performed on full analysis set which included all subjects who had a valid pre-vaccination serology result. Here, 'number of subjects analysed' = subjects evaluable for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination), Day 30 (post-vaccination) in study MET50 or MET43

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: For this endpoint, data were planned to be collected and analysed for pooled population of groups 1, 3 and 4 as pre-specified in the protocol.

End point values	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)	Pooled Groups 1, 3 and 4: MenACYW Conjugate Vaccine		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	134	376		
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A: Day 0 of MET50 or MET43(n=134,376)	35.8 (27.7 to 44.6)	54.5 (49.3 to 59.6)		
Serogroup A: Day 30 of MET50 or MET43(n=133,376)	81.2 (73.5 to 87.5)	94.7 (91.9 to 96.7)		
Serogroup C: Day 0 of MET50 or MET43(n=134,376)	12.7 (7.6 to 19.5)	18.6 (14.8 to 22.9)		
Serogroup C: Day 30 of MET50 or MET43(n=132,376)	74.2 (65.9 to 81.5)	98.1 (96.2 to 99.2)		
Serogroup Y: Day 0 of MET50 or MET43(n=134,376)	3.7 (1.2 to 8.5)	4.5 (2.7 to 7.1)		
Serogroup Y: Day 30 of MET50 or MET43(n=133,376)	88.7 (82.1 to 93.5)	97.9 (95.9 to 99.1)		
Serogroup W: Day 0 of MET50 or MET43(n=134,376)	40.3 (31.9 to 49.1)	39.9 (34.9 to 45.0)		
Serogroup W: Day 30 of MET50 or MET43(n=133,376)	93.2 (87.5 to 96.9)	100 (99.0 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs of Antibodies Against Meningococcal Serogroups A, C, Y, and W at Day 0 and 30 Days Post Vaccination in Either Study MET50 or MET43 and Pre Vaccination in Study MET59

End point title	GMTs of Antibodies Against Meningococcal Serogroups A, C, Y, and W at Day 0 and 30 Days Post Vaccination in Either Study MET50 or MET43 and Pre Vaccination in Study MET59[16]

End point description:

GMTs of antibodies against meningococcal serogroups A, C, Y, and W were measured by hSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on full analysis set which included all subjects who had a valid pre-vaccination serology result. Here, 'number of subjects analysed' = subjects evaluable for this endpoint and 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 (post-vaccination) in study MET50 or MET43; Day 0 (pre-vaccination) in study MET59

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: For this endpoint, data were planned to be collected and analysed for pooled population of groups 1, 3 and 4, as pre-specified in the protocol.

End point values	Group 2: MenACYW Conjugate vaccine (Menveo Vaccine-primed)	Pooled Groups 1, 3 and 4: MenACYW Conjugate Vaccine		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	140	380		
Units: titers				
geometric mean (confidence interval 95%)				
Serogroup A: Day 0 of MET50 or MET43(n=134,376)	5.72 (4.75 to 6.87)	7.28 (6.53 to 8.11)		
Serogroup A: Day 30 of MET50 or MET43(n=133,376)	32.8 (25.0 to 43.1)	45.2 (39.9 to 51.1)		
Serogroup A: Day 0 of MET59 (n=140,379)	11.6 (9.41 to 14.3)	12.5 (11.1 to 14.1)		
Serogroup C: Day 0 of MET50 or MET43(n=134,376)	2.98 (2.69 to 3.30)	3.48 (3.22 to 3.76)		
Serogroup C: Day 30 of MET50 or MET43(n=132,376)	49.7 (32.4 to 76.4)	417 (348 to 500)		
Serogroup C: Day 0 of MET59 (n=140,380)	11.0 (8.09 to 14.9)	37.5 (31.6 to 44.5)		
Serogroup Y: Day 0 of MET50 or MET43(n=134,376)	2.30 (2.13 to 2.48)	2.36 (2.22 to 2.50)		
Serogroup Y: Day 30 of MET50 or MET43(n=133,376)	36.1 (27.2 to 47.8)	91.0 (78.6 to 105)		
Serogroup Y: Day 0 of MET59 (n=140,379)	8.49 (6.50 to 11.1)	21.8 (18.8 to 25.1)		
Serogroup W: Day 0 of MET50 or MET43(n=134,376)	5.54 (4.57 to 6.72)	5.34 (4.76 to 6.00)		
Serogroup W: Day 30 of MET50 or MET43(n=133,376)	45.1 (34.3 to 59.4)	82.7 (73.6 to 92.9)		
Serogroup W: Day 0 of MET59 (n=140,379)	14.9 (11.9 to 18.6)	28.8 (25.1 to 33.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Vaccine Seroresponse Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1, 3 and 4

End point title	Percentage of Subjects With Vaccine Seroresponse Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1, 3 and 4[17]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by hSBA. The hSBA vaccine seroresponse was defined as a post-vaccination hSBA titer >=1:16 for subjects with pre-

vaccination hSBA titer <1:8, or a >= 4-fold increase in hSBA titer from pre-vaccination to post-vaccination for subjects with pre-vaccination hSBA titer >= 1:8. Analysis was performed on PPAS2 population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination) in study MET59

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: For this endpoint, data were planned to be collected and analysed for individual Groups 1, 3 and 4 and for pooled population of groups 3 and 4 only, as pre-specified in the protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 3: MenACYW Conjugate vaccine + Trumenba vaccine	Group 4: MenACYW Conjugate vaccine + Bexsero vaccine	Pooled Groups 3 and 4: MenACYW Conjugate Vaccine
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	174	90	89	179
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A (n=174,90,88,178)	94.8 (90.4 to 97.6)	93.3 (86.1 to 97.5)	95.5 (88.8 to 98.7)	94.4 (89.9 to 97.3)
Serogroup C (n=174,90,88,178)	97.1 (93.4 to 99.1)	97.8 (92.2 to 99.7)	96.6 (90.4 to 99.3)	97.2 (93.6 to 99.1)
Serogroup Y (n=174,89,89,178)	98.9 (95.9 to 99.9)	98.9 (93.9 to 100)	97.8 (92.1 to 99.7)	98.3 (95.2 to 99.7)
Serogroup W (n=174,90,88,178)	97.7 (94.2 to 99.4)	98.9 (94.0 to 100)	96.6 (90.4 to 99.3)	97.8 (94.3 to 99.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Vaccine Seroprotection Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1, 3 and 4

End point title	Percentage of Subjects With Vaccine Seroprotection Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1, 3 and 4[18]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by hSBA. Seroprotection was defined as hSBA titer >=1:8. Analysis was performed on PPAS2 population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 (post-vaccination) in study MET59

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For this endpoint, data were planned to be collected and analysed for individual Groups 1, 3 and 4 and for pooled population of groups 3 and 4, as pre-specified in the protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 3: MenACYW Conjugate vaccine + Trumenba vaccine	Group 4: MenACYW Conjugate vaccine + Bexsero vaccine	Pooled Groups 3 and 4: MenACYW Conjugate Vaccine
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	174	90	89	179
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A: Day 0 (n=174,90,88,178)	71.3 (63.9 to 77.9)	73.3 (63.0 to 82.1)	71.6 (61.0 to 80.7)	72.5 (65.3 to 78.9)
Serogroup A: Day 30 (n=174,90,89,179)	99.4 (96.8 to 100)	98.9 (94.0 to 100)	100 (95.9 to 100)	99.4 (96.9 to 100)
Serogroup C: Day 0 (n=174,90,89,179)	87.9 (82.1 to 92.4)	86.7 (77.9 to 92.9)	86.5 (77.6 to 92.8)	86.6 (80.7 to 91.2)
Serogroup C: Day 30 (n=174,90,88,178)	100 (97.9 to 100)	100 (96.0 to 100)	100 (95.9 to 100)	100 (97.9 to 100)
Serogroup Y: Day 0 (n=174,89,89,178)	79.9 (73.2 to 85.6)	89.9 (81.7 to 95.3)	80.9 (71.2 to 88.5)	85.4 (79.3 to 90.2)
Serogroup Y: Day 30 (n=174,90,89,179)	100 (97.9 to 100)	100 (96.0 to 100)	100 (95.9 to 100)	100 (98.0 to 100)
Serogroup W: Day 0 (n=174,90,88,178)	86.2 (80.2 to 91.0)	91.1 (83.2 to 96.1)	90.9 (82.9 to 96.0)	91.0 (85.8 to 94.8)
Serogroup W: Day 30 (n=174,90,89,179)	100 (97.9 to 100)	100 (96.0 to 100)	100 (95.9 to 100)	100 (98.0 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs of Antibodies Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1, 3 and 4

End point title	GMTs of Antibodies Against Meningococcal Serogroups A, C, Y, and W Following Vaccination With MenACYW Conjugate Vaccine in Study MET59: Group 1, 3 and 4[19]

End point description:

GMTs of antibodies against meningococcal serogroups A, C, Y, and W were measured by hSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on PPAS2 population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 (post-vaccination) in study MET59

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: For this endpoint, data were planned to be collected and analysed for individual Groups 1, 3 and 4 and for pooled population of groups 3 and 4, as pre-specified in the protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 3: MenACYW Conjugate vaccine + Trumenba vaccine	Group 4: MenACYW Conjugate vaccine + Bexsero vaccine	Pooled Groups 3 and 4: MenACYW Conjugate Vaccine
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	174	90	89	179
Units: titers				
geometric mean (confidence interval 95%)				
Serogroup A: Day 0 (n=174,90,88,178)	11.7 (9.89 to 13.8)	12.5 (9.78 to 16.0)	12.3 (9.37 to 16.2)	12.4 (10.4 to 14.9)
Serogroup A: Day 30 (n=174,90,89,179)	502 (388 to 649)	593 (426 to 825)	667 (477 to 933)	629 (498 to 794)
Serogroup C: Day 0 (n=174,90,89,179)	36.6 (28.8 to 46.7)	37.6 (26.6 to 53.3)	42.4 (29.4 to 61.0)	39.9 (31.1 to 51.2)
Serogroup C: Day 30 (n=174,90,88,178)	3708 (3146 to 4369)	4741 (3882 to 5791)	3472 (2667 to 4518)	4064 (3446 to 4793)
Serogroup Y: Day 0 (n=174,89,89,178)	20.5 (16.6 to 25.2)	25.5 (19.4 to 33.6)	21.0 (15.4 to 28.7)	23.2 (18.9 to 28.5)
Serogroup Y: Day 30 (n=174,90,89,179)	2308 (1925 to 2767)	2600 (2042 to 3311)	2469 (1881 to 3241)	2534 (2117 to 3034)
Serogroup W: Day 0 (n=174,90,88,178)	27.0 (22.0 to 33.1)	28.3 (22.0 to 36.4)	30.0 (22.5 to 40.1)	29.1 (24.1 to 35.2)
Serogroup W: Day 30 (n=174,90,89,179)	2290 (1934 to 2711)	2702 (2134 to 3422)	2064 (1601 to 2662)	2363 (1988 to 2810)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited adverse event (AE) data were collected from Day 0 (pre-vaccination) up to Day 30 (post-vaccination) in MET59. Solicited reactions (SR): within 7 days post-vaccination in MET59. Serious AEs data: up to 30 days days post-vaccination in MET59.

Adverse event reporting additional description:

Analysis performed on SafAS population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Group 1: MenACYW Conjugate Vaccine

Reporting group description:

Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single IM dose of MenACYW Conjugate vaccine, at Day 0 in the present study (MET59).

Reporting group title	Group 2: MenACYW Conjugate Vaccine (Menveo Vaccine-primed)

Reporting group description:

Subjects who received a single dose of Menveo vaccine in previous study MET50 or outside of Sanofi Pasteur trials, received a single IM dose of MenACYW Conjugate vaccine, at Day 0 in the present study (MET59).

Reporting group title	Group 3: MenACYW Conjugate Vaccine + Trumenba Vaccine

Reporting group description:

Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single IM dose of MenACYW Conjugate vaccine, concomitantly with 1 dose of Trumenba vaccine at Day 0 in the present study (MET59).

Reporting group title	Group 4: MenACYW Conjugate Vaccine + Bexsero Vaccine

Reporting group description:

Subjects who received a single dose of MenACYW Conjugate vaccine in previous studies MET50 or MET43, received a single IM dose of MenACYW Conjugate vaccine, concomitantly with 1 dose of Bexsero vaccine at Day 0 in the present study (MET59).

Serious adverse events	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate Vaccine (Menveo Vaccine-primed)	Group 3: MenACYW Conjugate Vaccine + Trumenba Vaccine
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 186 (1.08%)	2 / 184 (1.09%)	2 / 93 (2.15%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Accidental Overdose			

subjects affected / exposed	0 / 186 (0.00%)	0 / 184 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Major Depression			
subjects affected / exposed	0 / 186 (0.00%)	0 / 184 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal Ideation			
subjects affected / exposed	1 / 186 (0.54%)	1 / 184 (0.54%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 186 (0.54%)	1 / 184 (0.54%)	0 / 93 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 4: MenACYW Conjugate Vaccine + Bexsero Vaccine		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 92 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 92 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Major Depression			
subjects affected / exposed	0 / 92 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal Ideation			

subjects affected / exposed	0 / 92 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 92 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1: MenACYW Conjugate Vaccine	Group 2: MenACYW Conjugate Vaccine (Menveo Vaccine-primed)	Group 3: MenACYW Conjugate Vaccine + Trumenba Vaccine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	129 / 186 (69.35%)	116 / 184 (63.04%)	83 / 93 (89.25%)
Nervous system disorders			
Headache			
subjects affected / exposed	68 / 186 (36.56%)	67 / 184 (36.41%)	41 / 93 (44.09%)
occurrences (all)	69	67	42
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	12 / 186 (6.45%)	10 / 184 (5.43%)	15 / 93 (16.13%)
occurrences (all)	12	10	15
Injection Site Pain			
subjects affected / exposed	71 / 186 (38.17%)	63 / 184 (34.24%)	77 / 93 (82.80%)
occurrences (all)	71	63	114
Injection Site Swelling			
subjects affected / exposed	10 / 186 (5.38%)	3 / 184 (1.63%)	12 / 93 (12.90%)
occurrences (all)	10	3	13
Malaise			
subjects affected / exposed	50 / 186 (26.88%)	47 / 184 (25.54%)	36 / 93 (38.71%)
occurrences (all)	50	47	36
Musculoskeletal and connective tissue disorders			
Myalgia			

subjects affected / exposed	61 / 186 (32.80%)	64 / 184 (34.78%)	60 / 93 (64.52%)
occurrences (all)	61	64	61
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 186 (4.84%)	6 / 184 (3.26%)	5 / 93 (5.38%)
occurrences (all)	10	6	5
Upper Respiratory Tract Infection			
subjects affected / exposed	10 / 186 (5.38%)	8 / 184 (4.35%)	1 / 93 (1.08%)
occurrences (all)	10	8	1

Non-serious adverse events	Group 4: MenACYW Conjugate Vaccine + Bexsero Vaccine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	88 / 92 (95.65%)		
Nervous system disorders			
Headache			
subjects affected / exposed	36 / 92 (39.13%)		
occurrences (all)	36		
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	14 / 92 (15.22%)		
occurrences (all)	19		
Injection Site Pain			
subjects affected / exposed	85 / 92 (92.39%)		
occurrences (all)	123		
Injection Site Swelling			
subjects affected / exposed	15 / 92 (16.30%)		
occurrences (all)	19		
Malaise			
subjects affected / exposed	37 / 92 (40.22%)		
occurrences (all)	37		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	58 / 92 (63.04%)		
occurrences (all)	58		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 92 (2.17%) 2		
Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	1 / 92 (1.09%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 January 2020	Following changes were made: •Visit 3 was changed to Visit 2 for the main cohort (all subjects excluding the subset) following updates to the table of study procedures. •Visit 3 was replaced by Day 30 since this naming convention applies for all study subjects (main cohort and subset cohort).•FAS1 (full analysis set for Day 06) and FAS2 (full analysis set for Day 30) populations were defined (2 FAS analysis sets instead of 1). •Additional details were included to the statistical analysis: Geometric Mean Titer Ratio (GMTR) was added.
10 April 2020	Following changes were made: •Were completed to comply with changes requested by Center for Biologics Evaluation and Research (CBER)/Food and Drug Administration (FDA): - the primary objective and endpoint, and related statistical analyses, -one secondary objective; -observational objectives; calculation of sample size.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported