



Clinical trial results:

A Phase IIIb, Open-label, Multi-center Study to Evaluate the Immunogenicity and Safety of a Booster Dose and Describe the Immune Persistence of MenACYW Conjugate Vaccine with 5-and/or 10-year Booster Doses in Children and Adolescents who had been Primed with MenACYW Conjugate Vaccine as Toddlers

Summary

EudraCT number	2021-000104-38
Trial protocol	FI HU DE ES
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	08 March 2024
First version publication date	08 March 2024

Trial information

Trial identification

Sponsor protocol code	MEQ00073
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04936685
WHO universal trial number (UTN)	U1111-1255-4941

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	Discovery Drive, Swiftwater, Pennsylvania, United States, 18370-0187
Public contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.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?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	08 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 March 2023
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the vaccine seroresponse sufficiency of meningococcal serogroups A, C, W, and Y after the administration of a booster dose of MenACYW conjugate vaccine in subjects who received 1 dose of MenACYW conjugate vaccine approximately 5 years earlier as toddlers.

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	23 August 2022
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 41
Country: Number of subjects enrolled	Germany: 58
Country: Number of subjects enrolled	Hungary: 59
Country: Number of subjects enrolled	Spain: 51
Worldwide total number of subjects	209
EEA total number of subjects	209

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)	209
Adolescents (12-17 years)	0

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 26 centres in 4 countries from 23 August 2022 to 06 February 2023.

Pre-assignment

Screening details:

A total of 209 subjects were enrolled in this study. Results has been reported as per the primary completion date of 09 March 2023. Final analysis results will be reported at later date.

Period 1

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

Arms

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

Arm description:

Subjects received a first intramuscular (IM) booster dose of 0.5 millilitre (mL) of Meningococcal polysaccharide (Serogroups A, C, Y and W) (MenACYW conjugate vaccine) at Day 1 (visit 1, at child age approximately 5 years post priming dose as toddlers in study MET51) and will receive a second booster dose at Year 5 of the study (visit 3, at adolescent age approximately 5 years post booster dose as children in this study).

Arm type	Experimental
Investigational medicinal product name	MenACYW conjugate vaccine
Investigational medicinal product code	
Other name	MenQuadfi®
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered MenACYW conjugate vaccine through IM injection in the deltoid muscle of arm at Day 1 and at Year 5 of the study.

Arm title	MenACYW: Group 2
------------------	------------------

Arm description:

Subjects will receive a single IM booster dose of 0.5 mL of MenACYW conjugate vaccine at Year 5 (visit 2) of the study (approximately 10 years post priming dose as toddlers in study MET51).

Arm type	Experimental
Investigational medicinal product name	MenACYW conjugate vaccine
Investigational medicinal product code	
Other name	MenQuadfi®
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects will be administered MenACYW conjugate vaccine through IM injection in the deltoid muscle of arm at Year 5 of the study.

Number of subjects in period 1	MenACYW: Group 1	MenACYW: Group 2
Started	93	116
Completed	92	116
Not completed	1	0
Protocol Violation	1	-

Baseline characteristics

Reporting groups

Reporting group title	MenACYW: Group 1
Reporting group description:	
Subjects received a first intramuscular (IM) booster dose of 0.5 millilitre (mL) of Meningococcal polysaccharide (Serogroups A, C, Y and W) (MenACYW conjugate vaccine) at Day 1 (visit 1, at child age approximately 5 years post priming dose as toddlers in study MET51) and will receive a second booster dose at Year 5 of the study (visit 3, at adolescent age approximately 5 years post booster dose as children in this study).	
Reporting group title	MenACYW: Group 2
Reporting group description:	
Subjects will receive a single IM booster dose of 0.5 mL of MenACYW conjugate vaccine at Year 5 (visit 2) of the study (approximately 10 years post priming dose as toddlers in study MET51).	

Reporting group values	MenACYW: Group 1	MenACYW: Group 2	Total
Number of subjects	93	116	209
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	6.28	6.26	
standard deviation	± 0.578	± 0.440	-
Gender categorical			
Units: Subjects			
Female	35	60	95
Male	58	56	114
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	93	113	206
More than one race	0	1	1
Unknown or Not Reported	0	2	2

End points

End points reporting groups

Reporting group title	MenACYW: Group 1
Reporting group description: Subjects received a first intramuscular (IM) booster dose of 0.5 millilitre (mL) of Meningococcal polysaccharide (Serogroups A, C, Y and W) (MenACYW conjugate vaccine) at Day 1 (visit 1, at child age approximately 5 years post priming dose as toddlers in study MET51) and will receive a second booster dose at Year 5 of the study (visit 3, at adolescent age approximately 5 years post booster dose as children in this study).	
Reporting group title	MenACYW: Group 2
Reporting group description: Subjects will receive a single IM booster dose of 0.5 mL of MenACYW conjugate vaccine at Year 5 (visit 2) of the study (approximately 10 years post priming dose as toddlers in study MET51).	

Primary: Group 1: Percentage of Subjects With Sufficiency of Serum Bactericidal Assay Using Human Complement (hSBA) Vaccine Seroresponse at 30 Days Post Booster Dose

End point title	Group 1: Percentage of Subjects With Sufficiency of Serum Bactericidal Assay Using Human Complement (hSBA) Vaccine Seroresponse at 30 Days Post Booster Dose ^{[1][2]}
End point description: Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. hSBA vaccine seroresponse for serogroups A, C, W, and Y was defined as: percentage of subjects with a pre-vaccination titer < 1:8, who had achieved a post-vaccination titer ≥ 1:16 or subjects with a pre-vaccination titer ≥ 1:8, who had achieved a post-vaccination titer at least 4-fold greater than the pre-vaccination titer. The seroresponse sufficiency was demonstrated if the lower limit of 1-sided 97.5% confidence interval (CI) is > 75%. The Per-Protocol Analysis Sets 1 (PPAS1) was a subset of the Full analysis set (FAS). The FAS consisted of subjects who had received the study vaccine and had a valid post-vaccination serology result 5-years after priming vaccination at visit 1. Here, n= number of subjects whose titers met the hSBA vaccine seroresponse criteria are analysed and 9999= Only 1-sided CI was determined.	
End point type	Primary
End point timeframe: Baseline (Day 1) and 30 days after the MenACYW conjugate vaccine 5-year booster dose. Assessed until primary analysis date.	
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: As the endpoint is descriptive in nature, no statistical analysis is provided.

[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: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: percentage of subjects				
number (confidence interval 97.5%)				
Serogroup A (n= 82)	93.2 (85.7 to 9999)			
Serogroup C (n= 86)	97.7 (92.0 to 9999)			

Serogroup W (n= 87)	98.9 (93.8 to 99.9)			
Serogroup Y (n= 87)	98.9 (93.8 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Persistence of Meningococcal (Groups 1 and 2): Percentage of Subjects Achieving Titer (Seroprotection) $\geq 1:8$ hSBA and Serum Bactericidal Assay Using Baby Rabbit Complement (rSBA) Titer $\geq 1:8$ Approximately 5 Years After the Primary Vaccination

End point title	Antibody Persistence of Meningococcal (Groups 1 and 2): Percentage of Subjects Achieving Titer (Seroprotection) $\geq 1:8$ hSBA and Serum Bactericidal Assay Using Baby Rabbit Complement (rSBA) Titer $\geq 1:8$ Approximately 5 Years After the Primary Vaccination
-----------------	---

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA and the rSBA and the results were expressed as vaccine seroprotection. Seroprotection rate is defined as percentage of subjects with hSBA titer and rSBA titer ≥ 1.8 who received MenACYW conjugate vaccine 5 years earlier. Antibody persistence of meningococcal serogroups A, C, W, and Y in children at 5 years (Groups 1 and 2). The FAS3 consisted of subjects who had a valid baseline serology results (hSBA or rSBA accordingly). Only data from the subjects analysed were reported. Here, n= number of subjects analysed for each specific serogroup.

End point type	Secondary
----------------	-----------

End point timeframe:

Day 1 (Visit 1) up to 5 year after the administration of a priming dose as toddlers in study MET51.

End point values	MenACYW: Group 1	MenACYW: Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	116		
Units: percentage of subjects				
number (confidence interval 95%)				
hSBA titer ≥ 1.8 , Serogroup A (n= 72, 86)	78.3 (68.4 to 86.2)	74.1 (65.2 to 81.8)		
hSBA titer ≥ 1.8 , Serogroup C (n= 77, 100)	83.7 (74.5 to 90.6)	86.2 (78.6 to 91.9)		
hSBA titer ≥ 1.8 , Serogroup W (n= 78, 98)	84.8 (75.8 to 91.4)	84.5 (76.6 to 90.5)		
hSBA titer ≥ 1.8 , Serogroup Y (n= 66, 77)	71.7 (61.4 to 80.6)	66.4 (57.0 to 74.9)		
rSBA titer ≥ 1.8 , Serogroup A (n= 66, 71)	71.7 (61.4 to 80.6)	61.7 (52.2 to 70.6)		
rSBA titer ≥ 1.8 , Serogroup C (n= 55, 68)	59.8 (49.0 to 69.9)	58.6 (49.1 to 67.7)		
rSBA titer ≥ 1.8 , Serogroup W (n= 53, 65)	57.6 (46.9 to 67.9)	58.0 (48.3 to 67.3)		
rSBA titer ≥ 1.8 , Serogroup Y (n= 56, 66)	62.9 (52.0 to 72.9)	60.6 (50.7 to 69.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers Against Meningococcal Serogroups A, C, W, and Y

End point title	Geometric Mean Titers Against Meningococcal Serogroups A, C, W, and Y ^[3]
-----------------	--

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA and the rSBA and the results were expressed as geometric mean titers. The PPAS is a subset of the FAS and hSBA and rSBA PPAS1 individually consisted of subjects for Group 1 visit 1. Only data from the subjects analysed were reported. Here, n= number of subjects analysed at specific time point.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline (Day 1) and Day 31 after the administration of a 5-year booster dose. Assessed until primary analysis date.

Notes:

[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: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: titer				
geometric mean (confidence interval 95%)				
Day 1: hSBA, Serogroup A (n= 88)	17.2 (12.6 to 23.3)			
Day 31: hSBA, Serogroup A (n= 88)	1143 (820 to 1594)			
Day 1: hSBA, Serogroup C (n= 88)	36.9 (25.7 to 52.9)			
Day 31: hSBA, Serogroup C (n= 88)	8933 (6252 to 12764)			
Day 1: hSBA, Serogroup Y (n= 88)	14.6 (10.8 to 19.7)			
Day 31: hSBA, Serogroup Y (n= 88)	3727 (2908 to 4776)			
Day 1: hSBA, Serogroup W (n= 88)	29.3 (21.7 to 39.7)			
Day 31: hSBA, Serogroup W (n= 88)	8656 (6393 to 11721)			
Day 1: rSBA, Serogroup A (n= 88)	150 (81.7 to 275)			
Day 31: rSBA, Serogroup A (n= 88)	8454 (6869 to 10405)			
Day 1: rSBA, Serogroup C (n= 88)	31.5 (18.8 to 52.8)			

Day 31: rSBA, Serogroup C (n= 88)	20427 (14379 to 29018)			
Day 1: rSBA, Serogroup Y (n= 85)	64.5 (35.0 to 119)			
Day 31: rSBA, Serogroup Y (n= 88)	7814 (6111 to 9991)			
Day 1: rSBA, Serogroup W (n= 88)	49.7 (26.6 to 93.0)			
Day 31: rSBA, Serogroup W (n= 88)	23354 (17251 to 31615)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titer $\geq 1:4$ and $\geq 1:8$

End point title	Percentage of Subjects With hSBA Titer $\geq 1:4$ and $\geq 1:8$ ^[4]
-----------------	---

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. hSBA vaccine seroresponse is defined as a post-vaccination titer $\geq 1:16$ for subjects with pre-vaccination hSBA titer $< 1:8$, or a post-vaccination titer ≥ 4 -fold increase at post baseline for subjects with pre-vaccination hSBA titer $\geq 1:8$. The PPAS is a subset of the FAS and hSBA PPAS1 consisted of subjects for Group 1.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline (Day 1) and Day 31 after the administration of a 5-year booster dose. Assessed until primary analysis date.

Notes:

[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: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: percentage of subjects				
number (confidence interval 95%)				
Day 1: hSBA $\geq 1:4$ titer, Serogroup A	93.2 (85.7 to 97.5)			
Day 31: hSBA $\geq 1:4$ titer, Serogroup A	100 (95.9 to 100)			
Day 1: hSBA $\geq 1:8$ titer, Serogroup A	78.4 (68.4 to 86.5)			
Day 31: hSBA $\geq 1:8$ titer, Serogroup A	98.9 (93.8 to 100)			
Day 1: hSBA $\geq 1:4$ titer, Serogroup C	86.4 (77.4 to 92.8)			
Day 31: hSBA $\geq 1:4$ titer, Serogroup C	97.7 (92.0 to 99.7)			
Day 1: hSBA $\geq 1:8$ titer, Serogroup C	84.1 (74.8 to 91.0)			
Day 31: hSBA $\geq 1:8$ titer, Serogroup C	97.7 (92.0 to 99.7)			

Day 1: hSBA \geq 1:4 titer, Serogroup Y	78.4 (68.4 to 86.5)			
Day 31: hSBA \geq 1:4 titer, Serogroup Y	100 (95.9 to 100)			
Day 1: hSBA \geq 1:8 titer, Serogroup Y	73.9 (63.4 to 82.7)			
Day 31: hSBA \geq 1:8 titer, Serogroup Y	100 (95.9 to 100)			
Day 1: hSBA \geq 1:4 titer, Serogroup W	95.5 (88.8 to 98.7)			
Day 31: hSBA \geq 1:4 titer, Serogroup W	100 (95.9 to 100)			
Day 1: hSBA \geq 1:8 titer, Serogroup W	85.2 (76.1 to 91.9)			
Day 31: hSBA \geq 1:8 titer, Serogroup W	100 (95.9 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With rSBA Titer \geq 1:8 and \geq 1:128

End point title	Percentage of Subjects With rSBA Titer \geq 1:8 and \geq
-----------------	--

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the rSBA. rSBA vaccine seroresponse is defined as a post-vaccination titer \geq 1:32 for subjects with pre-vaccination rSBA titer $<$ 1:8, or a post-vaccination titer \geq 4-fold increase at post baseline for subjects with pre-vaccination rSBA titer \geq 1:8. The PPAS is a subset of the FAS and rSBA PPAS1 consisted of subjects for Group 1. Only data from the subjects analysed were reported. Here, n= number of subjects analysed at specific time point.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline (Day 1) and Day 31 after the administration of a 5-year booster dose. Assessed until primary analysis date.

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: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: percentage of subjects				
number (confidence interval 95%)				
Day 1: rSBA \geq 1:8 titer, Serogroup A (n= 88)	72.7 (62.2 to 81.7)			
Day 31: rSBA \geq 1:8 titer, Serogroup A (n= 88)	100 (95.9 to 100)			
Day 1: rSBA \geq 1:128 titer, Serogroup A (n= 88)	64.8 (53.9 to 74.7)			
Day 31: rSBA \geq 1:128 titer, Serogroup A (n= 88)	100 (95.9 to 100)			
Day 1: rSBA \geq 1:8 titer, Serogroup C (n= 88)	62.5 (51.5 to 72.6)			

Day 31: rSBA \geq 1:8 titer, Serogroup C (n= 88)	98.9 (93.8 to 100)			
Day 1: rSBA \geq 1:128 titer, Serogroup C (n= 88)	37.5 (27.4 to 48.5)			
Day 31: rSBA \geq 1:128 titer, Serogroup C (n= 88)	98.9 (93.8 to 100)			
Day 1: rSBA \geq 1:8 titer, Serogroup Y (n= 85)	63.5 (52.4 to 73.7)			
Day 31: rSBA \geq 1:8 titer, Serogroup Y (n= 88)	98.9 (93.8 to 100)			
Day 1: rSBA \geq 1:128 titer, Serogroup Y (n= 85)	56.5 (45.3 to 67.2)			
Day 31: rSBA \geq 1:128 titer, Serogroup Y (n= 88)	98.9 (93.8 to 100)			
Day 1: rSBA \geq 1:8 titer, Serogroup W (n= 88)	58.0 (47.0 to 68.4)			
Day 31: rSBA \geq 1:8 titer, Serogroup W (n= 88)	98.9 (93.8 to 100)			
Day 1: rSBA \geq 1:128 titer, Serogroup W (n= 88)	50.0 (39.1 to 60.9)			
Day 31: rSBA \geq 1:128 titer, Serogroup W (n= 88)	98.9 (93.8 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titer \geq 4-Fold Rise From Pre-Vaccination to Post-Vaccination

End point title	Percentage of Subjects With hSBA Titer \geq 4-Fold Rise From Pre-Vaccination to Post-Vaccination ^[6]
-----------------	---

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. hSBA vaccine seroresponse is defined as a post-vaccination titer \geq 1:16 for subjects with pre-vaccination hSBA titer $<$ 1:8, or a post-vaccination titer \geq 4-fold increase at post baseline for subjects with pre-vaccination hSBA titer \geq 1:8. The PPAS is a subset of the FAS and hSBA PPAS1 consisted of subjects for Group 1.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline (Day 1) and Day 31 after the administration of a 5-year booster dose. Assessed until primary analysis date.

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: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A	93.2 (85.7 to 97.5)			
Serogroup C	97.7 (92.0 to 99.7)			

Serogroup Y	98.9 (93.8 to 100)			
Serogroup W	98.9 (93.8 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With rSBA Titer \geq 4-Fold Rise From Pre-Vaccination to Post-Vaccination

End point title	Percentage of Subjects With rSBA Titer \geq 4-Fold Rise From Pre-Vaccination to Post-Vaccination ^[7]
-----------------	---

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the rSBA. rSBA vaccine seroresponse is defined as a post-vaccination titer \geq 1:32 for subjects with pre-vaccination rSBA titer $<$ 1:8, or a post-vaccination titer \geq 4-fold increase at post baseline for subjects with pre-vaccination rSBA titer \geq 1:8. The PPAS is a subset of the FAS and rSBA PPAS1 consisted of subjects for Group 1. Only data from the subjects analysed were reported. Here, n= number of subjects analysed for each specific serogroup.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline (Day 1) and Day 31 after the administration of a 5-year booster dose. Assessed until primary analysis date.

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: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A (n= 88)	89.8 (81.5 to 95.2)			
Serogroup C (n= 88)	96.6 (90.4 to 99.3)			
Serogroup Y (n= 85)	91.8 (83.8 to 96.6)			
Serogroup W (n= 88)	97.7 (92.0 to 99.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With \geq 0.01 International Units (IU)/mL and \geq 0.1 IU/mL Anti-Tetanus Antibody Concentration

End point title	Percentage of Subjects With \geq 0.01 International Units (IU)
-----------------	--

End point description:

Anti-tetanus antibodies were measured by diphtheria, tetanus, pertussis multiplexed electrochemiluminescent (DTP-ECL) assay, a multiplexed serological assay that allowed for the simultaneous quantification of human antibodies to 6 specific antigens including diphtheria toxoid, tetanus toxoid, and 4 pertussis antigens: pertussis toxin, filamentous hemagglutinin, fimbriae and pertactin. The captured antibodies were then detected using a sulfotag-conjugated anti-human immunoglobulin (Ig)G conjugate. The PPAS is a subset of the FAS and hSBA PPAS1 consisted of subjects for Group 1.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline (Day 1) and Day 31 after the administration of a 5-year booster dose. Assessed until primary analysis date.

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: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: percentage of subjects				
number (confidence interval 95%)				
Day 1: ≥ 0.01 IU/mL	100 (95.9 to 100)			
Day 31: ≥ 0.01 IU/mL	100 (95.9 to 100)			
Day 1: ≥ 0.1 IU/mL	95.5 (88.8 to 98.7)			
Day 31: ≥ 0.1 IU/mL	100 (95.9 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentrations of Anti-Tetanus Antibody Concentration

End point title	Geometric Mean Concentrations of Anti-Tetanus Antibody Concentration ^[9]
-----------------	---

End point description:

Anti-tetanus antibodies were measured by DTP-ECL assay, a multiplexed serological assay that allowed for the simultaneous quantification of human antibodies to 6 specific antigens including diphtheria toxoid, tetanus toxoid, and 4 pertussis antigens: pertussis toxin, filamentous haemagglutinin, fimbriae and pertactin. The captured antibodies were then detected using a sulfotag-conjugated anti-human Ig G conjugate. The PPAS is a subset of the FAS and hSBA PPAS1 consisted of subjects for Group 1.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline (Day 1) and Day 31 after the administration of a 5-year booster dose. Assessed until primary analysis date.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: IU/mL				
geometric mean (confidence interval 95%)				
Day 1	2.41 (1.77 to 3.30)			
Day 31	13.7 (12.0 to 15.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Immediate Unsolicited Systemic Adverse Events (AEs)

End point title	Number of Subjects With Immediate Unsolicited Systemic Adverse Events (AEs) ^[10]
-----------------	---

End point description:

An AE is any untoward medical occurrence in a subject or clinical study subject, temporally associated with the use of study vaccine, whether or not considered related to the study vaccine. An unsolicited AE is an observed AE that does not fulfill the conditions of solicited reactions (i.e, pre-listed in the case report book (CRB) in terms of diagnosis and/or onset window post-vaccination). The Safety analysis set 1 (SafAS 1) consisted of subjects who had received the study vaccine 5 years after priming vaccination (Visit 1) and had any safety data available (Group 1).

End point type	Secondary
----------------	-----------

End point timeframe:

Within 30 minutes after vaccination. Assessed until primary analysis date.

Notes:

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

Justification: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: subjects	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Solicited Injection Site Reactions and Systemic Reactions

End point title	Number of Subjects With Solicited Injection Site Reactions and Systemic Reactions ^[11]
-----------------	---

End point description:

All noxious and unintended responses to a study vaccine related to any dose was considered adverse reactions (AR). A solicited reaction is an "expected" AR (sign or symptom) observed and reported under the conditions (nature and onset) pre-listed in the protocol and CRB. An injection/administration site reaction is an AR at and around the injection/administration site. Injection/administration site reactions are commonly inflammatory reactions. They were considered to be related to the study vaccine administered. Systemic reactions were all ARs that were not injection or administration site reactions and included systemic manifestations such as headache, fever, as well as localised or topical manifestations that are not associated with the vaccination or administration site. The SafAS 1 consisted of subjects who had received the study vaccine 5 years after priming vaccination (Visit 1) and had any safety data available (Group 1).

End point type	Secondary
----------------	-----------

End point timeframe:

7 days after vaccination. Assessed until primary analysis date.

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: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: subjects				
Solicited injection site reactions	67			
Solicited systemic reactions	45			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Unsolicited AEs

End point title	Number of Subjects With Unsolicited AEs ^[12]
-----------------	---

End point description:

An AE is any untoward medical occurrence in a subject or clinical study subject, temporally associated with the use of study vaccine, whether or not considered related to the study vaccine. An unsolicited AE is an observed AE that does not fulfill the conditions of solicited reactions (i.e. pre-listed in the CRB in terms of diagnosis and/or onset window post-vaccination). Unsolicited AEs included both serious and non-serious unsolicited AEs. The SafAS 1 consisted of subjects who had received the study vaccine 5 years after priming vaccination (Visit 1) and had any safety data available (Group 1).

End point type	Secondary
----------------	-----------

End point timeframe:

Within 30 days after vaccination. Assessed until primary analysis date.

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: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: subjects	28			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious AEs (SAEs) and Adverse Event of Special Interest (AESI)

End point title	Number of Subjects With Serious AEs (SAEs) and Adverse Event of Special Interest (AESI) ^[13]
-----------------	---

End point description:

A SAEs is defined as any untoward medical occurrence, at any dose that resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent disability/incapacity, was a congenital anomaly/birth defect, or other important medical event. An AESI (serious or non-serious) is defined as one of scientific and medical concern specific to the Sponsor's study vaccination or program, for which ongoing monitoring and rapid communication by the Investigator to the Sponsor was appropriate. The SafAS 1 consisted of subjects who had received the study vaccine 5 years after priming vaccination (Visit 1) and had any safety data available (Group 1).

End point type	Secondary
----------------	-----------

End point timeframe:

From the first study vaccine administration to the last study vaccine administration (approximately 5.5 years). Assessed until primary analysis date.

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: Only subjects in reporting group "MenACYW: Group 1" were analysed at the time of primary analysis date.

End point values	MenACYW: Group 1			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: subjects				
SAE	3			
AESI	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first study vaccine administration up to primary completion date of 09 March 2023, approximately 28 weeks.

Adverse event reporting additional description:

Analysis was performed on SafAS1 population.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	26.0
--------------------	------

Reporting groups

Reporting group title	MenACYW Group 1
-----------------------	-----------------

Reporting group description:

Subjects received a first IM booster dose of 0.5 mL of MenACYW conjugate vaccine at Day 1 (visit 1, at child age approximately 5 years post priming dose as toddlers in study MET51).

Serious adverse events	MenACYW Group 1		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 93 (3.23%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Wrist Fracture			
subjects affected / exposed	1 / 93 (1.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Giardiasis			
subjects affected / exposed	1 / 93 (1.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 93 (1.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	MenACYW Group 1		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	72 / 93 (77.42%)		
Nervous system disorders			
Headache			
subjects affected / exposed	20 / 93 (21.51%)		
occurrences (all)	20		
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	36 / 93 (38.71%)		
occurrences (all)	36		
Injection Site Pain			
subjects affected / exposed	60 / 93 (64.52%)		
occurrences (all)	60		
Injection Site Swelling			
subjects affected / exposed	28 / 93 (30.11%)		
occurrences (all)	28		
Malaise			
subjects affected / exposed	23 / 93 (24.73%)		
occurrences (all)	23		
Pyrexia			
subjects affected / exposed	14 / 93 (15.05%)		
occurrences (all)	14		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	31 / 93 (33.33%)		
occurrences (all)	31		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 February 2022	Amended to add a study arm in order to describe the immunogenicity and safety of a booster dose and the persistence of a priming dose of MenACYW conjugate vaccine (MenQuadfi®) in adolescents who had been vaccinated with MenACYW conjugate vaccine approximately 10 years earlier as toddlers as part of the MET51 study. It was also to increase the study duration in the initial study arm to describe the immunogenicity and safety of a second booster dose (as adolescents approximately 5 years after the first booster dose) and the persistence of a first booster dose of MenACYW conjugate vaccine in adolescents who had been primed with MenACYW conjugate vaccine as toddlers as part of the MET51 study and had received a first booster dose as children approximately 5 years after the priming dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported