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Safety and Immunogenicity of a Quadrivalent Meningococcal Conjugate Vaccine in Healthy Meningococcal-Naïve Children 2–9 Years of Age: A Phase III, Randomized Study

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Background: Invasive meningococcal disease is a major cause of meningitis in children. An investigational meningococcal (serogroups A, C, Y, and W) tetanus toxoid conjugate vaccine (MenACYW-TT) could offer protection against invasive meningococcal disease in this population. This phase III study assessed the immunogenicity and safety of MenACYW-TT in children compared with a licensed quadrivalent meningococcal vaccine conjugated with diphtheria protein CRM_{197} (MenACWY-CRM).

Methods: Healthy children 2–9 years of age in the United States, including Puerto Rico, were randomized (1:1) to receive MenACYW-TT (n = 499) or MenACWY-CRM (n = 501) (NCT03077438). Meningococcal antibody titers to the 4 vaccine serogroups were measured using a serum bactericidal antibody assay with human complement (hSBA) before and at day 30 after vaccination. Noninferiority between the vaccine groups was assessed by comparing seroresponse rates (postvaccination titers ≥1:16 when prevaccination titers were <1:8, or ≥4-fold increase if prevaccination titers were ≥1:8) to the 4 serogroups at day 30. Safety was monitored.

Results: The proportion of participants achieving seroresponse at day 30 in the MenACYW-TT group was noninferior to the MenACWY-CRM group (A: 55.4% vs. 47.8%; C: 95.2% vs. 47.8%; W: 78.8% vs. 64.1%; Y: 91.5% vs. 79.3%, respectively). Geometric mean titers for serogroups C, W, and Y were higher with MenACYW-TT than for MenACWY-CRM. Both vaccines were well-tolerated and had similar safety profiles.

Conclusions: MenACYW-TT was well-tolerated in children and achieved noninferior immune responses to MenACWY-CRM against each of the 4 vaccine serogroups.

Key Words: children, conjugate vaccine, invasive meningococcal disease, MenACWY-CRM, MenACYW-TT, meningococcal vaccination, noninferiority

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INTRODUCTION

Neisseria meningitidis is responsible for invasive meningococcal disease (IMD) presenting most commonly as meningitis and septicemia. Children are particularly vulnerable.[1] Survivors may experience long-term sequelae including amputation, loss of hearing, brain damage, and neurologic impairments. In Europe, the United States, and Canada, the incidence of IMD cases per 100,000 population was 0.70, 0.12, and 0.30, respectively, in 2015.[2] *N. meningitidis* can be classified into 12 meningococcal serogroups, of which 6 (A, B, C, W, X, and Y) are considered to be the primary cause of IMD worldwide.[3] However, the prevalence of the serogroups varies over time by age and region. In Europe, the most common cause of IMD is serogroup B; in recent years, cases caused by serogroup W and Y have increased.[4] In the United States in 2017, there were approximately 350 total cases of IMD reported, with serogroups B, C, and Y the most common cause.[5] In the United States, serogroups B and C are also the most common cause of IMD, with incidence rates up to 4.5 per 100,000 reported.[6] In the Asia Pacific region, IMD is underrecognized, with limited data indicating that serogroups B, C, and W are dominant.[7] Serogroups A and W have been the predominant cause of IMD in Africa,[8] with rates of disease exceeding 200 cases per 100,000 population reported in several countries.[6] In general, the incidence of IMD is highest in children under 5 years of age.[8] Accurate global incidence rates are difficult to ascertain due to limitations in surveillance and underreporting, particularly in developing countries. The global case-fatality ratio of IMD has been estimated to be 10%–15% even with appropriate antibiotic treatment.[9,10]

Meningococcal vaccines have helped to reduce the incidence of IMD to <1 case per 100,000 population per year in developed countries with established meningococcal vaccine programs.[3] In sub-Saharan Africa, the introduction of the meningococcal serogroup A vaccine has led to the virtual elimination of this serogroup as a cause of epidemic IMD in some countries in the region.[11,12] Nonetheless, the disease incidence continues to vary geographically overtime, with periodic epidemics/outbreaks caused by different IMD serogroups. The temporal dynamic changes in the disease-causing serogroups highlights the need for meningococcal vaccines that provide protection against a broad range of serogroups.[8]

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Qualified researchers may request access to patient level data and related study documents including the clinical study report, study protocol with any amendments, blank case report form, statistical analysis plan, and dataset specifications. Patient level data will be anonymized and study documents will be redacted to protect the privacy of study participants. Further details on Sanofi's data sharing criteria, eligible studies, and process for requesting access can be found at: https://www.clinicalstudydatarequest.com.

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An investigational quadrivalent meningococcal polysaccharide (serogroups A, C, Y, and W) tetanus toxoid conjugate vaccine (MenACYW-TT, Sanofi Pasteur) has been developed for use in individuals ≥6 weeks of age. We compared the immunogenicity and safety profile of a single dose of MenACYW-TT with a licensed quadrivalent diphtheria protein (CRM_{197}) conjugate meningococcal vaccine (MenACWY-CRM, Menveo®, GlaxoSmithKline Vaccines Srl; formerly Novartis Vaccines) in children 2–9 years of age in the United States, including Puerto Rico.

MATERIALS AND METHODS

Study Design and Participants

This was a Phase III, modified double-blind, randomized, parallel-group, active-controlled study conducted from February 2017 to October 2017 at 36 sites across the United States including Puerto Rico (ClinicalTrials.gov: NCT03077438).

The appropriate independent ethics committees and institutional review boards approved the study before its initiation. The conduct of this study was consistent with standards established by the Declaration of Helsinki and compliant with the International Conference on Harmonisation guidelines for Good Clinical Practice, including all local and national regulations and directives. Parents or guardians were required to provide signed informed consent before the start of the study. In addition, participants (≥7 years of age) were asked to sign an assent form (as required by local regulations).

Healthy meningococcal vaccine-naïve children 2–9 years of age were recruited. Participants were excluded if they had been involved in another clinical trial of a drug, vaccine, or medical device in the 4 weeks before the start of the present study, or had planned simultaneous participation in another trial. Those who received another vaccine in the 4 weeks preceding the study vaccination or planned to receive another vaccine before immunologic assessment at day 30 were also excluded. Other exclusion criteria included a history of Guillain-Barré syndrome and meningococcal infection confirmed clinically, serologically, or microbiologically, or a demonstrable high risk of meningococcal infection during the study. Participants with known systemic hypersensitivity to any of the vaccine's components, or a history of a life-threatening reaction to these components, were also excluded.

Eligible participants were randomly assigned in a 1:1 ratio via an interactive web response system (stratified by the age groups of 2–5 and 6–9 years) to receive a single dose (0.5 mL) of either MenACYW-TT conjugate vaccine or MenACWY-CRM at day 0. Participants, their parents/guardians, and investigators were unaware of treatment assignments throughout the study. The vaccines were administered by an unblinded administrator who was not involved in safety data collection. Serology testing was performed by the sponsor and laboratory personnel who remained blinded to treatment assignments throughout the study.

MenACYW-TT (Sanofi Pasteur, Swiftwater, PA) was presented as a liquid solution in single-dose vials; each 0.5 mL dose contained 10 μg of each serogroup (A, C, W, and Y) and approximately 55 μg of tetanus toxoid protein carrier. MenACWY-CRM (GlaxoSmithKline Vaccines Srl; formerly Novartis Vaccines) was presented as a lyophilized powder of the serogroup A vaccine component and a liquid serogroup C, W, and Y vaccine component in 2 separate vials which were combined for a single dose of 0.5 mL. Each dose contained 10, 5, 5, and 5 μg of serogroups A, C, W, and Y oligosaccharide, respectively, and approximately 32.7–64.1 μg of CRM_{197} protein carrier. Both vaccines were administered intramuscularly in the right or left deltoid region.

Immunogenicity

Blood samples for immunogenicity assessments were collected at baseline (day 0; prevaccination) and at day 30 (up to day 44) postvaccination. Functional antibody titers against meningococcal serogroups A, C, W, and Y were measured prevaccination and at day 30 postvaccination by serum bactericidal antibody assays using human complement (hSBA; Global Clinical Immunology Laboratory, Sanofi Pasteur, Swiftwater, PA) and baby rabbit complement (rSBA; Public Health England, Manchester, United Kingdom), as previously described.[13,14] A subset of participants (100 participants from each age group in the 2 vaccine groups) was used to measure rSBA. The lower limit of quantification for the hSBA and rSBA assays was 1:4. Bactericidal antibody titers determined by the hSBA and rSBA assays were converted into geometric mean titers (GMTs), as described previously.[15]

The primary objective was to demonstrate the noninferiority of immune response following administration of a single dose of MenACYW-TT relative to MenACWY-CRM in terms of hSBA seroresponse to serogroups A, C, W, and Y at day 30. An hSBA seroresponse was defined as postvaccination titers ≥1:16 for a participant with prevaccination titers of <1:8, or at least a 4-fold increase in titers if the prevaccination titers were ≥1:8. Secondary objectives were to evaluate the hSBA GMTs at day 0 and day 30 in the total population (those 2–9 years of age) and also for the 2 age groups, 2–5 and 6–9 years. hSBA vaccine seroresponse was also assessed by age subgroups (2–5 and 6–9 years). In addition, the study described antibody titers measured by hSBA in all participants, and titers measured by rSBA in a subset of participants. Seroprotection was defined as hSBA titers ≥1:8 or rSBA titers ≥1:128.

Safety

All participants were observed for 30 minutes after vaccination to assess the occurrence of any immediate adverse events (AEs)/reactions. Participants' parents/guardians were provided with diary cards and instructed to record information on solicited injection site (pain, erythema, and swelling) and systemic reactions (fever, headache, malaise, and myalgia) from day 0 to day 7 postvaccination (see Table, Supplemental Digital Content 1, http://links.lww.com/INF/E64 and 2, http://links.lww.com/INF/E65), and unsolicited AEs through to day 30 (+14 days).

Serious AEs (SAEs) were recorded throughout the duration of the study. Parents or guardians were asked to inform the investigators of any potential SAEs immediately. AEs of special interest (AESI) monitored based on the guidance received from the European Medicines Agency included the following: Kawasaki disease; Guillain-Barré syndrome; generalized seizures, including febrile seizures; and idiopathic thrombocytopenic purpura.

Statistical Analyses

For the primary objective, the noninferiority of hSBA seroresponse with MenACYW-TT relative to MenACWY-CRM at day 30 as tested for each of the serogroups A, C, W, and Y separately. If the lower limit of the 2-sided 95% confidence interval (CI) of the difference between the 2 seroresponse rates was greater than –10%, the inferiority hypothesis was rejected. Overall noninferiority was demonstrated if all 4 individual inferiority hypotheses were rejected.

Assuming a 10% noninferiority margin, with 400 evaluable participants in each vaccine group, the study would have 90% power to declare the noninferiority of the hSBA seroresponse of MenACYW-TT to that of MenACWY-CRM. A total of 1000 participants needed to be enrolled to meet the power requirements assuming a 20% dropout rate, which would result in approximately 800 participants in the Per Protocol Analysis Set (PPAS) available for immunogenicity analyses. Power was calculated with the assumption that the seroresponse estimate from the MenACYW-TT equaled that of MenACWY-CRM.

All immunogenicity analyses were performed on the PPAS, which was composed of participants who had received the study vaccine and had at least 1 valid postvaccination serology result and met all protocol-specified inclusion criteria. Safety assessments were carried out on the Safety Analysis Set, which included all participants who received the study vaccine and had safety data available.

Categorical variables were summarized and presented as frequency counts with 95% CIs calculated using the normal approximation for quantitative data and the exact binomial distribution (Clopper-Pearson method).[16] Bactericidal antibody titers and corresponding 95% CIs were calculated on Log_{10} transformed data assuming normal distribution for the transformed data, with antilog transformations applied to provide GMTs and their 95% CI.[17]

RESULTS

Study Participants

A total of 1000 participants were enrolled and randomized to receive either MenACYW-TT (n = 499) or MenACWY-CRM (n = 501). The participant disposition through the study is shown in Figure, Supplemental Digital Content 3 (http://links.lww.com/INF/E66). Of the total randomized participants, 498 (MenACYW-TT [n = 251]; MenACWY-CRM [n = 247]) were 2–5 years of age, and 502 (MenACYW-TT [n = 248]; MenACWY-CRM [n = 254]) were 6–9 years of age. All participants provided blood samples at day 0 and day 30 after vaccination. The PPAS comprised 458 and 460 participants in the MenACYW-TT and MenACWY-CRM groups, respectively. A total of 974 participants completed the study in the MenACYW-TT (n = 487) and MenACWY-CRM (n = 487) groups. Baseline demographic characteristics are summarized for the 2 groups in Table 1.

Immunogenicity

MenACYW-TT was demonstrated to be noninferior to MenACWY-CRM in terms of hSBA seroresponse against all 4 serogroups at day 30 (Table 2). In the MenACYW-TT group, higher proportions of participants had an hSBA seroresponse with nonoverlapping 95% CIs against serogroups C, W, and Y compared with MenACWY-CRM (Table 2).

TABLE 1. Baseline Demographics (All Randomized Participants)

	MenACYW-TT (n = 499)	MenACWY-CRM (n = 501)
Gender, n (%)		
Male	254 (50.9)	265 (52.9)
Mean age, y (mean [SD])		
2–5	4.0 (1.2)	3.9 (1.2)
6–9	7.9 (1.2)	8.0 (1.1)
Racial origin, n (%)		
White	402 (80.6)	417 (83.2)
Asian	2 (0.4)	2 (0.4)
Black/African American	66 (13.2)	61 (12.2)
American Indian/Alaska Native	1 (0.2)	0 (0.0)
Native Hawaiian/Pacific Islander	4 (0.8)	0 (0.0)
Mixed origin	21 (4.2)	21 (4.2)
Missing	3 (0.6)	0 (0.0)
Ethnicity, n (%)		
Hispanic or Latino	114 (22.8)	116 (23.2)
Non-Hispanic or Latino	384 (77.0)	385 (76.8)
Missing	1 (0.2)	0 (0.0)

The hSBA GMTs for all serogroups increased between day 0 and day 30 in both vaccine groups (Figure 1). At day 30, GMTs for serogroups C, W, and Y achieved with MenACYW-TT were higher than those with MenACWY-CRM, with nonoverlapping 95% CIs (Figure 1). The GMTs for serogroup A were comparable between vaccine groups (overlapping 95% CIs).

The proportion of participants with hSBA titers ≥1:8 increased from baseline to day 30 for all serogroups, regardless of vaccine group (Table 3). The proportion of participants with seroprotective hSBA titers were higher in the MenACYW-TT group than the MenACWY-CRM group for serogroups C, W, and Y, with similar proportions in both groups achieving seroprotective titers against serogroup A. For rSBA titers, the proportion of participants with titers ≥1:128 was similar in both groups at day 30, except for serogroup C for which the proportion of participants was higher in the MenACYW-TT group (see Table, Supplemental Digital Content 4, http://links.lww.com/INF/E67).

The immune response tended to be stronger in those 6–9 years than those 2–5 years of age, with similar trends observed for GMTs (see Figure, Supplemental Digital Content 5, http://links.lww.com/INF/E68), seroresponse rates (see Table, Supplemental Digital Content 6, http://links.lww.com/INF/E69), and seroprotective titers (see Figure, Supplemental Digital Content 7, http://links.lww.com/INF/E70). For both age groups, in those who received MenACYW-TT, GMTs and seroresponse rates were highest against serogroup C; in those who received MenACWY-CRM, GMTs and seroresponse rates were highest against serogroup Y. In both age groups, the greatest proportion of participants with seroprotection (hSBA titers ≥1:8) were seen against serogroup Y in both vaccine groups.

Safety

The safety profile of MenACYW-TT was comparable to that of MenACWY-CRM. The proportion of participants reporting solicited systemic reactions and injection site reactions was similar in both vaccine groups (Table 4). No participant discontinued because of AEs or reactions. One AESI (temporal partial seizure) was reported in the MenACWY-CRM group, and it was assessed as not related to the vaccination by the Investigator. There were no SAEs considered related to vaccination in either group. When vaccine groups were stratified by age (2–5 and 6–9 years), the safety profiles were comparable.

DISCUSSION

This is the first study to assess the safety and immunogenicity of MenACYW-TT compared with MenACWY-CRM in children 2–9 years of age. The noninferiority of MenACYW-TT to MenACWY-CRM in terms of the hSBA seroresponse was demonstrated for all 4 meningococcal serogroups at day 30 postvaccination. The safety profile of MenACYW-TT was similar to that of MenACWY-CRM, with no safety concerns identified.

The proportion of participants achieving an hSBA seroresponse against serogroups C, W, and Y was higher with MenACYW-TT than MenACWY-CRM, with a similar proportion of participants achieving seroresponse against serogroup A. Consistent with these observations, GMTs were higher with MenACYW-TT than MenACWY-CRM for serogroups C, W, and Y, but similar between the 2 study groups for serogroup A. hSBA GMTs against serogroup C were notably high in the MenACYW-TT group, but the clinical benefit of these high GMT levels has not yet been established. The observed differences in immune response may be due to heterogeneity in the MenACYW-TT and MenACWY-CRM vaccine formulations. While higher titers may be anticipated to lead to longer persistence of protection, we currently cannot make any

TABLE 2. Noninferiority of the Proportion of Participants (%) Who Had Achieved hSBA Vaccine Seroresponse[a] at Day 30 Between Vaccine Groups (Per Protocol Analysis Set)

	MenACYW-TT (n = 458)		MenACWY-CRM (n = 460)		MenACYW-TT–MenACWY-CRM
Serogroup	n/M	% (95% CI)	n/M	% (95% CI)	Difference, % (95% CI)
A	252/455	55.4 (50.7-60.0)	219/458	47.8 (43.2-52.5)	7.6 (1.1-14.0)
C	436/458	95.2 (92.8-97.0)	219/458	47.8 (43.2-52.5)	47.4 (42.2-52.2)
W	361/458	78.8 (74.8-82.5)	294/459	64.1 (59.5-68.4)	14.8 (8.9-20.5)
Y	419/458	91.5 (88.5-93.9)	364/459	79.3 (75.3-82.9)	12.2 (7.7-16.7)

[a]hSBA vaccine seroresponse was demonstrated if a participant had prevaccination titers <1:8, then the postvaccination titer had to be ≥1:16, or for a participant with a prevaccination titer ≥1:8, the postvaccination titer had to be at least 4-fold greater than the prevaccination titer; 95% CIs of the single proportion was calculated from the exact binomial method.

CI, confidence interval; PPAS, Per Protocol Analysis Set; n, number of participants who achieved an hSBA vaccine seroresponse; M, number of participants with available data for the endpoint; N, number of participants in the PPAS.

The overall noninferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > –10% for all 4 serogroups.

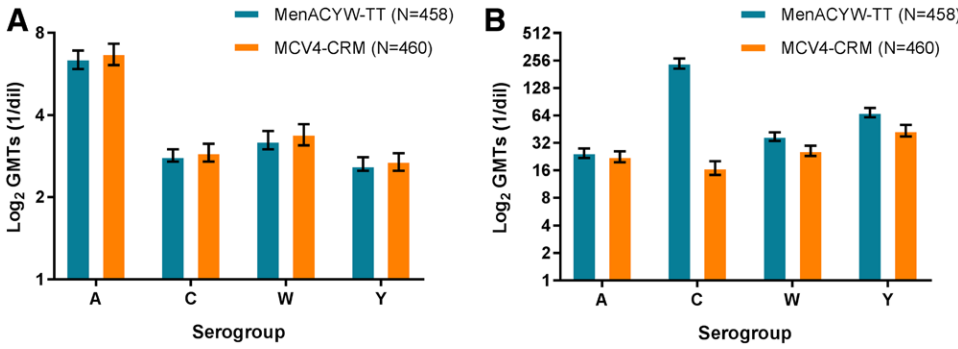

FIGURE 1. hSBA GMTs at (A) baseline (day 0) and (B) day 30 (Per Protocol Analysis Set).

TABLE 3. Proportion of Participants With hSBA Titers ≥1:8 at Day 0 and at Day 30 (Per Protocol Analysis Set)

		MenACYW-TT (n = 458)		MenACWY-CRM (n = 460)	
Serogroups	Time Point	n/M	% (95% CI)	n/M	% (95% CI)
A	Day 0	225/457	49.2 (44.6-53.9)	224/460	48.7 (44.0-53.4)
	Day 30	394/456	86.4 (82.9-89.4)	363/458	79.3 (75.3-82.9)
C	Day 0	56/458	12.2 (9.4-15.6)	59/459	12.9 (9.9-16.3)
	Day 30	448/458	97.8 (96.0-98.9)	308/459	67.1 (62.6-71.4)
W	Day 0	90/458	19.7 (16.1-23.6)	93/460	20.2 (16.6-24.2)
	Day 30	434/458	94.8 (92.3-96.9)	396/459	86.3 (82.8-89.3)
Y	Day 0	54/458	11.8 (9.0-15.1)	57/460	12.4 (9.5-15.8)
	Day 30	451/458	98.5 (96.9-99.4)	417/459	90.8 (87.8-93.3)

CI, confidence interval; M, number of participants with a valid serology result for the particular serogroup and time point; n, number of participants experiencing the endpoint.

Titers ≥1:8 were considered seroprotective.

predictions from the current study data. Ongoing persistence and booster studies with MenACYW-TT will be able to provide additional information.

Routine conjugate meningococcal vaccination schedules against IMD have been introduced in 21 countries based on their established efficacy, safety profile, and immunogenicity,[18] with more countries in the African meningitis belt expected to follow by 2020.[19] School-based immunization programs have shown to be effective in reducing cases of IMD, for example, the meningococcal C vaccine was administered in children and adolescents in the United Kingdom, leading to vaccine uptake of >85% in these age groups.[20] In the present study, similar trends for protective titers and GMTs were observed for both age subgroups (2–5 and 6–9 years). There tended to be more participants who had achieved an hSBA seroresponse in the older compared with younger age group, consistent with other studies of MenACYW-TT that found a higher proportion of adults and adolescents achieved protective titers compared with children.[21,22] However, this is unlikely to have any clinical significance and is an observation likely driven by physiologic differences in immune responses. Taken together, the results of the present study suggest that MenACYW-TT could be suitable for protection against IMD in either preschool or school-age children, dependent on the immunization program of a particular country.[18,23]

Overall, both MenACYW-TT and MenACWY-CRM were well-tolerated. The safety profiles of MenACYW-TT and MenACWY-CRM were consistent with previous studies assessing other vaccines against IMD in children.[24,25] There were no AESIs or SAEs assessed as related to vaccination in either group.

The study has some limitations. While hSBA ≥1:8 or rSBA ≥1:128 titer thresholds are widely used as serologic correlates of protection for meningococcal vaccines, and have been accepted globally by health regulatory agencies,[26–28] the absolute clinical benefit of these protective titers is yet to be determined.[29,30] This study benefitted from enrolling a large number of study participants across 36 sites in the United States, including Puerto Rico; however, analyses comparing the populations of mainland United States and Puerto Rico have not been conducted. A high rate of adherence to the protocol among enrolled participants added to the strength of this study. High baseline titers for serogroup A were

TABLE 4. Summary Safety Outcomes (Safety Analysis Set)

	MenACYW-TT (n = 498)		MenACWY-CRM (n = 494)	
	n/M	% (95% CI)	n/M	% (95% CI)
AEs within 30 min after vaccine injection				
Immediate unsolicited AE	0/498	0.0 (0.0-0.7)	0/494	0.0 (0.0-0.7)
Immediate unsolicited AR	0/498	0.0 (0.0-0.7)	0/494	0.0 (0.0-0.7)
AEs within 30 d after vaccine injection				
Solicited reaction	270/487	55.4 (50.9-59.9)	296/486	60.9 (56.4-65.3)
Solicited injection site reaction	228/487	46.8 (42.3-51.4)	262/486	53.9 (49.4-58.4)
Pain	188/487	38.6 (34.3-43.1)	206/486	42.4 (37.9-46.9)
Erythema	110/487	22.6 (18.9-26.6)	153/485	31.5 (27.4-35.9)
Swelling	67/484	13.8 (10.9-17.2)	104/483	21.5 (17.9-25.5)
Solicited systemic reaction	168/487	34.5 (30.3-38.9)	180/486	37.0 (32.7-41.5)
Fever	9/485	1.9 (0.9-3.5)	13/479	2.7 (1.5-4.6)
Headache	61/487	12.5 (9.7-15.8)	56/486	11.5 (8.8-14.7)
Malaise	103/487	21.1 (17.6-25.0)	99/486	20.4 (16.9-24.2)
Myalgia	98/487	20.1 (16.7-24.0)	112/486	23.0 (19.4-27.1)
Unsolicited AE	121/498	24.3 (20.6-28.3)	145/494	29.4 (25.4-33.6)
Unsolicited AR	10/498	2.0 (1.0-3.7)	17/494	3.4 (2.0-5.5)
Related SAE	0/498	0.0 (0.0-0.7)	0/494	0.0 (0.0-0.7)
AEs during the study				
SAE	0/498	0.0 (0.0-0.7)	0/494	0.0 (0.0-0.7)
MAAEs between visits 1 and 2	65/498	13.1 (10.2-16.3)	76/494	15.4 (12.3-18.9)
MAAE between visit 2 to 6-month follow-up	155/498	31.1 (27.1-35.4)	136/494	27.5 (23.6-31.7)

AEs, adverse events; AR, adverse reaction; CI, confidence interval; M, number of participants with available data for the endpoint; MAAE, medically-attended AE; n, number of participants experiencing the endpoint. SAE, serious AE.

seen among the participants in this study, and another similar study in adolescents.[21] Given that there is no recommendation for infant or toddler vaccination with meningococcal vaccines in the United States, the exact origin of these titers cannot be explained. Because of the potential variability of baseline titers, an advantage of using seroresponse as an endpoint for assessing immunogenicity is that it accounts for baseline seropositivity.

Our findings suggest that MenACYW-TT may have the potential to prevent IMD when administered as a single dose to meningococcal vaccine-naïve children 2–9 years of age. MenACYW-TT could also have potential in catch-up immunization programs alongside routine recommendations.

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