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Meningococcal (Groups A, C, Y, and W) Conjugate Vaccine (MenQuadfi®)

Extension of use to include infants from 6 weeks of age

Agenda

Public health burden of invasive meningococcal disease

Rationale for clinical development

Clinical data from infant studies

Summary

Public health burden of meningococcal disease

- Meningococcal disease remains a *major global health challenge* because it can strike quickly and with devastating effect, taking a life in < 24 hours [1,2]
  - Case-fatality rate is *~10% to 15%* even with appropriate treatment[2]
  - *~1 in 5 survivors suffer permanent sequelae[3,4]*

Limb amputation

Deafness

Brain damage

- Since introduction of the first MenACWY conjugate vaccine in 2005, MenACWY-D, IMD caused by serogroups *C, W, and Y has declined by > 90% among adolescents and young adults[5]*
- Infants continue to have the highest incidence of IMD, so we would like to share information about the performance of Sanofi's MenACYW-TT in this population

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1. Thompson MJ, et al. *Lancet*. 2006;367(9508):397-403. **2.** WHO. https://www.who.int/en/news-room/fact-sheets/detail/meningococcal-meningitis [accessed March 2020]. **3.** CDC. *MMWR*. 2013;62(RR-2):1-22. **4.** Rosenstein NE, et al. *N Engl J Med.* 2001;344(18):1378-1388. **5.** MacNeil JR, et al. *Clin Infect Dis* 2018; 66:1276–81.

What is MenQuadfi (MenACYW-TT)?

- A quadrivalent meningococcal conjugate vaccine to help *prevent invasive meningococcal disease caused by serogroups A, C, W, and Y*
- FDA approved on 23 April 2020 for use in *persons 2 years of age and older*
- Developed with the ambition of being:
  - Used across a *broad age range*
    - *Studies to support expansion of age indication to include infants as young as 6 weeks of age are completed*
  - Incorporated in *various immunization schedules that exist worldwide*
- Conjugated to *tetanus toxoid* (approximately 55 µg)
  - Each 0.5-mL intramuscular dose contains *10 µg each* of the 4 meningococcal polysaccharides
- Fully liquid solution that *does not require reconstitution* and supplied in a single-dose vial

Proposed Schedule for Primary Vaccination with MenACYW-TT

Age at First Dose	Primary Vaccination Schedule
Infants aged from 6 weeks	4-dose series at 2, 4, 6 and between 12 and 18 months of age. The first dose may be given as early as 6 weeks.
Infants aged 6 months through 23 months	2-dose series with the second dose administered in the second year of life and at least 3 months after the first dose.
Individuals 2 years of age and older	A single dose

Overview of MenQuadfi Clinical Development

MenQuadfi Clinical Development Program in Infants and Toddlers

Toddlers
(12–23 Months)

MET54
Phase II
Control MCV4-TT
(single dose)
Finland
NCT03205358

MET51
Phase III
Control: MCV4-TT
(single dose)
Germany, Spain, Finland, Hungary
NCT02955797

MET57
Phase III
Single dose co-ad* with MMR + varicella, DTaP-IPV-HB-Hib, or PCV13 (single dose)
No Meninge vaccine control
South Korea, Russia, Mexico, Thailand
NCT03205371

MEQ00065
Phase III
NI / Superiority
Controls MenC-conj and MCV4-TT
(single-dose)
Denmark, Finland, Germany
NCT03890367

MEQ00086
Interchangeability
Toddlers (12–23M)
Toddlers primed with MenACWY-CRM or MCV4-TT during 1Y
Argentina
ONGOING

Infants
(6 Weeks–11 Months)

&

Toddlers
(12–23 Months)

MET33
Phase III
Schedule: 2+1 (2 or 3, 6, 12M)
Control MenACWY-CRM in 3 +1 (2, 4, 6, 12M)
Russia, Mexico
NCT03630705

MET52
Phase III
Schedule: 1+1 (3, 12–13M)
NI when co-ad MenB and standard of care vaccines§
(multi-dose)
UK
NCT03632720

MET41
Phase III
Schedule: 3+1 (2, 4, 6, 12M)
Control MenACWY-CRM
USA
NCT03673462

MET58
Phase III
Schedule: 2+1 (2, 4, 12–18M) and 3+1 (2, 4, 6, 12–18M)
Control MCV4-TT
Europe*
NCT03547271

MET42
Phase III
Schedule: 3+1 (2, 4, 6, 12–18M)
Control MenACWY-CRM
USA
NCT03537508

MEQ00089
Phase III
Schedule: 1+1 (6M+): 6-7 +12-13 M
Control: MCV4-TT
EU
ONGOING

MET61
Phase III
Schedule: 1+1 (6M+)
Controls MenACWY-CRM, MenACWY-D
USA
NCT03691610

Coadministration study

Booster dose study

MenACWY-TT = MenQuadfi, MenACWY-CRM = Menveo, MenACWY-D = Menactra, MCV4-TT= Nimenrix (not licensed in US)
-Studies in *green font* are completed
-Studies in ***black font*** are ongoing

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MET42

Immunogenicity and Safety Study of a Quadrivalent Meningococcal Conjugate Vaccine (MenACYW-TT) when Co-administered with Routine Pediatric Vaccines in Healthy Infants and Toddlers in the US and Puerto Rico

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MET42: Study design and demographic data

Short Study Title		Immune Non-inferiority, Safety and Co-administration study in infants & toddlers	
Study Population		Age group	≥ 42 to ≤ 89 days
		Number of participants	2627
		Meningococcal-vaccine naïve	
Vaccine Groups		Group 1: MenACYW-TT + Routine pediatric vaccines Group 2: MenACWY-CRM + Routine pediatric vaccines	
Vaccination Schedule		Single dose of MenACYW-TT or MenACWY-CRM (2, 4, 6, and 12 months)	
Safety follow up	**Immediate Unsolicited Systemic AEs**	Within 30 minutes after each vaccination	
	Solicited AEs	Day 0 to Day 7 after each vaccination	
	Unsolicited AEs	D0 to D30 after each vaccination	
	SAEs (AESIs and MAAEs)	Visit 1 (day of first vaccination) until the end of the 6-month follow-up period after the last vaccination.	

Baseline Characteristics	Group 1 (N=1746)	Group 2 (N=881)
Sex: n (%)		
Male	918 (52.6)	466 (52.9)
Female	828 (47.4)	415 (47.1)
Sex ratio: Male/Female	1.11	1.12
Age: (Days)		
Mean (SD)	65.3 (8.02)	65.3 (7.81)
Min ; Max	42.0 ; 89.0	42.0 ; 89.0
Median	64.0	64.0
Racial origin: n (%)		
American Indian or Alaska Native	11 (0.6)	3 (0.3)
Asian	15 (0.9)	10 (1.1)
Black or African American	204 (11.7)	99 (11.2)
Native Hawaiian or Other Pacific Islander	7 (0.4)	6 (0.7)
White	1428 (81.8)	722 (82.0)
Mixed Origin	44 (2.5)	30 (3.4)
Unknown	19 (1.1)	6 (0.7)
Ethnicity: n (%)		
Hispanic or Latino	838 (48.0)	410 (46.5)
Not Hispanic or Latino	897 (51.4)	465 (52.8)
Unknown	3 (0.2)	4 (0.5)
Not reported	8 (0.5)	2 (0.2)

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Immunogenicity and Safety of a Quadrivalent Meningococcal Conjugate Vaccine When Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers in the US. ClinicalTrials.gov, Sanofi Pasteur, 15 Oct. 2024, https://clinicaltrials.gov/study/NCT03537508

AESI: Adverse events of special interest, MAAE: Medically attended adverse events.

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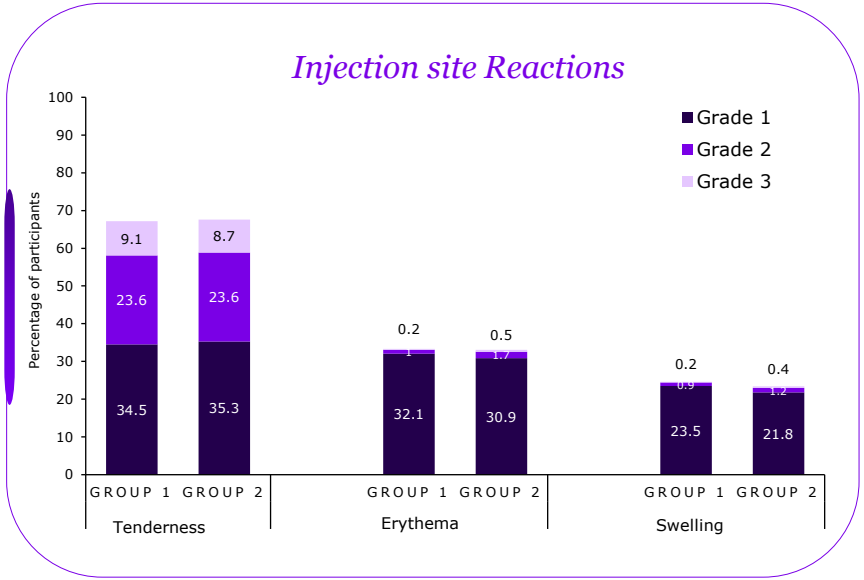
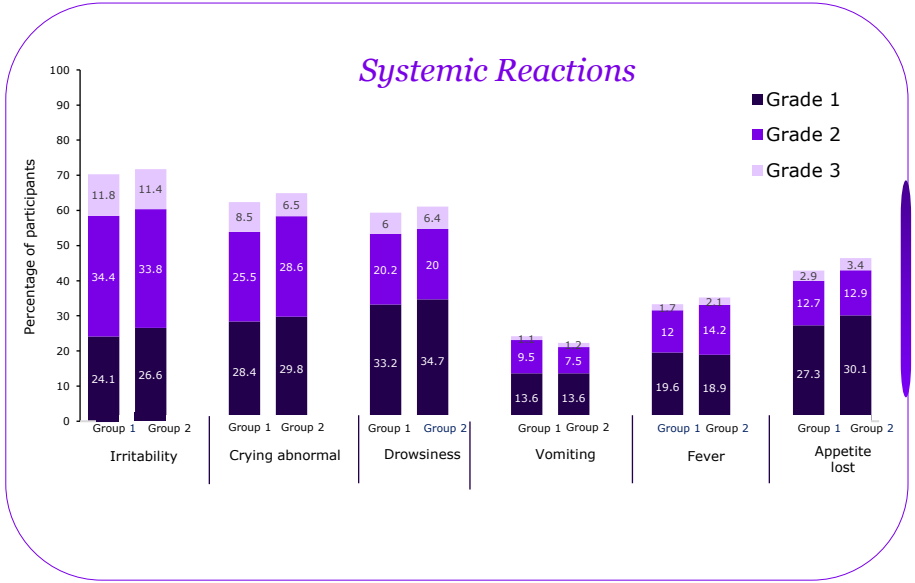
Safety

MET42: Solicited injection site & systemic reactions within 7 days after any dose





Tenderness was the most frequently reported solicited injection site reaction. Erythema and swelling were reactions less frequently experienced. Most solicited injection site reactions were of Grade 1 or 2 intensity.

Irritability was the most frequently reported solicited systemic reaction, followed by crying abnormal, drowsiness & appetite lost. Fever (33.4% vs 35.2%) and vomiting were reactions less frequently experienced. Most solicited systemic reactions were of Grade 1 or 2 intensity

Group 1: MenACYW-TT and routine pediatric vaccines; Group 2: MenACWY-CRM and routine pediatric vaccines

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Immunogenicity and Safety of a Quadrivalent Meningococcal Conjugate Vaccine When Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers in the US. ClinicalTrials.gov, Sanofi Pasteur, 15 Oct. 2024, https://clinicaltrials.gov/study/NCT03537508

MET42: Summary of results

Summary of SAEs, AESIs and unsolicited AEs after any vaccine injections

99 subjects (5.7%) in Group 1 (MenACYW-TT), 38 subjects (4.4%) in Group 2 (MenACWY-CRM) reported SAEs during the study

- 2 subjects reported SAEs related to study vaccines during the study:
  - 1 instance of *febrile seizure* in a participant in Group 1 (MenACYW-TT) with prior history of seizures. The Febrile seizure was an AESI (13 days after 15-month dose)
  - 1 subject reported *fever* post vaccination in Group 2 (MenACWY-CRM) (8 hours following 2-month dose)

18 subjects reported AESI during the study: 13 subjects (0.8%) in Group 1 (MenACYW-TT) and 5 (0.6%) subjects in Group 2 (MenACWY-CRM)

- All AESIs were nonrelated to the study vaccines, except the one SAE mentioned above

There were 2 subjects (both in Group 1-MenACYW-TT) who discontinued due to SAEs (*Infantile spasms, Cardiac arrest*)

- There was one death reported in the study. It was deemed unrelated to the study vaccine by the investigator and sponsor

AESI: adverse events of special interest

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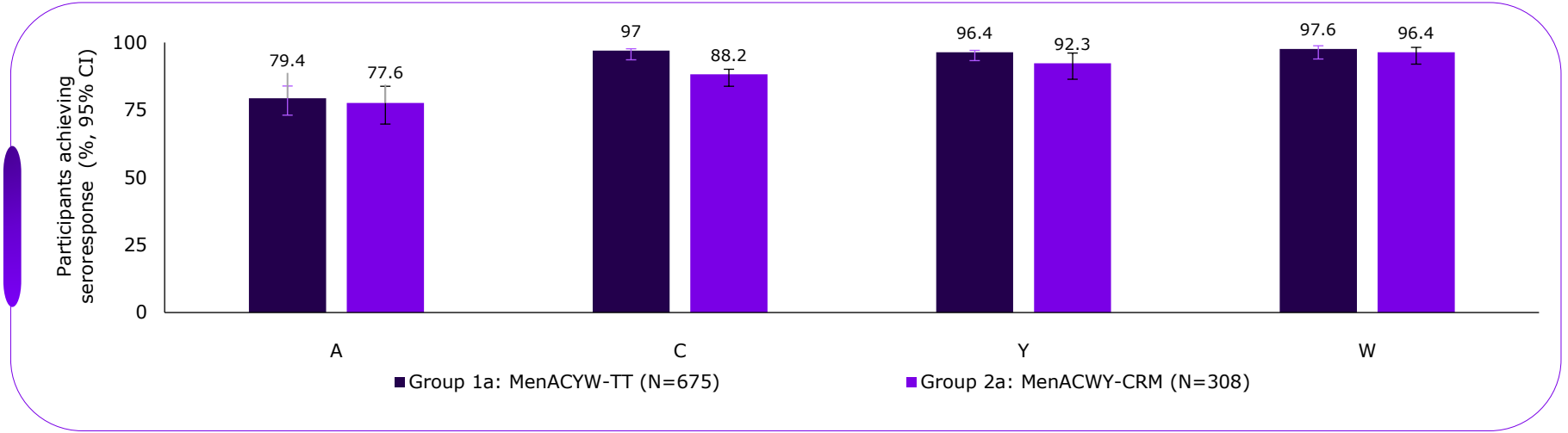
Immunogenicity

MET42: Post booster, MenACYW-TT seroresponse rates were comparable to those for MenACWY-CRM for serogroups A, Y, W and higher for serogroup C

Primary objective 1 was met: The percentage of subjects who **achieved vaccine seroresponse rate post-dose 4** for meningococcal serogroups A, C, W, and Y in MenACYW-TT (Group 1a) are **non-inferior** to the corresponding percentages in MenACWY-CRM (Group 2a), as the lower limit of the 2-sided 95% confidence interval (CI) of the difference between MenACYW-TT (Group 1a) and MenACWY-CRM (Group 2a) were higher than -10% for all 4 serogroups

Percentage of subjects with vaccine seroresponse



Vaccine seroresponse* at day 30 after the booster dose (Group 1 vs Group 2) in Per-protocol Analysis Set

95% CI of the single proportion calculated from the exact binomial method.
Group 1a: MenACYW-TT and routine vaccines at 2, 4, 6, and 12 to 15 months of age
Group 2a: MenACWY-CRM at 2, 4, 6, and 12 months of age and routine vaccines at 2, 4, 6, 12, and 15 to 18 months of age

*__hSBA vaccine seroresponse__ for serogroups A, C, Y, and W was defined as:
- For a subject with a pre-vaccination titer < 1:8, the post-vaccination titer had to be ≥ 1:16
- For a subject with a pre-vaccination titer ≥ 1:8, the post-vaccination titer had to be ≥ 4-fold greater than the pre-vaccination titer

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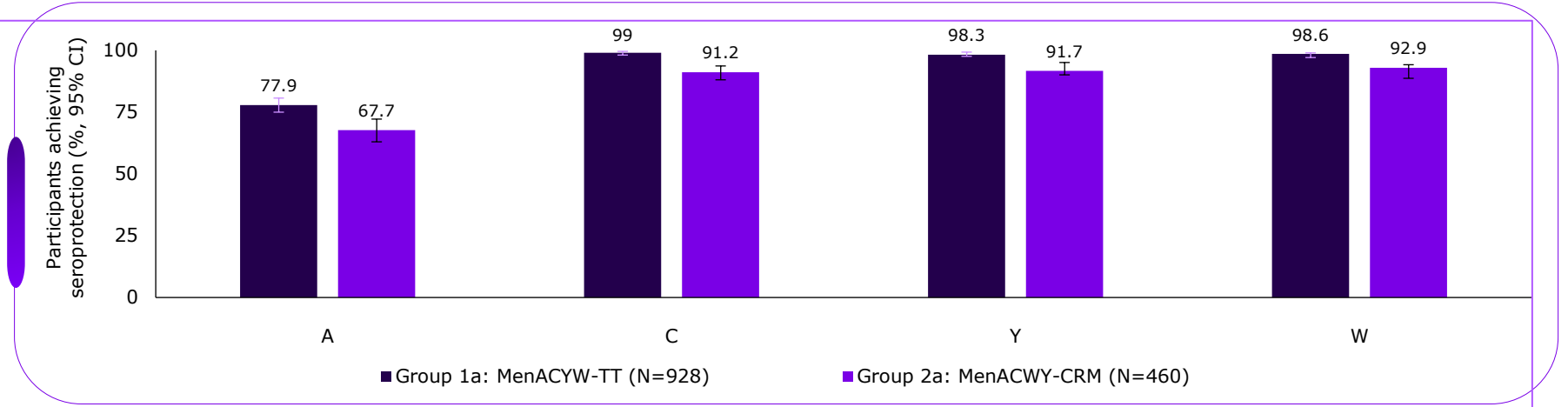
Immunogenicity and Safety of a Quadrivalent Meningococcal Conjugate Vaccine When Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers in the US. ClinicalTrials.gov, Sanofi Pasteur, 15 Oct. 2024, https://clinicaltrials.gov/study/NCT03537508

MET42: Post 3-dose infant series, MenACYW-TT seroprotection rates were higher than those for MenACWY-CRM for all 4 serogroups

Primary objective 2 was met: Non-inferiority of the percentage of subjects with hSBA titers to meningococcal serogroups A, C, Y, and W ≥ 1:8 **following administration of 3 doses** of MenACYW-TT compared to 3 doses of MenACWY-CRM when **given concomitantly with pediatric routine vaccines** to infants and toddlers **at 6 to 7 months of age** was demonstrated as the lower limit of the 2-sided 95% CI of the difference in hSBA seroprotection rates (antibody titers ≥ 1:8) were > -10% for all 4 serogroups

Percentage of subjects with hSBA titer >= 1:8 (seroprotection)



N: number of subjects in per-protocol analysis set 2, for booster series.
95% CI of the single proportion calculated from the exact binomial method.
Group 1a: MenACYW-TT and routine vaccines at 2, 4, 6, and 12 to 15 months of age
Group 2a: MenACWY-CRM at 2, 4, 6, and 12 months of age and routine vaccines at 2, 4, 6, 12, and 15 to 18 months of age
PPAS, Per-Protocol Analysis Set

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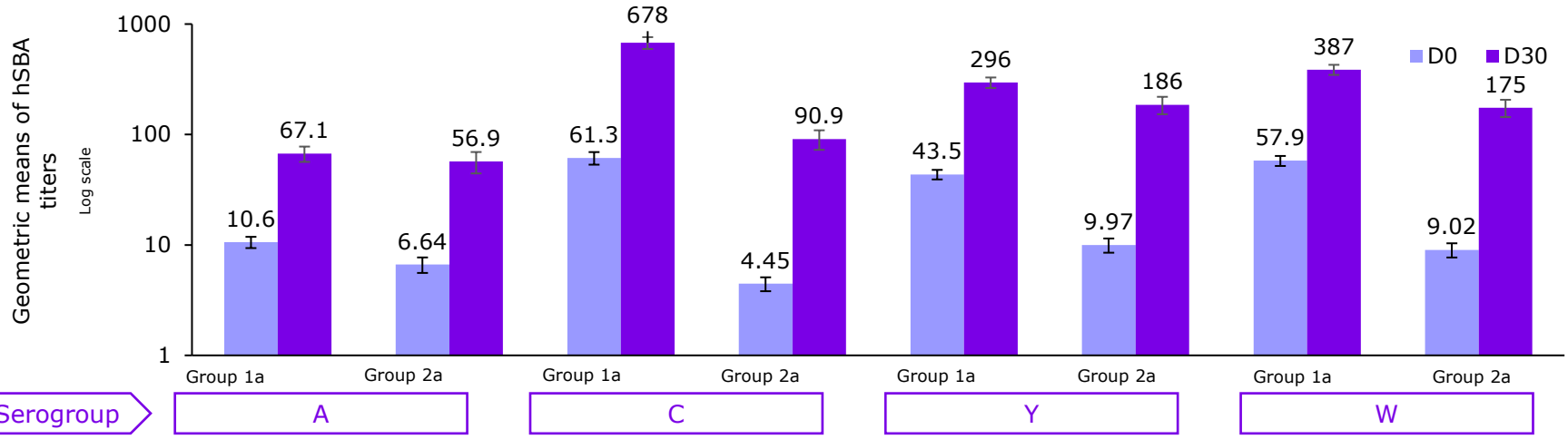
MET42: Geometric mean of hSBA antibody titers pre- and post- 4th dose

Summary of secondary immunogenicity results

Secondary objective 2: Geometric mean of hSBA antibody titers against meningococcal serogroups A, C, Y and W after 4th dose of MenACYW-TT were comparable or generally higher for all serogroups for Group 1a vs Group 2a

Summary of geometric means of hSBA titers at D0 before the 4th dose and D30 after the 4th dose - Per-Protocol Analysis Set 3



D, day;
95% CI calculated using calculation for normal distribution on log10(titer) following by antilog transformation
Group 1a: MenACYW-TT and routine vaccines at 2, 4, 6, and 12 to 15 months of age
Group 2a: MenACWY-CRM at 2, 4, 6, and 12 months of age and routine vaccines at 2, 4, 6, 12, and 15 to 18 months of age

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MET42: Results on concomitant administration of pediatric vaccines

Secondary objective 1 was met: Non-inferiority of immune responses of the routine pediatric vaccines administered concomitantly with MenACYW-TT as compared with MenACWY-CRM in infants and toddlers 6 weeks old to 18 months of age was demonstrated

Evaluation Time	Antigen	Endpoint	Non-inferiority margin	Non-inferiority?
1st Year, 30 days after the 6-month vaccination	Hepatitis B	% ≥ 10 mIU/mL	10%	Yes
	PRP	% ≥ 0.15 µg/mL	5%	Yes
	PRP	% ≥ 1.0 µg/mL	10%	Yes
	Polio†	% ≥ 1:8	5%	Yes
	Rotavirus	% ≥ 3-fold rise	10%	Yes
	Rotavirus	GMC (G1/G2 ratio)	1.5	Yes
	Pertussis*	GMC (G1/G2 ratio)	1.5	Yes
	Pneumococcal‡	GMC (G1/G2 ratio)	2	Yes
2nd Year, 30 days after the 12-month vaccination	Measles	% ≥ 255 mIU/mL	10%	Yes
	Mumps	% ≥ 10 mumps Ab units/mL	10%	Yes
	Rubella	% ≥ 10 IU/mL	10%	Yes
	Varicella	% ≥ 5 gpELISA units/mL	10%	Yes
	Pneumococcal‡	GMC (G1a/G2a ratio)	2	Yes
2nd Year, 30 days after the 15-month vaccination	PRP	% ≥ 1.0µg/mL	10%	Yes
	Polio†	% ≥ 1:8	5%	Yes
	Pertussis*	Response rate	10%	Yes

Ab, antibody; ELISA, enzyme-linked immunosorbent assay; GMC, geometric mean concentrations; PRP, anti polyribosyl-ribitol phosphate
*Pertussis antigen: PT, FHA, PRN, and FIM; †Polioviruses: type 1, type 2, type 3; ‡Pneumococcal serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F

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Immunogenicity and Safety of a Quadrivalent Meningococcal Conjugate Vaccine When Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers in the US. ClinicalTrials.gov, Sanofi Pasteur, 15 Oct. 2024, https://clinicaltrials.gov/study/NCT03537508

MET42: Summary of results

Primary immunogenicity objectives were met

- MenACYW-TT was **non-inferior** to MenACWY-CRM, based on **hSBA vaccine seroresponse** after the 4th dose, when the vaccines were given at 2, 4, 6, and 12 months of age, along with routine pediatric vaccines
- MenACYW-TT was **non-inferior** to MenACWY-CRM, based on **seroprotection** after the 3rd dose, when the vaccines were given at 2, 4, 6, and 12 months of age along with routine pediatric vaccines

Secondary immunogenicity objectives were met

- **Non-inferiority** of *immune responses to routine pediatric vaccines* administered concomitantly with *MenACYW-TT* as compared with MenACWY-CRM in infants and toddlers 6 weeks old to 18 months of age was **demonstrated**
- Geometric mean of hSBA titers against meningococcal serogroups A, C, Y and W after 3rd dose of *MenACYW-TT* were comparable or higher for all *serogroups* in the MenACYW-TT group vs MenACWY-CRM group

Safety

- There were no new safety concerns identified
- The safety profile and tolerance of MenACYW-TT was comparable to MenACWY-CRM
- Safety data from *3211 subjects who received 4 doses of MenACYW-TT (MET41 and MET42) are shown on later slides*

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Immunogenicity and Safety of a Quadrivalent Meningococcal Conjugate Vaccine When Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers in the US. ClinicalTrials.gov, Sanofi Pasteur, 15 Oct. 2024, https://clinicaltrials.gov/study/NCT03537508

MET41

Safety of a Quadrivalent Meningococcal Conjugate Vaccine (MenACYW-TT) Administered Concomitantly with Routine Pediatric Vaccines in Healthy Infants and Toddlers

MET41: Phase III study of MenACYW-TT conjugate vaccine administered to healthy infants and toddlers

Short Study Title		Immune Non-inferiority, Safety and Co-administration study in infants & toddlers
Study Population	Age	≥ 42 to ≤ 89 days
	Number of participants	2797
	Meningococcal-vaccine naïve	
Study Design		Group 1: MenACYW-TT + Routine pediatric vaccines Group 2: MenACWY-CRM + Routine pediatric vaccines
Vaccination Schedule		Single dose of MenACYW-TT or MenACWY-CRM (2, 4, 6, and 12 months)
Safety follow up	**Immediate Unsolicited Systemic AEs**	Within 30 minutes after each vaccination
	Solicited AEs	Day 0 to Day 7 after each vaccination
	Unsolicited AEs	Day 0 until the next study visit
	SAEs (AESIs and MAAEs)	Visit 1 (day of first vaccination) until the end of the 6-month follow-up period after the last vaccination.

Baseline Characteristics	Group 1 (N=2099)	Group 2 (N=362)
Sex: n (%)		
Male	1101 (52.5)	362 (51.9)
Female	998 (47.5)	336 (48.1)
Sex ratio: Male/Female	1.10	1.08
Age: (Days)		
Mean (SD)	64.7 (6.63)	64.9 (6.77)
Min ; Max	42.0 ; 89.0	42.0 ; 89.0
Median	63.0	63.0
Racial origin: n (%)		
American Indian or Alaska Native	8 (0.4)	0
Asian	28 (1.3)	12 (1.7)
Black or African American	210 (10.0)	67 (9.6)
Native Hawaiian or Other Pacific Islander	10 (0.5)	5 (0.7)
White	1719 (81.9)	580 (83.1)
Mixed Origin	102 (4.9)	31 (4.4)
Unknown	12 (0.6)	0
Ethnicity: n (%)		
Hispanic or Latino	566 (27)	197 (28.2)
Not Hispanic or Latino	1526 (72.7)	499 (71.5)
Unknown	0	0
Not reported	7 (0.3)	9 (0.3)

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Safety of a Quadrivalent Meningococcal Conjugate Vaccine Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers (MET41). ClinicalTrials.gov, Sanofi Pasteur, 14 Dec. 2023, https://clinicaltrials.gov/study/NCT03673462

MET41: Summary of results

Summary of SAEs, AESIs and unsolicited AEs after any vaccine injections

- The most common non-serious unsolicited adverse events (AEs) were in the "Infections and Infestations", with respiratory and gastrointestinal infections being the most frequently reported

129/2797 (4.6%) subjects reported *serious adverse events (SAEs).* None of these SAEs were assessed to be related to the study vaccines.

- 108/2080 (5.2%) of subjects in the MenACYW-TT group reported SAEs.
- 21/697 (3%) of subjects in the MenACWY-CRM group reported SAEs.

20/2797 (0.7%) subjects reported 24 AESIs (*febrile or non-febrile seizures*), none related to the study vaccines.

- 19/2080 (0.9%) of AESIs occurred in the MenACYW-TT group.
- 1/697 (0.1%) of AESIs occurred in the MenACWY-CRM group.

- *Confounding factors* were identified in 21/24 (87.5%) of the AESI cases.
- 22/24 (92%) of AESI cases did not meet the Brighton Collaboration* case definition criteria for febrile and non-febrile seizures.

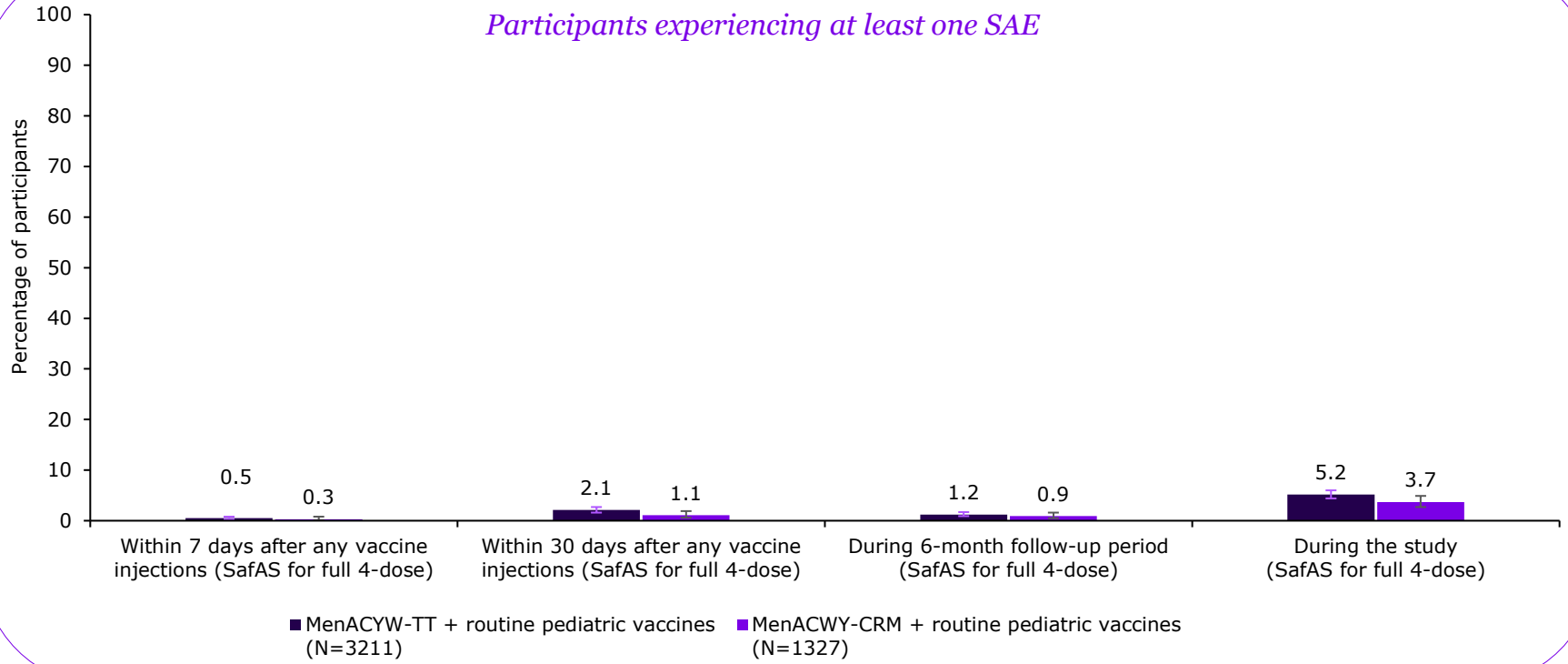
12 discontinuations occurred due to AEs throughout the study

- 7 subjects (all in MenACYW-TT) discontinued due to SAEs, including 3 deaths *(non-accidental injury to the head, sudden unexplained death in infancy, found unresponsive)*
- None were considered related to the study vaccine or procedure by the investigator and sponsor.

AESIs, adverse events of special interest; *Brighton Collaboration is a Global Standard for Case Definitions (and Guidelines) for Adverse Events Following Immunization (AEFI) and adverse events of special interest (AESI).

Safety of a Quadrivalent Meningococcal Conjugate Vaccine Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers (MET41). ClinicalTrials.gov, Sanofi Pasteur, 14 Dec. 2023, https://clinicaltrials.gov/study/NCT03673462

MET41 and MET42 pooled safety analysis



1. Safety of a Quadrivalent Meningococcal Conjugate Vaccine Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers (MET41). ClinicalTrials.gov, Sanofi Pasteur, 14 Dec. 2023, https://clinicaltrials.gov/study/NCT03673462 **2.** Immunogenicity and Safety of a Quadrivalent Meningococcal Conjugate Vaccine When Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers in the US. ClinicalTrials.gov, Sanofi Pasteur, 15 Oct. 2024, https://clinicaltrials.gov/study/NCT03537508

MET61

Phase III, modified double -blind, randomized, parallel group, active -controlled, multicenter study of Quadrivalent Meningococcal Conjugate Vaccine (MenACYW-TT) in infants & toddlers from 6 through 23 months of age in the United States

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MET61: Phase III Study of immunogenicity and safety of a quadrivalent meningococcal conjugate vaccine administered concomitantly with routine pediatric vaccines in healthy infants and toddlers

Short Study Title	Immune Non-inferiority, Safety and Co-administration study in infants & toddlers	
Study Population	**Age**	Infants 6 to 7 months; Toddlers 17 to 19 months
	Number of participants	950
Study Design	**Group 1**: MenACYW-TT conjugate vaccine + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age	**Group 3**: MenACYW-TT conjugate vaccine at 17 to 19 months of age and 20 to 23 months of age
	Group 2: MenACWY-CRM + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age	**Group 4**: MenACWY-D at 17 to 19 months of age and 20 to 23 months of age
Safety follow up	Immediate Unsolicited Systemic AEs: 30 minutes post-vaccination. Solicited AEs: D0 to D7 post-vaccination Unsolicited AEs: D0 until the next visit SAEs (AESIs and MAAEs): Visit 1 to 6-month follow-up	

Baseline Characteristics	Group 1+2	Group 3+4
Characteristic (950)	n=750	n=200
Sex, n (%) Male	398 (53.1)	100 (50.0)
Female	352 (46.9)	100 (50.0)
Age in years, mean (SD)	6.01 (0.570)	17.9 (0.652)
Race, n (%) White	541 (72.1)	166 (83.0)
African-American	138 (18.4)	22 (11.0)
Mixed Origin	35 (4.5)	9 (4.5)
Ethnicity, n (%) Hispanic or Latino	330 (44.0)	66 (33.0)

Immunogenicity and Safety Study of a Quadrivalent Meningococcal Conjugate Vaccine Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers. ClinicalTrials.gov, Sanofi Pasteur, 25 June 2024, https://clinicaltrials.gov/study/NCT03691610

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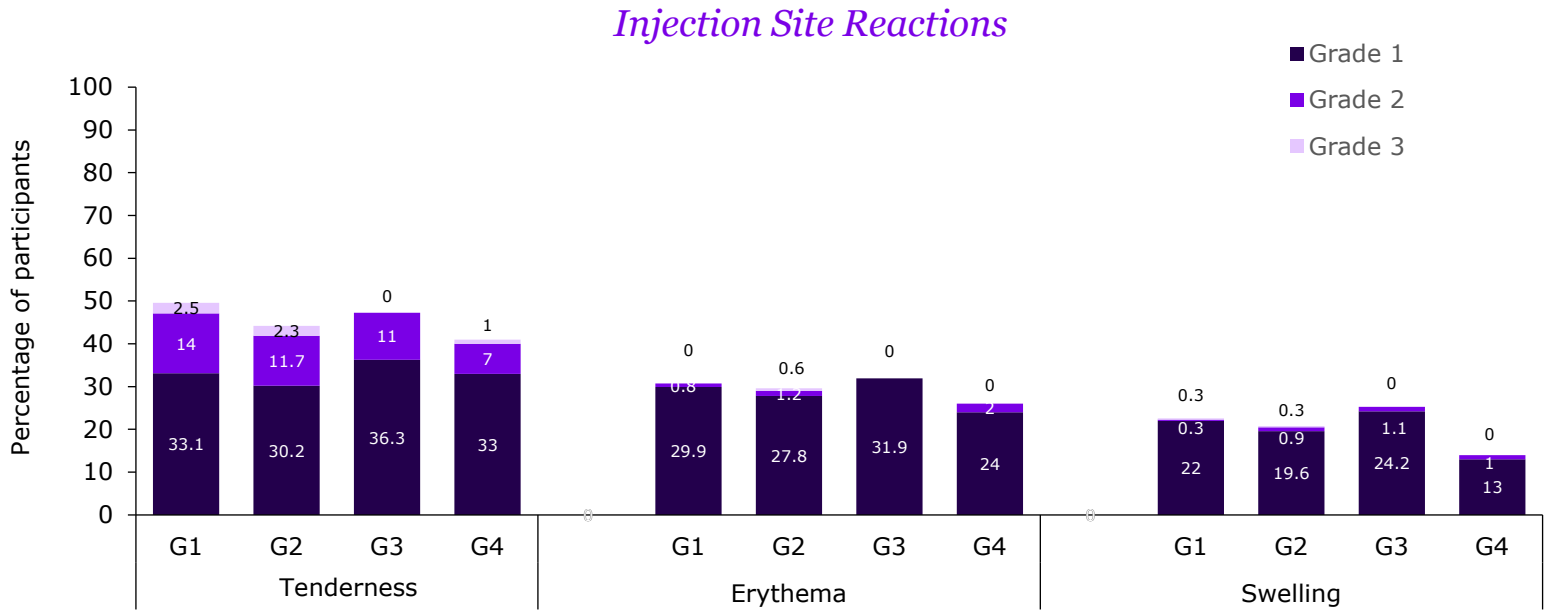
MET61

Safety

MET61: Solicited injection site reactions within 7 days after any dose



Majority of injection site reactions were Grade 1 (erythema and swelling) and Grade 1 & 2 (tenderness)

Group 1 (G1): MenACYW-TT vaccine + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age
Group 2 (G2): MenACWY-CRM vaccine + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age
Group 3 (G3): MenACYW-TT vaccine at 17 to 19 months of age and 20 to 23 months of age
Group 4 (G4): MenaACWY-D vaccine at 17 to 19 months of age and 20 to 23 months of age

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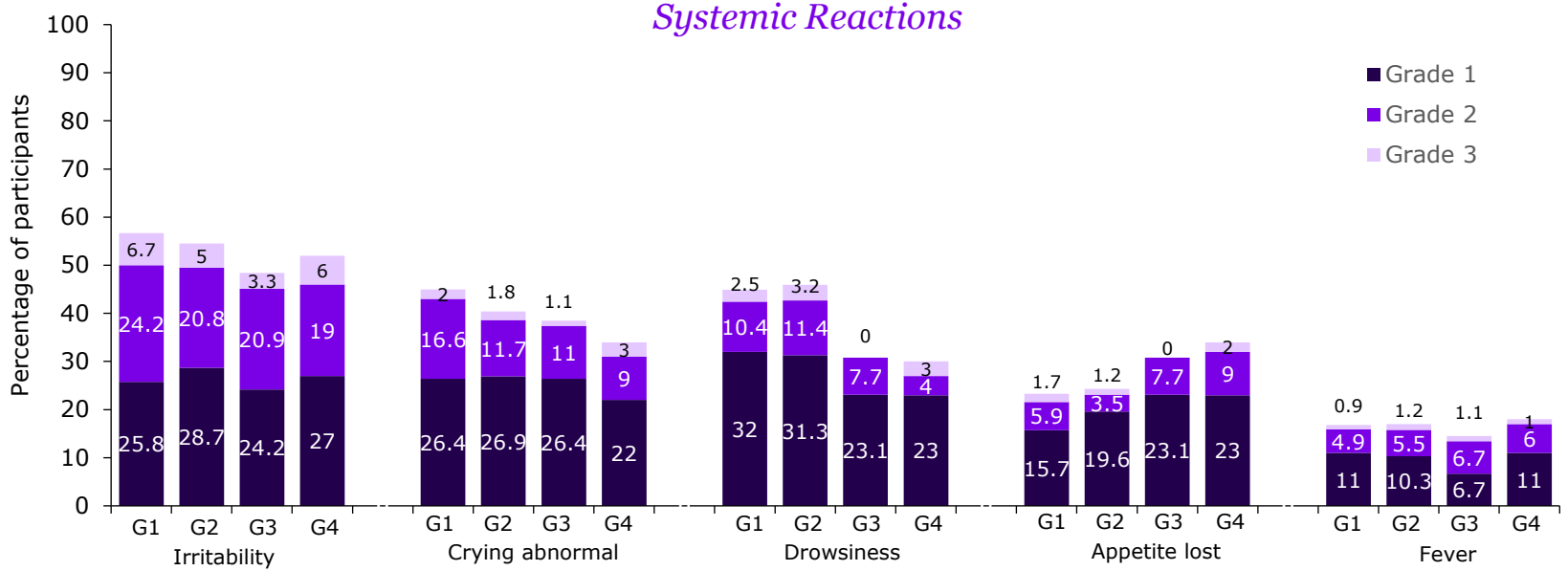
Immunogenicity and Safety Study of a Quadrivalent Meningococcal Conjugate Vaccine Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers. ClinicalTrials.gov, Sanofi Pasteur, 25 June 2024, https://clinicaltrials.gov/study/NCT03691610

MET61: Solicited systemic reactions within 7 days after any dose



Vomiting occurred less frequently, with 11.8%, 10.8%, 7.7%, and 9% reported in groups 1, 2, 3, and 4, respectively

Group 1 (G1): MenACYW-TT vaccine + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age
Group 2 (G2): MenACWY-CRM vaccine + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age
Group 3 (G3): MenACYW-TT vaccine at 17 to 19 months of age and 20 to 23 months of age
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MET61: Summary of results

Summary of safety events after any vaccine injections

- A total of 6 participants (1.6%) in Group 1 (MenACYW-TT), 12 participants (3.3%) in Group 2 (MenACWY-CRM), 1 participant (1.0%) in Group 3 (MenACYW-TT), and 4 participants (3.9%) in Group 4 (MenACWY-D) reported SAEs during the study
  - One participant in Group 2 (MenACWY-CRM) experienced an immediate unsolicited AE (head injury)
  - There was 1 SAE (acute myeloid leukemia not related to the study vaccines), leading to study discontinuation in Group 2 (MenACWY-CRM)

- One participant (1.0%) in Group 4 (MenACWY-D) experienced an SAE (febrile convulsions) that was considered related to vaccination. This was reported as an adverse event of special interest (AESI).

  - One participant (0.3%) in Group 1 (MenACYW-TT), 2 participants (0.6%) in Group 2 (MenACWY-CRM), and 2 participants (1.9%) in Group 4 (MenACWY-D) reported an AESI during the study. None of these AESI were related to the study vaccines.

- All other SAEs were evaluated as non-related to vaccination by Investigators and Sponsor
  - No deaths were reported during the study

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AESIs, adverse events of special interest

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MET61

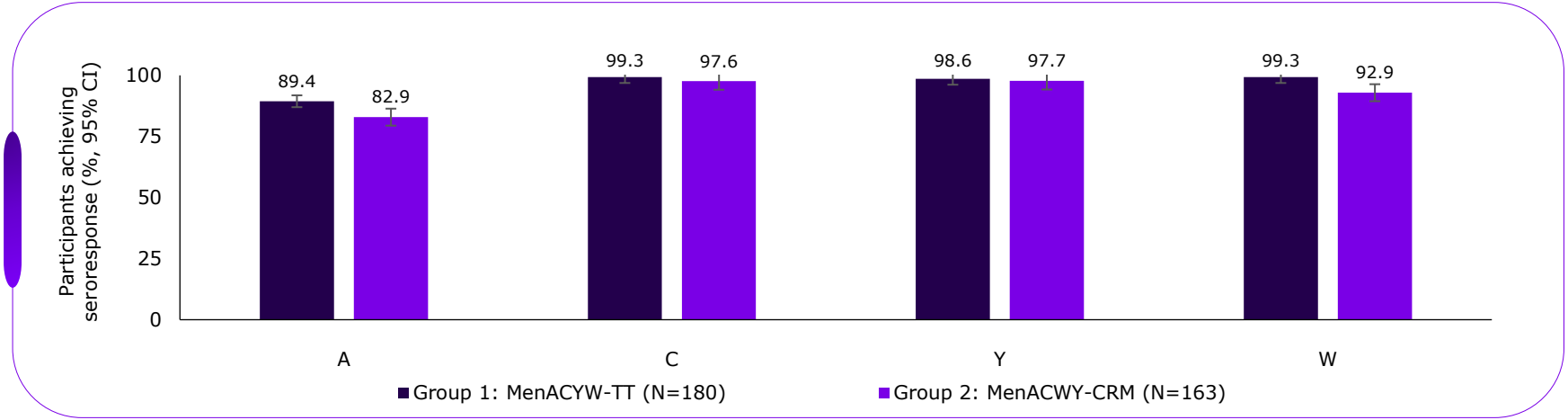
Immunogenicity

MET61: Post booster, MenACYW-TT seroresponse rates were high and comparable to those for MenACWY-CRM for all 4 serogroups

Primary objective 1 was met: Post second vaccination at 12 to 13 months of age, non-inferiority of the group 1 *vs*. group 2 showed the lower limit of the 95% confidence interval (CI) of the difference in hSBA *seroresponse* for meningococcal serogroups A, C, W, and Y was above -10%

Vaccine seroresponse* at day 30 after the booster dose (Group 1 vs Group 2) in Per-protocol Analysis Set

Percentage of subjects with vaccine seroresponse



95% CI of the single proportion calculated from the exact binomial method.
Group 1: MenACYW-TT vaccine + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age
Group 2: MenACWY-CRM + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age

*hSBA vaccine seroresponse for serogroups A, C, Y, and W was defined as:
- For a subject with a pre-vaccination titer < 1:8, the post-vaccination titer had to be ≥ 1:16
- For a subject with a pre-vaccination titer ≥ 1:8, the post-vaccination titer had to be ≥ 4-fold greater than the pre-vaccination titer

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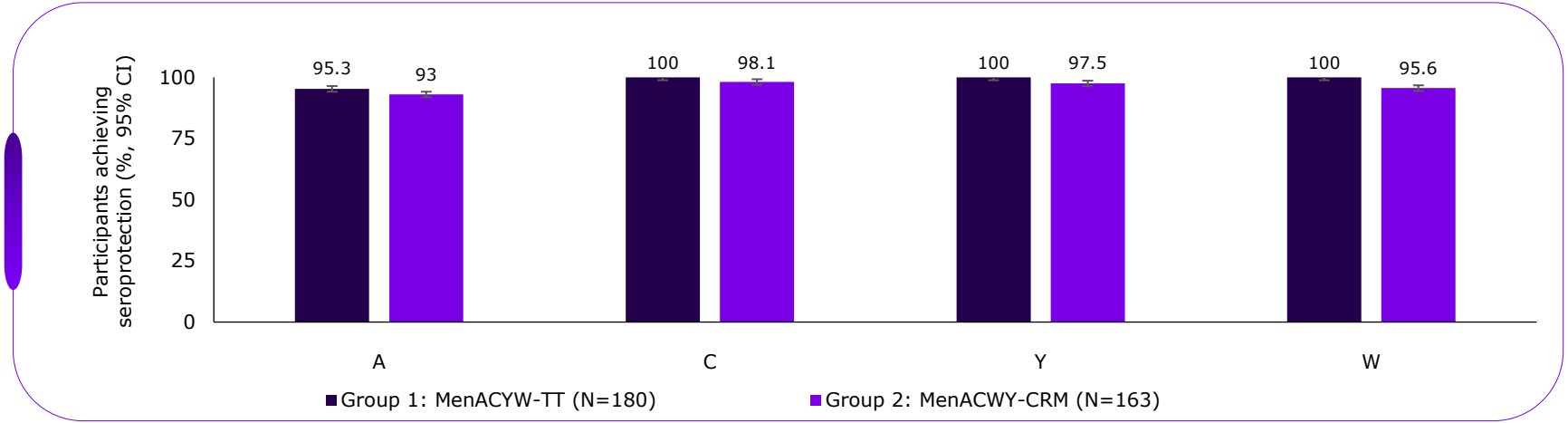
MET61: Post booster, MenACYW-TT seroprotection rates were high and comparable to those for MenACWY-CRM for all 4 serogroups

Secondary objective was met: Post-second vaccination at 12-13 months, group 1 demonstrated that at D30, the lower limit of the 95% confidence interval (CI) for the difference in subjects achieving seroprotection (hSBA ≥1:8) for serogroups A, C, W, and Y was above -10% compared to group 2.

Seroprotection: hSBA antibody titers ≥ 1:8

Percentage of subjects with seroprotection



N: number of subjects in per-protocol analysis set 2, for booster series.
95% CI of the single proportion calculated from the exact binomial method.
Group 1: MenACYW- TT vaccine + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age
Group 2: MenACWY-CRM + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age
PPAS, Per-Protocol Analysis Set

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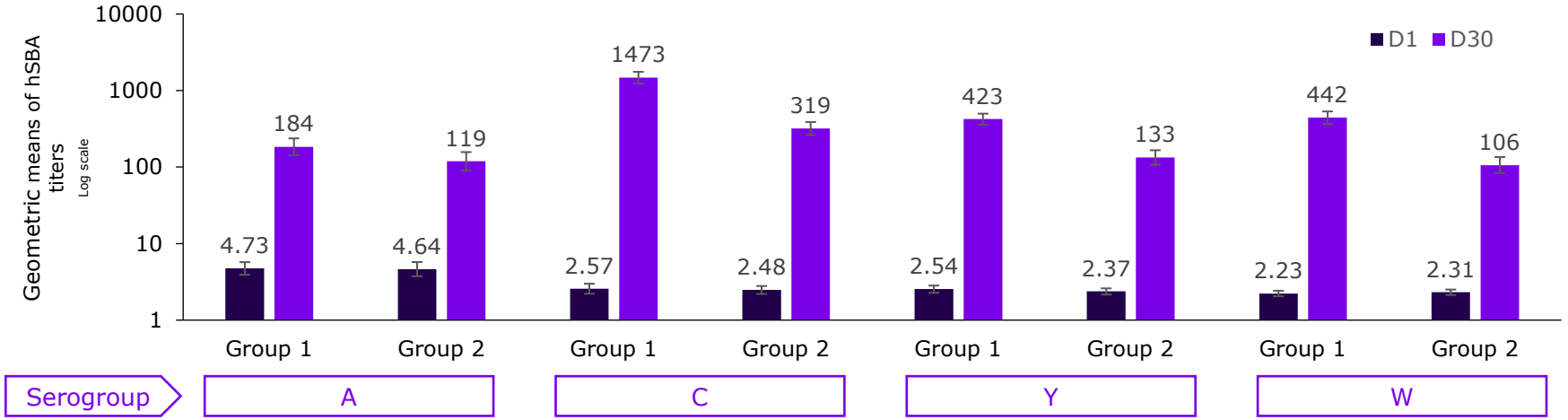
MET61: Geometric mean of hSBA antibody titers pre- and post-2nd vaccination with MenACYW-TT and MenACWY-CRM

Summary of secondary immunogenicity results

Secondary objective: At D0 (pre-dose 1), baseline hSBA GMTs for serogroups A, C, Y, and W were comparable between groups, but at D30 post-dose 2 (12–13 months), they were higher in Group 1 for all serogroups

Summary of geometric means of hSBA titers at pre-dose D1 and D30 after the 2nd vaccination at 12-13 months dose - Per-Protocol Analysis Set 2



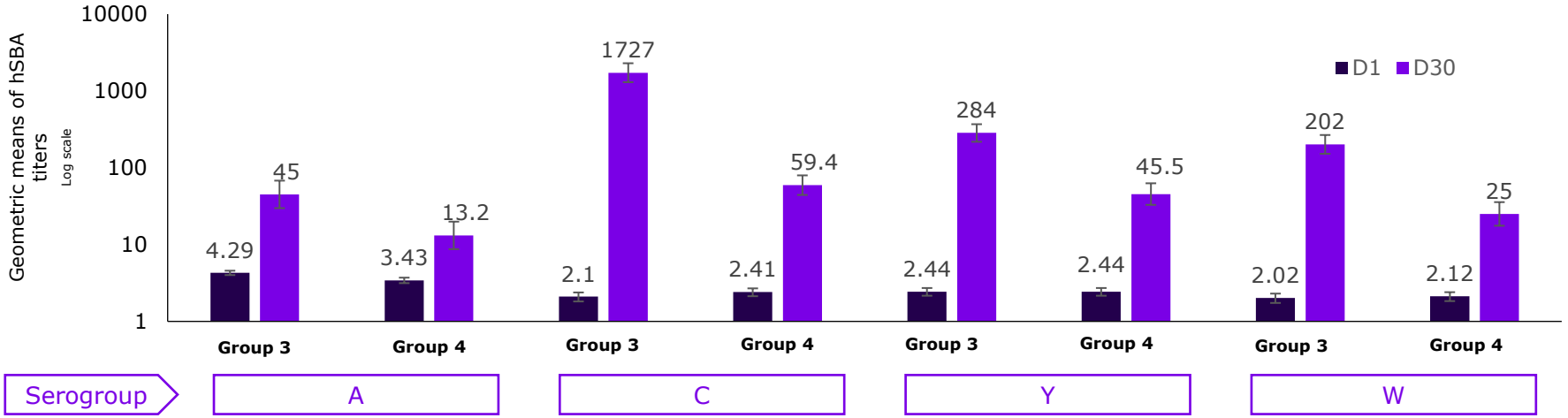
D, day; GMT, geometric mean titer; hSBA, human serum bactericidal assay;
95% CI calculated using calculation for normal distribution on log10(titer) following by antilog transformation
Group 1: MenACYW-TT vaccine + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age
Group 2: MEenACWY-CRM vaccine + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age

MET61: Geometric mean hSBA titers pre- and post-2nd vaccination with MenACYW-TT and MenACWY-D

Summary of secondary immunogenicity results

Secondary objective: At D0 (pre-dose 1), hSBA GMTs were comparable between groups, but at 30 days post-dose 2 (20–23 months), they were higher in Group 3 for all serogroups

Summary of geometric means of hSBA titers at pre-dose D1 and D30 after the 2nd vaccination at 20-33 months dose - Per-Protocol Analysis Set 2



D, day; GMT, geometric mean titer; hSBA, human serum bactericidal assay;
95% CI calculated using calculation for normal distribution on log10(titer) following by antilog transformation
Group 3: MenACYW-TT vaccine at 17 to 19 months of age and 20 to 23 months of age
Group 4: MenACWY-D at 17 to 19 months of age and 20 to 23 months of age

MET61: Summary of results

Summary of immunogenicity findings

Seroresponses **at day 30 following the first dose** of MenACYW-TT vaccine co-administered with routine pediatric vaccines were **non-inferior** to those seen after administration of a primary dose of MenACWY-CRM with routine pediatric vaccines

Six to 7 months following administration of a dose of MenACYW-TT vaccine to **infants 6-7 months of age**, *geometric mean titers (GMTs)* were **comparable** to those seen after administration of a dose of MenACWY-CRM for serogroup A **and higher for serogroups C, W, and Y**

- The **percentages of participants** in both groups **with ≥4-fold rise in titers pre- vs 30 days post-dose 2 were comparable for all 4 serogroups**

Thirty days after dose 2 administered at 20-23 months of age, the hSBA **GMTs were higher for all serogroups** in participants administrated MenACYW-TT vaccine compared to those who received MenACWY-D

- The **percentages of participants** with a **≥ 4-fold rise in hSBA GMTs** for serogroups C, Y, and W were **comparable** between the 2 vaccine groups and **higher for serogroup A** after MenACYW-TT vaccine administration compared to MenACWY-D

MenACYW-TT vaccine is immunogenic and demonstrates an acceptable safety profile when administered to infants 6 months through 23 months of age in a 2-dose schedule.

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Conclusion

MenACYW-TT demonstrated robust immunogenicity & reassuring safety profile in infants & toddlers starting vaccination as early as 6 weeks of age

- The expanded indication for MenACYW-TT is a *valuable public health option* to facilitate *immunization across the lifespan* from 6 weeks & above
- *Immunogenicity* results demonstrate *non-inferior* immune responses, administered with routine pediatric vaccines, compared to currently licensed MenACWY conjugate vaccines
- *No unexpected safety concerns* were found in infants and toddlers (from 6 weeks to 23 months) compared to the safety profile in individuals ≥2 years and other licensed MenACWY conjugate vaccines
  - *No relevant safety profile differences* were observed based on *sex or race*
  - The safety profile of 237 infants with a history of *preterm birth* (31-36 weeks gestational age)** was comparable to infants who had been born full-term, with no new safety concerns or AEs leading to study discontinuation

** all prematurely born infants were either enrolled in studies MET41 and MET42

Thank *you*

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