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

Authors: James D. Campbell[1], Sandeep Gupta[2*], Betzana Zambrano[3], Mandeep Singh Dhingra[2], Lucia Gan[2], Siham B'Chir[4], Julie Chaix[4], Olga Syrkina[5], Julie Masson[4], Olga Lyabis[4], Christine Rehm[2]

Affiliations: [1]University of Maryland School of Medicine, Center for Vaccine Development and Global Health, Baltimore, Maryland, US; [2]Sanofi, Swiftwater, Pennsylvania, US; [3]Sanofi, Montevideo, Uruguay; [4]Sanofi, Marcy L' Etoile, France; [5]Sanofi, Cambridge, Massachusetts, US

Campbell et al.

DISCLOSURES

SG, BZ, MSD, LG, SB, JC, OS, JM, OL and CR are employees of Sanofi and may hold company stocks and/or stock options. JDC has no conflicts of interest. All relevant financial disclosures have been mitigated.

Background

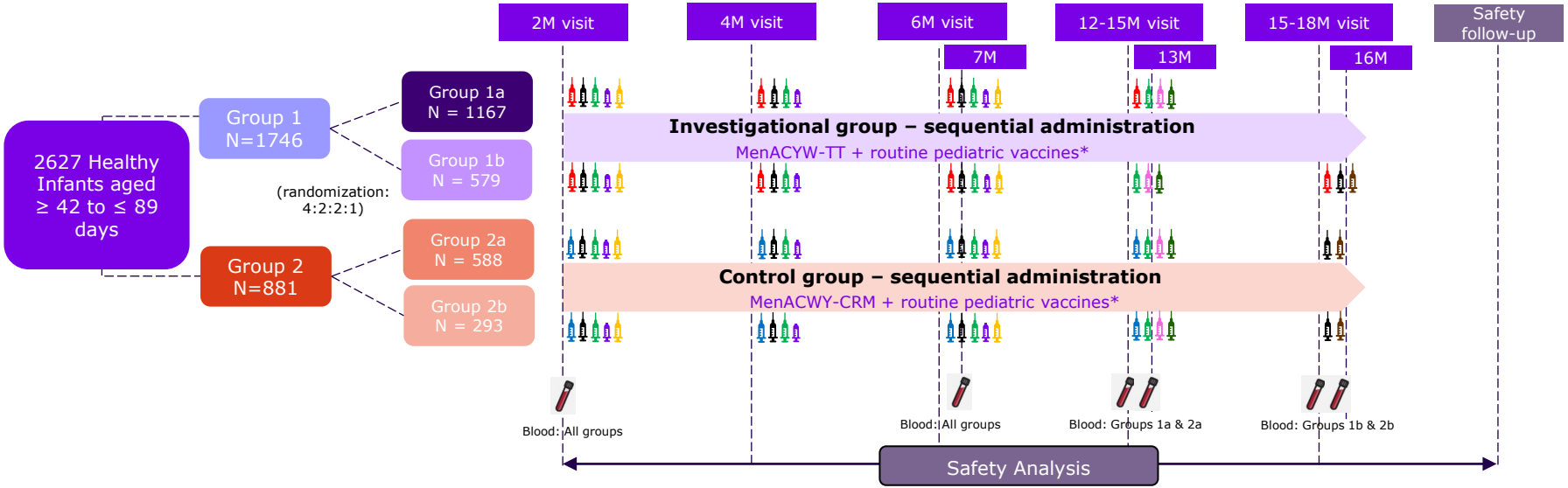
Study Design Overview

MET42 Main study features (NCT03537508)

- Invasive meningococcal disease (IMD) is a serious, potentially fatal, illness caused by *Neisseria meningitidis*,[1-3] with the highest incidence among infants (<1 year of age) and also high incidence among children 1–4 years of age.[1,4,5]
- The most common manifestations of IMD are meningitis and septicemia, which progress rapidly,[1,3,4] and can lead to death within 24–48 hours of onset.[3] Among survivors, IMD can lead to amputations and scarring due to sepsis and other long-term complications, including neurological and psychological sequelae.[1,3,6]
- Sanofi's **MenACYW-TT** (MenQuadfi®, Sanofi, Swiftwater, PA) is a quadrivalent meningococcal tetanus toxoid-conjugate vaccine developed to provide broad protection against IMD caused by serogroups A, C, W, and Y.[7] MenACYW-TT is licensed in different parts of the world including Europe, Australia, Canada for use from ≥12 months of age.[8-10] In the United States (US), MenACYW-TT is licensed for use in individuals ≥2 years of age.[7]
- A Phase III, partially modified double-blind, randomized, parallel-group, active-controlled, multi-center study was conducted in the US to compare the immunogenicity and safety of **MenACYW-TT** vs MENVEO® (Meningococcal [Groups A, C, Y, and W-135] Oligosaccharide Diphtheria CRM197 Conjugate Vaccine) when administered concomitantly with routine pediatric vaccines to healthy infants and toddlers.

References: 1. ECDC fact sheet. **2.** CDC 2024 about. **3.** WHO fact sheet 2023. **4.** Pardo 2023. **5.** CDC surveillance. **6.** Olbrich 2018. **7.** Menquadfi® US PI. **8.** Menquadfi® EU PIs. **9.** Menquadfi® Aus PIs. **10.** Menquadfi® Canada PIs.

Study Design



MenACYW-TT [(at 2, 4, 6, 12 to 15 months of age for Group 1a) & (at 2, 4, 6, 15 to 18 months of age for Group 1b)]
MenACWY-CRM at 2, 4, 6, and 12 months of age
*Routine pediatric vaccines include -
Pentacel® (DTaP-IPV//Hib) at 2, 4, 6, and 15 to 18 months of age
PREVNAR 13® (Pneumococcal 13-valent conjugate vaccine; PCV13) at 2, 4, 6, and 12 to 15 months of age
RotaTeq® (Rotavirus vaccine) at 2, 4, and 6 months of age
ENGERIX-B® (Hepatitis B vaccine) at 2 and 6 months of age
M-M-R® II (Measles, mumps, and rubella vaccine) at 12 to 15 months of age
VARIVAX® (Varicella vaccine) at 12 to 15 months of age
HAVRIX® (hepatitis A vaccine) at 15 to 18 months of age, received by groups 1b and 2
M, Months of age; SafAS3, Safety summary after the third dose at 6 months of age; SafAS4, Safety summary after the fourth dose at 12 months of age

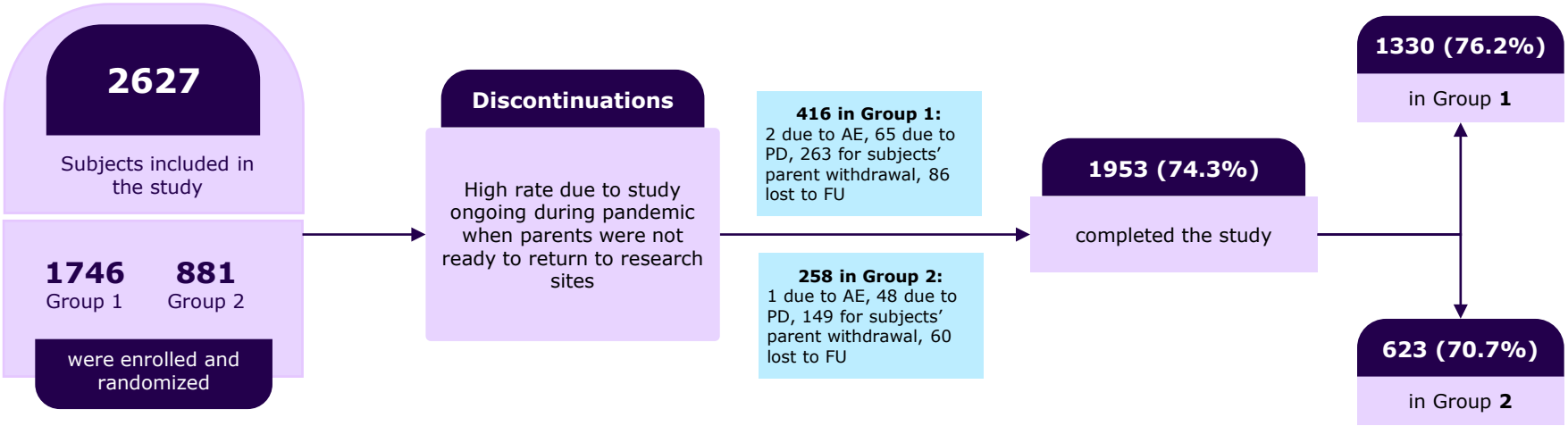
Study Objectives

MET42 Main Objectives	
Primary Objectives (Immunogenicity)	• To demonstrate the non-inferiority of vaccine seroresponse to serogroups A, C, Y, and W following the administration of a 4-dose series of **MenACYW-TT** vs MenACWY-CRM, when given concomitantly with routine pediatric vaccines in infants and toddlers 6 weeks old to 15 months of age • To demonstrate the non-inferiority of the hSBA antibody response to serogroups A, C, Y, and W following the administration of 3 doses in infancy of **MenACYW-TT** vs MenACWY-CRM, when given concomitantly with routine pediatric vaccines to infants at 2, 4, and 6 months of age
Key Secondary Objectives (Immunogenicity)	• To demonstrate the non-inferiority of immune responses of routine pediatric vaccines administered concomitantly with MenACYW-TT as compared with MenACWY-CRM after dose 3 and dose 4 • To assess the antibody responses against meningococcal serogroups A, C, Y, and W after the administration of the 4th dose of MenACYW-TT or MenACWY-CRM when both are given concomitantly with routine pediatric vaccines at 12 months of age
Safety Objectives (Descriptive)	• To describe the safety profile of **MenACYW-TT** and MenACWY-CRM when administered concomitantly with routine pediatric vaccines to healthy infants
Safety Endpoints (Descriptive)	• Immediate unsolicited adverse events (AEs) and adverse reactions (ARs) measured within 30 min post vaccinations • Solicited injection site & systemic ARs measured within the 7 days post-vaccinations • Unsolicited AEs & ARs measured within the 30 days post-vaccinations • Serious adverse events (SAEs) measured throughout the study duration

hSBA, serum bactericidal assay using human complement

Results

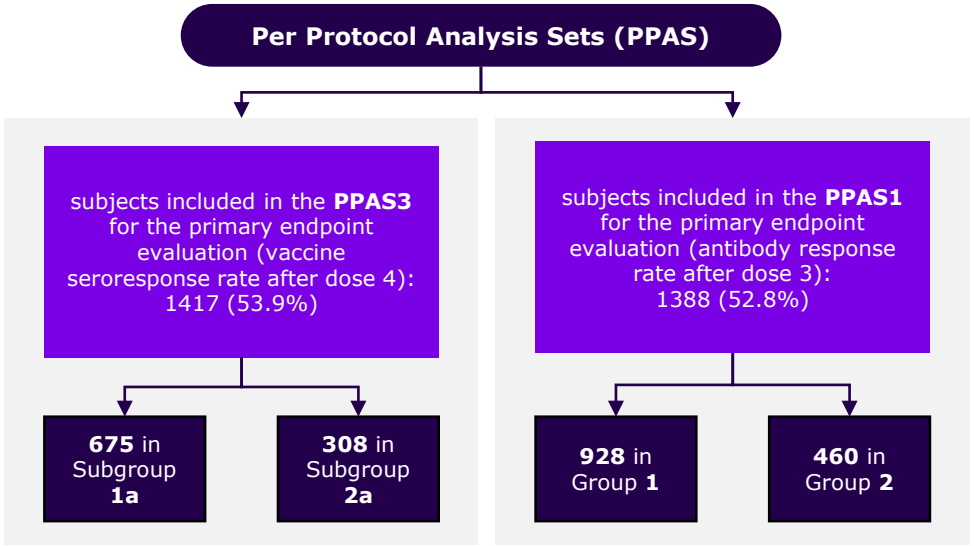
Disposition

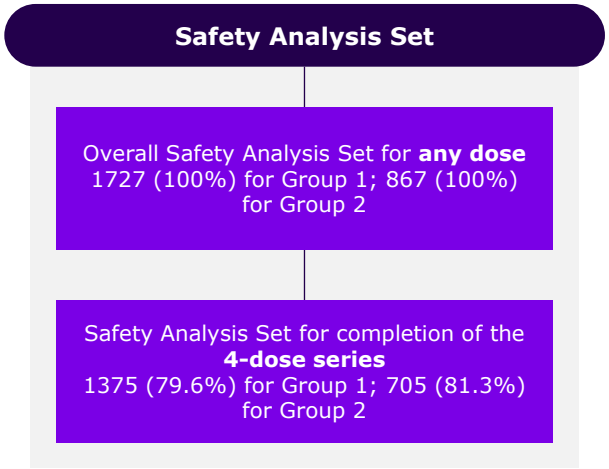


FU, follow up; PD, protocol deviation;
Group 1 (Group 1a and 1b): MenACYW-TT and routine pediatric vaccines; Group 2 (Group 2a and 2b): MenACWY-CRM and routine pediatric vaccines

Results

Disposition





hSBA vaccine seroresponse for serogroups A, C, W, and Y is defined as: for a subject with a pre-vaccination titer < 1:8, the post-vaccination titer must be ≥ 1:16; for a subject with a pre-vaccination titer ≥ 1:8, the post-vaccination titer must be ≥ 4-fold greater than the pre-vaccination titer. Antibody response is defined as with hSBA antibody titers >=1:8 for serogroups A, C, W, and Y
PPAS, Per Protocol Analysis Sets;
Group 1 (Group 1a and 1b): MenACYW-TT and routine pediatric vaccines; Group 2 (Group 2a and 2b): MenACWY-CRM and routine pediatric vaccines

Results

Demographics

1243 subjects (47.3%) were female and 1384 (52.7%) were male. The mean age was 65.3 days for Group 1, and 65.3 days for Group 2. 81.8% of the subjects were White.

	Group 1 (N=1746)	Group 2 (N=881)	Group 1a (N=1167)	Group 1b (N=579)	Group 2a (N=588)	Group 2b (N=293)	All (N=2627)
Sex: n (%)							
Male	918 (52.6)	466 (52.9)	618 (53.0)	300 (51.8)	324 (55.1)	142 (48.5)	1384 (52.7)
Female	828 (47.4)	415 (47.1)	549 (47.0)	279 (48.2)	264 (44.9)	151 (51.5)	1243 (47.3)
Sex ratio: Male/Female	1.11	1.12	1.13	1.08	1.23	0.94	1.11
Age: (Days)							
M	1746	881	1167	579	588	293	2627
Mean (SD)	65.3 (8.02)	65.3 (7.81)	65.3 (8.12)	65.3 (7.80)	65.4 (7.75)	65.0 (7.93)	65.3 (7.95)
Min ; Max	42.0 ; 89.0	42.0 ; 89.0	42.0 ; 89.0	42.0 ; 89.0	42.0 ; 89.0	42.0 ; 89.0	42.0 ; 89.0
Median	64.0	64.0	64.0	64.0	64.0	64.0	64.0
Q1 ; Q3	61.0 ; 69.0	61.0 ; 69.0	61.0 ; 69.0	61.0 ; 69.0	61.0 ; 69.0	61.0 ; 69.0	61.0 ; 69.0
Racial origin: n (%)							
American Indian or Alaska Native	11 (0.6)	3 (0.3)	6 (0.5)	5 (0.9)	3 (0.5)	0	14 (0.5)
Asian	15 (0.9)	10 (1.1)	8 (0.7)	7 (1.2)	6 (1.0)	4 (1.4)	25 (1.0)
Black or African American	204 (11.7)	99 (11.2)	142 (12.2)	62 (10.7)	63 (10.7)	36 (12.3)	303 (11.5)

n: number of subjects fulfilling the item listed in the first column
M: number of subjects with available data for the relevant endpoint
N: number of subjects randomized in each study group
Percentages are based on N. Q1; Q3: first quartile; third quartile. SD: standard deviation
Group 1 (Group 1a and 1b): MenACYW-TT and routine pediatric vaccines
Group 2 (Group 2a and 2b): MenACWY-CRM and routine pediatric vaccines

Results

Demographics (Contd.)

	Group 1 (N=1746)	Group 2 (N=881)	Group 1a (N=1167)	Group 1b (N=579)	Group 2a (N=588)	Group 2b (N=293)	All (N=2627)
Native Hawaiian or Other Pacific Islander	7 (0.4)	6 (0.7)	5 (0.4)	2 (0.3)	4 (0.7)	2 (0.7)	13 (0.5)
White	1428 (81.8)	722 (82.0)	950 (81.4)	478 (82.6)	491 (83.5)	231 (78.8)	2150 (81.8)
Mixed Origin	44 (2.5)	30 (3.4)	31 (2.7)	13 (2.2)	16 (2.7)	14 (4.8)	74 (2.8)
Unknown	19 (1.1)	6 (0.7)	14 (1.2)	5 (0.9)	3 (0.5)	3 (1.0)	25 (1.0)
Not Reported	18 (1.0)	5 (0.6)	11 (0.9)	7 (1.2)	2 (0.3)	3 (1.0)	23 (0.9)
Ethnicity: n (%)							
Hispanic or Latino	838 (48.0)	410 (46.5)	549 (47.0)	289 (49.9)	278 (47.3)	132 (45.1)	1248 (47.5)
Not Hispanic or Latino	897 (51.4)	465 (52.8)	611 (52.4)	286 (49.4)	305 (51.9)	160 (54.6)	1362 (51.8)
Unknown	3 (0.2)	4 (0.5)	2 (0.2)	1 (0.2)	3 (0.5)	1 (0.3)	7 (0.3)
Not Reported	8 (0.5)	2 (0.2)	5 (0.4)	3 (0.5)	2 (0.3)	0	10 (0.4)

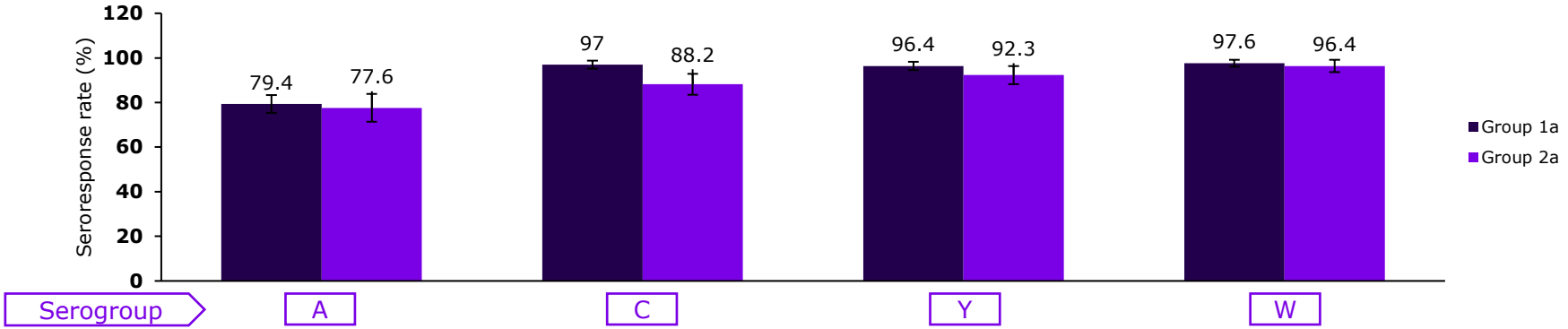
n: number of subjects fulfilling the item listed in the first column
M: number of subjects with available data for the relevant endpoint
N: number of subjects randomized in each study group
Percentages are based on N. Q1; Q3: first quartile; third quartile. SD: standard deviation
Group 1 (Group 1a and 1b): MenACYW-TT and routine pediatric vaccines
Group 2 (Group 2a and 2b): MenACWY-CRM and routine pediatric vaccines

Results

Summary of primary immunogenicity results

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

hSBA vaccine seroresponse rate at D30 after the 4th dose - Per-Protocol Analysis Set 3



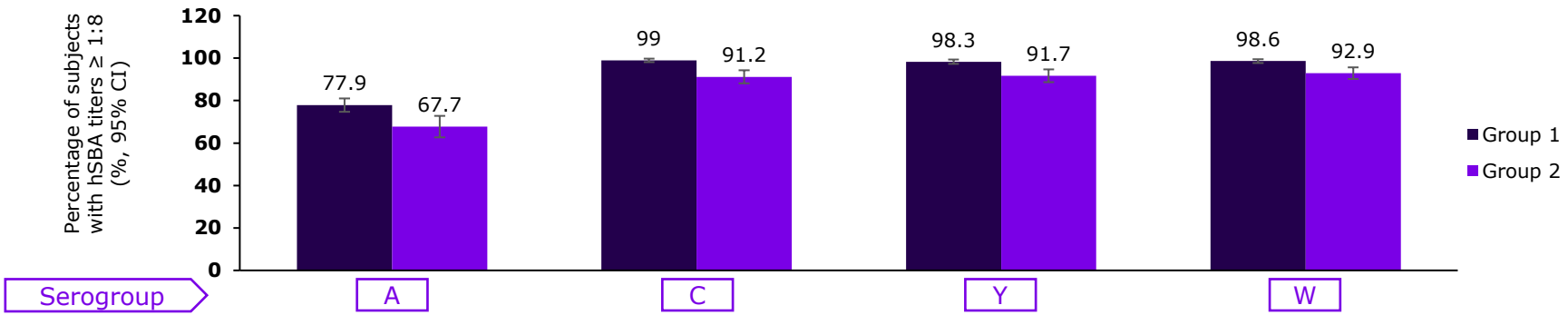
CI, confidence interval;
hSBA vaccine seroresponse: for a subject with a pre-1st dose (D0 before 2-month) vaccinations titer < 1:8, the post-4th dose (D30 after 12-month) vaccinations titer must be >= 1:16;
For a subject with a pre-1st dose vaccinations titer >= 1:8, the post-4th vaccinations titer must be at least 4-fold greater than the pre-1st dose vaccinations titer.
95% CI of the single proportion calculated from the exact binomial method. ; 95% CI of the difference calculated from the Wilson Score method without continuity correction.
The overall non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.
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

Results

Summary of primary immunogenicity results

Primary objective 2 was met: Non-inferiority of the **percentage of subjects with hSBA antibody titers** against 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 the percentage of subjects with hSBA antibody titer ≥ 1:8 were > -10% for all 4 serogroups.

Percentage of subjects with hSBA antibody titers >=1:8 at D30 after the 3rd dose - Per-Protocol Analysis Set 1



95% CI of the single proportion calculated from the exact binomial method
95% CI of the difference calculated from the Wilson Score method without continuity correction
The overall non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups
Group 1: MenACYW-TT and routine pediatric vaccines
Group 2: MenACWY-CRM and routine pediatric vaccines

Results

Summary of key secondary immunogenicity results

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

Summary of non-inferiority outcome for the secondary objectives

Evaluation Time	Comparison Groups (G)	Antigen	Endpoint	Non-inferiority margin	Hypothesis #	Non-inferiority?
1st Year, 30 days after the 6-month vaccination (PPAS1)	G1 vs G2	Hepatitis B	% ≥ 10 mIU/mL	10%	1	Yes
		PRP	% ≥ 0.15 µg/mL	5%	2	Yes
		PRP	% ≥ 1.0 µg/mL	10%	3	Yes
		Polio†	% ≥ 1:8	5%	4	Yes
		Rotavirus	% ≥ 3-fold rise	10%	5	Yes
		Rotavirus	GMC (G1/G2 ratio)	1.5	6	Yes
		Pertussis*	GMC (G1/G2 ratio)	1.5	7	Yes
		Pneumococcal‡	GMC (G1/G2 ratio)	2	8	Yes
2nd Year, 30 days after the 12-month vaccination (PPAS3)	G1a vs G2a	Measles	% ≥ 255 mIU/mL	10%	9	Yes
		Mumps	% ≥ 10 mumps Ab units/mL	10%	10	Yes
		Rubella	% ≥ 10 IU/mL	10%	11	Yes
		Varicella	% ≥ 5 gpELISA units/mL	10%	12	Yes
		Pneumococcal‡	GMC (G1a/G2a ratio)	2	13	Yes
2nd Year, 30 days after the 15-month vaccination (PPAS3)	G1b vs G2b	PRP	% ≥ 1.0µg/mL	10%	14	Yes
		Polio†	% ≥ 1:8	5%	15	Yes
		Pertussis*	Response rate	10%	16	Yes

Ab, antibody; ELISA, enzyme-linked immunosorbent assay; GMC, geometric mean concentrations; PPAS1, per-protocol analysis set 1; PPAS3, per-protocol analysis set 3; PRP, Anti polyribosyl-ribitol phosphate

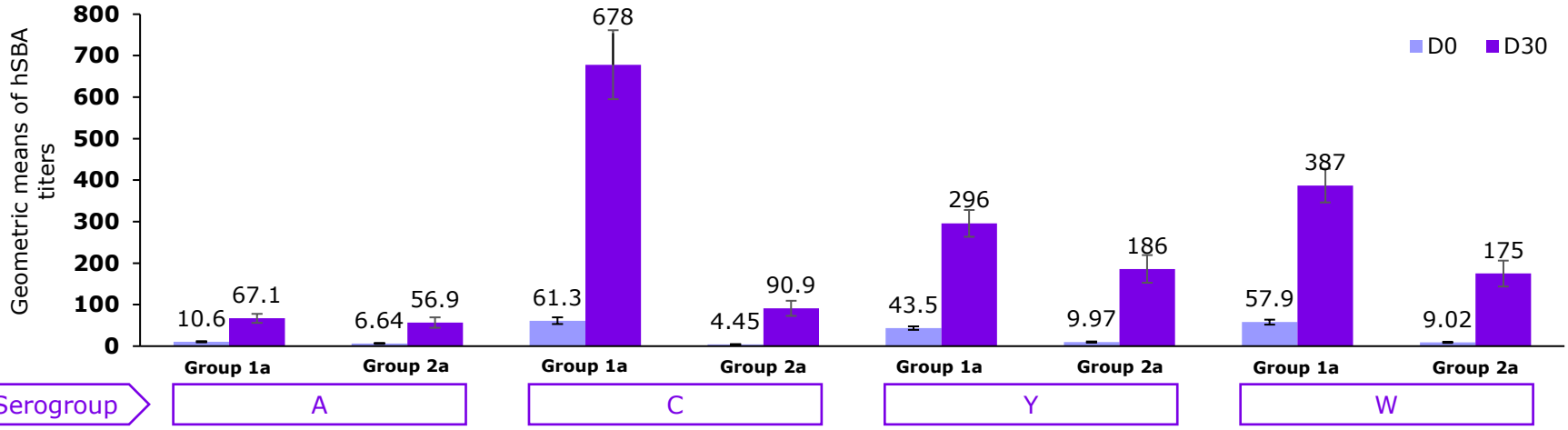
#Hypothesis number; *Pertussis: PT, FHA, PRN, and FIM; †Polio: type 1, type 2, type 3; ‡Pneumococcal: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F

Results

Summary of primary immunogenicity results

Secondary objective 2: Geometric mean of hSBA antibody titers against meningococcal serogroups A, C, Y and W after 4th dose of MenACYW 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

Results

Safety overview after any dose

	Group 1 (N=1727)			Group 2 (N=867)		
Subjects experiencing at least one:	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Within 30 mins after any vaccine injections						
Immediate unsolicited AE	1/1727	<0.1	(0 ; 0.3)	1/867	0.1	(0 ; 0.6)
Immediate unsolicited AR	0/1727	0	(0 ; 0.2)	0/867	0	(0 ; 0.4)
Solicited reaction from D0 to D7 within solicited period after any vaccine injections	1424/1644	86.6	(84.9 ; 88.2)	729/831	87.7	(85.3 ; 89.9)
Solicited injection site reaction	1280/1642	78.0	(75.9 ; 79.9)	663/831	79.8	(76.9 ; 82.5)
Solicited injection site reaction after injection of MenACYW-TT or MenACWY-CRM	1176/1641	71.7	(69.4 ; 73.8)	590/831	71.0	(67.8 ; 74.1)
Solicited injection site reaction after injection of PENTACEL	1111/1636	67.9	(65.6 ; 70.2)	586/827	70.9	(67.6 ; 73.9)
Solicited injection site reaction after injection of PREVNAR 13	1145/1639	69.9	(67.6 ; 72.1)	587/830	70.7	(67.5 ; 73.8)
Solicited injection site reaction after injection of ENGERIX-B	919/1634	56.2	(53.8 ; 58.7)	472/829	56.9	(53.5 ; 60.3)
Solicited injection site reaction after injection of M-M-R II	525/1279	41.0	(38.3 ; 43.8)	262/641	40.9	(37.0 ; 44.8)
Solicited injection site reaction after injection of VARIVAX	497/1275	39.0	(36.3 ; 41.7)	268/640	41.9	(38.0 ; 45.8)
Solicited injection site reaction after injection of HAVRIX	173/402	43.0	(38.1 ; 48.0)	235/595	39.5	(35.5 ; 43.6)
Solicited systemic reaction	1313/1642	80.0	(77.9 ; 81.9)	681/831	81.9	(79.2 ; 84.5)
Within 30 days after any vaccine injections						
Unsolicited AE	930/1727	53.9	(51.5 ; 56.2)	467/867	53.9	(50.5 ; 57.2)
Unsolicited AR	94/1727	5.4	(4.4 ; 6.6)	55/867	6.3	(4.8 ; 8.2)

n: number of subjects experiencing the endpoint listed in the first column; M: number of subjects with available data for the relevant endpoint N: number of subjects in overall safety analysis set for any dose ; Percentages are based on M.
"Immediate unsolicited AE" is collected only for immediate unsolicited systemic AEs; "MAAE" is medically-attended adverse event. "AESI" is adverse events of special interest. "Unsolicited AE" also includes immediate and serious unsolicited AEs. "Unsolicited non-serious AE" includes any unsolicited AE that is non-serious.
AR: Reactions related to study vaccine (MenACYW-TT/MenACWY-CRM); Unsolicited injection site reactions related to NIMP (routine vaccines) are reported separately For 4 AEs, the relationship to the exact vaccine (IMP/NIMP) cannot be determined.
Group 1: MenACYW-TT and routine pediatric vaccines; Group 2: MenACWY-CRM and routine pediatric vaccines

Results

Safety overview after any dose (Contd.)

	Group 1 (N=1727)			Group 2 (N=867)		
Subjects experiencing at least one:	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Unsolicited non-serious AE	916/1727	53.0	(50.7 ; 55.4)	466/867	53.7	(50.4 ; 57.1)
Unsolicited non-serious AR	93/1727	5.4	(4.4 ; 6.6)	55/867	6.3	(4.8 ; 8.2)
Unsolicited non-serious injection site AR related to MenACYW-TT or MenACWY-CRM	86/1727	5.0	(4.0 ; 6.1)	48/867	5.5	(4.1 ; 7.3)
Unsolicited non-serious injection site AR related to PENTACEL	96/1727	5.6	(4.5 ; 6.7)	38/867	4.4	(3.1 ; 6.0)
Unsolicited non-serious injection site AR related to PREVNAR 13	89/1727	5.2	(4.2 ; 6.3)	39/867	4.5	(3.2 ; 6.1)
Unsolicited non-serious injection site AR related to ENGERIX-B	37/1727	2.1	(1.5 ; 2.9)	19/867	2.2	(1.3 ; 3.4)
Unsolicited non-serious injection site AR related to M-M-R II	30/1727	1.7	(1.2 ; 2.5)	17/867	2.0	(1.1 ; 3.1)
Unsolicited non-serious injection site AR related to VARIVAX	21/1727	1.2	(0.8 ; 1.9)	15/867	1.7	(1.0 ; 2.8)
Unsolicited non-serious injection site AR related to HAVRIX	6/1727	0.3	(0.1 ; 0.8)	9/867	1.0	(0.5 ; 2.0)
Unsolicited non-serious systemic AE	870/1727	50.4	(48.0 ; 52.8)	442/867	51.0	(47.6 ; 54.4)
Unsolicited non-serious systemic AR	9/1727	0.5	(0.2 ; 1.0)	7/867	0.8	(0.3 ; 1.7)
AE leading to study discontinuation	1/1727	<0.1	(0 ; 0.3)	1/867	0.1	(0 ; 0.6)
SAE	39/1727	2.3	(1.6 ; 3.1)	11/867	1.3	(0.6 ; 2.3)
Death	1/1727	<0.1	(0 ; 0.3)	0/867	0	(0 ; 0.4)
AESI	3/1727	0.2	(0 ; 0.5)	0/867	0	(0 ; 0.4)
MAAE	689/1727	39.9	(37.6 ; 42.2)	368/867	42.4	(39.1 ; 45.8)

n: number of subjects experiencing the endpoint listed in the first column; M: number of subjects with available data for the relevant endpoint
N: number of subjects in overall safety analysis set for any dose ; Percentages are based on M.
"Immediate unsolicited AE" is collected only for immediate unsolicited systemic AEs; "MAAE" is medically-attended adverse event. "AESI" is adverse events of special interest.
"Unsolicited AE" also includes immediate and serious unsolicited AEs. "Unsolicited non-serious AE" includes any unsolicited AE that is non-serious.
AR: Reactions related to study vaccine (MenACYW-TT/MenACWY-CRM); Unsolicited injection site reactions related to NIMP (routine vaccines) are reported separately
For 4 AEs, the relationship to the exact vaccine (IMP/NIMP) cannot be determined.
Group 1: MenACYW-TT and routine pediatric vaccines; Group 2: MenACWY-CRM and routine pediatric vaccines

Results

Safety overview after any dose (Contd.)

	Group 1 (N=1727)			Group 2 (N=867)		
Subjects experiencing at least one:	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
During the study						
SAE	99/1727	5.7	(4.7 ; 6.9)	38/867	4.4	(3.1 ; 6.0)
Death	1/1727	<0.1	(0 ; 0.3)	0/867	0	(0 ; 0.4)
AESI	13/1727	0.8	(0.4 ; 1.3)	5/867	0.6	(0.2 ; 1.3)
MAAE	1050/1727	60.8	(58.5 ; 63.1)	526/867	60.7	(57.3 ; 63.9)

n: number of subjects experiencing the endpoint listed in the first column; M: number of subjects with available data for the relevant endpoint
N: number of subjects in overall safety analysis set for any dose ; Percentages are based on M.
"Immediate unsolicited AE" is collected only for immediate unsolicited systemic AEs; "MAAE" is medically-attended adverse event. "AESI" is adverse events of special interest.
"Unsolicited AE" also includes immediate and serious unsolicited AEs. "Unsolicited non-serious AE" includes any unsolicited AE that is non-serious.
AR: Reactions related to study vaccine (MenACYW-TT/MenACWY-CRM); Unsolicited injection site reactions related to NIMP (routine vaccines) are reported separately
For 4 AEs, the relationship to the exact vaccine (IMP/NIMP) cannot be determined.
Group 1: MenACYW-TT and routine pediatric vaccines Group 2: MenACWY-CRM and routine pediatric vaccines

Results

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

99 subjects (5.7%) in Group 1, 38 subjects (4.4%) in Group 2 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 the MenACYW-TT group with prior history of seizures. The Febrile seizure was an AESI
  - 1 subject reported **Fever** post vaccination in the MenACWY-CRM group

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

- All other AESI were nonrelated to the study vaccines (except the one mentioned above)

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

- The subject with Cardiac arrest was the only death reported in the study. It was deemed unrelated to the study vaccine by the investigator and sponsor

AESIs, adverse events of special interest;

Conclusion

Primary immunogenicity objectives were met

- Non-inferiority of hSBA seroresponses to meningococcal serogroups A, C, W, and Y when 4-doses of MenACYW-TT vaccine (at 2, 4, 6 and 12 months of age) is administered concomitantly with pediatric vaccines compared to 4 doses of MenACWY-CRM given with pediatric vaccines, was demonstrated
- 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 (at 2, 4, 6 months of age) 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

Secondary immunogenicity objectives were 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
- Geometric mean of hSBA titers against meningococcal serogroups A, C, Y and W after 4th dose of MenACYW were comparable for all serogroups in Group 1 vs Group 2

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 available

POSTERS:

P-632

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

Moskow et al.

P-662

Phase III, modified double-blind, randomized, parallel group, active-controlled, multi-center study of meningococcal quadrivalent ACWY conjugated vaccine in infants from 6 through 23 months of age in the United States

Duffy et al.

ACKNOWLEDGEMENTS:

• The authors would like to thank all participants who volunteered to take part in the study, the study investigators and their site staff; and the MET42 Sanofi team, who designed and coordinated the conduct of the study

• Medical writing support was provided by Sowmya Srinivasan, PhD (Sanofi)

• The study was sponsored by Sanofi

Thank *you!*

Back-ups

Results

Secondary objective 1

Hypothesis 1: Non-inferiority of the percentage of subjects with anti-hepatitis B antibody concentrations ≥10 mIU/mL at D30 after the 6-month vaccination - **met**

							Group 1- Group 2		
Criterion	n/M	Group 1 (N=928) %	95% CI	n/M	Group 2 (N=460) %	95% CI	Difference (%)	95% CI	Non-Inferiority
≥10 mIU/mL	754/765	98.6	(97.4 ; 99.3)	341/348	98.0	(95.9 ; 99.2)	0.57	(-0.95 ; 2.75)	Yes

n: Number of subjects with anti-hepatitis B antibody concentrations that met the criterion.
M: Number of subjects with available data for the endpoint.
N: number of subjects in per-protocol analysis set 1, for infant vaccinations.
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction
Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is >-10%
Group 1: MenACYW-TT and routine pediatric vaccines
Group 2: MenACWY-CRM and routine pediatric vaccines

Results

Secondary objective 1

Hypothesis 2 & 3: Non-inferiority of the percentage of subjects with anti-PRP antibody concentrations ≥0.15 and ≥1.0µg/mL at D30 after the 6-month vaccinations - **met**

							Group 1- Group 2		
Criterion	n/M	Group 1 (N=928) %	95% CI	n/M	Group 2 (N=460) %	95% CI	Difference (%)	95% CI	Non-Inferiority
≥0.15 µg/mL*	873/882	99.0	(98.1 ; 99.5)	405/420	96.4	(94.2 ; 98.0)	2.55	(0.89 ; 4.84)	Yes
≥1.0µg/mL **	805/882	91.3	(89.2 ; 93.0)	360/420	85.7	(82.0 ; 88.9)	5.56	(1.90 ; 9.60)	Yes

n: Number of subjects with anti- PRP antibody concentrations that met the criterion
N: number of subjects in per-protocol analysis set 1, for infant vaccinations; M: Number of subjects with available data for the endpoint.
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction
*Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is >-5%
**Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is >-10%
Group 1: MenACYW-TT and routine pediatric vaccines
Group 2: MenACWY-CRM and routine pediatric vaccines

Results

Secondary objective 1

Hypothesis 4: Non-inferiority of the percentage of subjects with anti-polio antibody titers ≥1:8 at D30 after the 6-month vaccinations - **met**

							Group 1- Group 2		
Serotypes	n/M	Group 1 (N=928) %	95% CI	n/M	Group 2 (N=460) %	95% CI	Difference (%)	95% CI	Non-Inferiority
Anti-polio 1	839/839	100	(99.6 ; 100)	412/412	100	(99.1 ; 100)	0	(-0.46 ; 0.92)	Yes
Anti-polio 2	838/838	100	(99.6 ; 100)	406/406	100	(99.1 ; 100)	0	(-0.46 ; 0.94)	Yes
Anti-polio 3	854/854	100	(99.6 ; 100)	415/415	100	(99.1 ; 100)	0	(-0.45 ; 0.92)	Yes

n: Number of subjects with anti- polio antibody titers that met the criterion M: Number of subjects with available data for the endpoint.
N: number of subjects in per-protocol analysis set 1, for infant vaccinations 95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction
Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is > -5% for all three serotypes
Group 1: MenACYW-TT and routine pediatric vaccines
Group 2: MenACWY-CRM and routine pediatric vaccines

Results

Secondary objective 1

Hypothesis 5: Non-inferiority of the percentage of subjects with anti-rotavirus IgA antibody concentrations ≥3-fold rise at D30 after the 6-month vaccinations - **met**

							Group 1- Group 2		
Antigen	n/M	Group 1 (N=928) %	95% CI	n/M	Group 2 (N=460) %	95% CI	Difference (%)	95% CI	Non-Inferiority
Anti-rotavirus	603/663	91.0	(88.5 ; 93.0)	298/321	92.8	(89.4 ; 95.4)	-1.88	(-5.26 ; 2.00)	Yes

n: Number of subjects with anti-rotavirus IgA antibody concentrations that met the criterion;
M: Number of subjects with available data for the endpoint. N: number of subjects in per-protocol analysis set 1, for infant vaccinations
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is > -10%
Group 1: MenACYW-TT and routine pediatric vaccines
Group 2: MenACWY-CRM and routine pediatric vaccines

Results

Secondary objective 1

Hypothesis 6: Non-inferiority of geometric mean concentrations (GMCs) of anti-rotavirus IgA antibody at D30 after the 6-month vaccinations - **met**

							Group 1- Group 2		
Antigen	n/M	Group 1 (N=928) GMC	95% CI	n/M	Group 2 (N=460) GMC	95% CI	GMC Ratio	95% CI	Non-Inferiority
Anti-rotavirus	857	272	(244 ; 303)	403	308	(264 ; 360)	0.881	(0.728 ; 1.07)	Yes

n: Number of subjects with anti-rotavirus IgA antibody concentrations that met the criterion;
M: Number of subjects with available data for the endpoint. N: number of subjects in per-protocol analysis set 1, for infant vaccinations
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is > -10%
Group 1: MenACYW-TT and routine pediatric vaccines
Group 2: MenACWY-CRM and routine pediatric vaccines

Results

Secondary objective 1

Hypothesis 7: Non-inferiority of geometric mean concentrations (GMCs) of anti-pertussis antibody at D30 after the 6-month vaccinations - **met**

							Group 1- Group 2		
Antigen	n/M	Group 1 (N=928) GMC	95% CI	n/M	Group 2 (N=460) GMC	95% CI	GMC Ratio	95% CI	Non-Inferiority
PT	906	75.8	(72.2 ; 79.6)	444	78.6	(72.8 ; 84.9)	0.964	(0.880 ; 1.06)	Yes
FHA	906	95.7	(90.9 ; 101)	444	98.6	(91.7 ;106)	0.970	(0.887 ; 1.06)	Yes
PRN	906	39.4	(36.8 ; 42.3)	444	42.1	(37.9 ; 46.6)	0.938	(0.830 ;1.06)	Yes
FIM	906	309	(291 ; 330)	444	311	(284 ; 341)	0.996	(0.892 ; 1.11)	Yes

M: Number of subjects with available data for the endpoint.
N: number of subjects in per-protocol analysis set 1, for infant vaccinations
95% CI calculated using calculation for normal distribution on log10(concentration) following by antilog transformation
Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is >2/3
Group 1: MenACYW-TT and routine pediatric vaccines
Group 2: MenACWY-CRM and routine pediatric vaccines

Results

Secondary objective 1

Hypothesis 8: Non-inferiority of geometric mean concentrations (GMCs) of anti-pneumococcal antibody at D30 after the 6-month vaccinations - **met**

							Group 1- Group 2		
Antigen	n/M	Group 1 (N=928) GMC	95% CI	n/M	Group 2 (N=460) GMC	95% CI	GMC Ratio	95% CI	Non-Inferiority
1	872	2.26	(2.13 ; 2.40)	420	1.93	(1.77 ; 2.12)	1.17	(1.05 ; 1.30)	Yes
3	869	0.607	(0.577 ; 0.638)	412	0.544	(0.505 ; 0.585)	1.12	(1.02; 1.22)	Yes
4	872	1.46	(1.40 ; 1.53)	420	1.33	(1.24 ; 1.42)	1.10	(1.01; 1.19)	Yes
5	873	1.54	(1.46 ; 1.63)	420	1.26	(1.15 ; 1.37)	1.23	(1.11; 1.36)	Yes
6A	874	4.01	(3.82 ; 4.22)	420	3.34	(3.09 ; 3.62)	1.20	(1.09; 1.32)	Yes
6B	874	2.47	(2.29 ; 2.67)	420	1.97	(1.75 ; 2.21)	1.26	(1.09; 1.44)	Yes
7F	874	3.48	(3.32 ; 3.64)	419	3.40	(3.18 ; 3.63)	1.02	(0.946; 1.11)	Yes
9V	873	1.88	(1.78 ; 1.99)	420	1.61	(1.48 ; 1.74)	1.17	(1.06; 1.29)	Yes
14	872	6.95	(6.53 ; 7.41)	420	7.17	(6.58 ; 7.81)	0.970	(0.870; 1.08)	Yes
18C	874	1.95	(1.86 ; 2.04)	420	1.82	(1.69 ; 1.96)	1.07	(0.983; 1.16)	Yes
19A	874	2.21	(2.10 ; 2.32)	420	2.00	(1.86 ; 2.14)	1.10	(1.01; 1.20)	Yes
19F	874	3.36	(3.21 ; 3.52)	420	2.98	(2.77 ; 3.21)	1.13	(1.03; 1.23)	Yes
23F	872	1.59	(1.49 ; 1.69)	420	1.30	(1.18 ; 1.44)	1.22	(1.09; 1.37)	Yes

M: Number of subjects with available data for the endpoint.
N: number of subjects in per-protocol analysis set 1, for infant vaccinations
95% CI calculated using calculation for normal distribution on log10(concentration) following by antilog transformation
Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is >1/2 for all thirteen serotypes
Group 1: MenACYW-TT and routine pediatric vaccines
Group 2: MenACWY-CRM and routine pediatric vaccines

Results

Secondary objective 1

Hypothesis 9, 10, 11: Non-inferiority of M-M-R II vaccine response rates at D30 after the 12-month vaccinations - **met**

		Group 1a (N=675)			Group 2a (N=308)			Group 1a- Group 2a		
Antigens	Criterion	n/M	%	95% CI	n/M	%	95% CI	Difference (%)	95% CI	Non-Inferiority
Anti-measles	≥255 mIU/mL	646/662	97.6	(96.1 ; 98.6)	293/301	97.3	(94.8 ; 98.8)	0.24	(-1.73 ; 2.90)	Yes
Anti-mumps	≥10 mumps Ab units/mL	630/660	95.5	(93.6 ; 96.9)	294/301	97.7	(95.3 ; 99.1)	-2.22	(-4.44 ; 0.53)	Yes
Anti-rubella	≥10 IU/mL	648/662	97.9	(96.5 ; 98.8)	295/301	98.0	(95.7 ; 99.3)	-0.12	(-1.89 ; 2.32)	Yes

n: Number of subjects with specific antibody concentrations that met the corresponding criterion M: Number of subjects with available data for the endpoint.
N: number of subjects in per-protocol analysis set 3, for 2nd year of life vaccinations 95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction
For each antigen, non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is >-10%
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

Results

Secondary objective 1

Hypothesis 12: Non-inferiority of VARIVAX vaccine response rates at D30 after the 12-month vaccinations - **met**

		Group 1a (N=675)			Group 2a (N=308)			Group 1a- Group 2a		
Antigens	Criterion	n/M	%	95% CI	n/M	%	95% CI	Difference (%)	95% CI	Non-Inferiority
Anti-varicella	≥5 gpELISA units /mL	638/662	96.4	(94.7 ; 97.7)	285/301	94.7	(91.5 ; 96.9)	1.69	(-0.96 ; 5.05)	Yes

n: Number of subjects with specific antibody concentrations that met the corresponding criterion
M: Number of subjects with available data for the endpoint.
N: number of subjects in full analysis set 3, for 2nd year of life vaccinations
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction
Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is >-10%
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

Results

Secondary objective 1

Hypothesis 13: Non-inferiority of geometric mean concentrations (GMCs) of anti-pneumococcal antibody at D30 after the 12-month vaccinations - **met**

							Group 1a/Group 2a		
Antigen	n/M	Group 1a (N=675) GMC	95% CI	n/M	Group 2a (N=308) GMC	95% CI	GMC Ratio	95% CI	Non-Inferiority
1	652	3.81	(3.56 ; 4.08)	299	3.44	(3.12 ; 3.81)	1.11	(0.980 ; 1.25)	Yes
3	651	0.771	(0.728 ; 0.817)	299	0.751	(0.690 ; 0.818)	1.03	(1.927 ; 1.14)	Yes
4	652	2.08	(1.95 ; 2.22)	299	2.00	(1.83 ; 2.18)	1.04	(1.933 ; 1.16)	Yes
5	652	2.70	(2.53 ; 2.88)	300	2.46	(2.25 ; 2.69)	1.10	(1.980 ; 1.23)	Yes
6A	652	9.65	(9.09 ; 10.2)	300	9.51	(8.72 ; 10.4)	1.01	(1.912 ; 1.13)	Yes
6B	649	7.41	(6.92 ; 7.93)	300	6.37	(5.77 ; 7.03)	1.16	(1.03 ; 1.31)	Yes
7F	652	5.40	(5.08 ; 5.73)	298	6.04	(5.56 ; 6.55)	0.894	(0.806 ; 0.992)	Yes
9V	652	3.53	(3.31 ; 3.77)	299	3.62	(3.30 ; 3.96)	0.976	(0.871 ; 1.09)	Yes
14	653	7.80	(7.26 ; 8.38)	300	9.20	(8.37 ; 10.1)	0.847	(0.752 ; 0.954)	Yes
18C	652	2.60	(2.44 ; 2.78)	300	2.92	(2.68 ; 3.19)	0.890	(0.799 ; 0.992)	Yes
19A	649	6.19	(5.82 ; 6.59)	300	5.86	(5.32 ; 6.45)	1.06	(0.945 ; 1.18)	Yes
19F	652	6.49	(6.11 ; 6.90)	300	6.01	(5.45 ; 6.62)	1.08	(0.967 ; 1.21)	Yes
23F	652	3.88	(3.60 ; 4.17)	300	3.41	(3.09 ; 3.78)	1.14	(0.999 ; 1.29)	Yes

M: Number of subjects with available data for the endpoint.
N: number of subjects in per-protocol analysis set 3, for 2nd year of life vaccinations
95% CI calculated using calculation for normal distribution on log10(concentration) following by antilog transformation
Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is > 1/2 for all thirteen serotypes
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

Results

Secondary objective 1

Hypothesis 14: Non-inferiority of the percentage of subjects with anti-PRP antibody concentrations ≥1.0 µg/mL at D30 after the 15-month vaccinations - **met**

	Group 1b (N=308)			Group 2b (N=126)			Group 1b-Group 2b		
Criterion	n/M	%	95% CI	n/M	%	95% CI	Difference (%)	95% CI	Non-Inferiority
≥1.0µg/mL	292/297	98.3	(96.1 ; 99.5)	123/125	98.4	(94.3 ; 99.8)	-0.08	(-2.57 ; 4.08)	Yes

n: Number of subjects with anti- PRP antibody concentrations that met the criterion
M: Number of subjects with available data for the endpoint.
N: number of subjects in per-protocol analysis set 3, for 2nd year of life vaccinations
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction
Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is > -10%
Group 1b: MenACYW-TT at 2, 4, 6, and 15 to 18 months of age and routine vaccines at 2, 4, 6, 12 to 15 months of age
Group 2b: 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

Results

Secondary objective 1

Hypothesis 15: Non-inferiority of the percentage of subjects with anti-polio antibody titers ≥1:8 at D30 after the 15-month vaccinations - **met**

							Group 1b - Group 2b		
Serotypes	n/M	Group 1b (N=308) %	95% CI	n/M	Group 2b (N=126) %	95% CI	Difference (%)	95% CI	Non-Inferiority
Anti-polio 1	286/286	100	(98.7 ; 100)	122/122	100	(97.0 ; 100)	0	(-1.33 ; 3.05)	Yes
Anti-polio 2	291/291	100	(98.7 ; 100)	122/122	100	(97.0 ; 100)	0	(-1.30 ; 3.05)	Yes
Anti-polio 3	289/289	100	(98.7 ; 100)	122/122	100	(97.0 ; 100)	0	(-1.31 ; 3.05)	Yes

n: Number of subjects with anti- polio antibody titers that met the criterion
M: Number of subjects with available data for the endpoint.
N: number of subjects in per-protocol analysis set 3, for 2nd year of life vaccinations
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction
Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is > -5% for all three serotypes
Group 1b: MenACYW-TT at 2, 4, 6, and 15 to 18 months of age and routine vaccines at 2, 4, 6, 12 to 15 months of age
Group 2b: 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

Results

Secondary objective 1

Hypothesis 16: Non-inferiority for pertussis antigens of the vaccine response rates at D30 after the 15-month vaccinations - **met**

							Group 1b - Group 2b		
Serotypes	n/M	Group 1b (N=308) %	95% CI	n/M	Group 2b (N=126) %	95% CI	Difference (%)	95% CI	Non-Inferiority
PT	269/273	98.5	(96.3 ; 99.6)	119/121	98.3	(94.2 ; 99.8)	0.19	(-2.35 ; 4.46)	Yes
FHA	264/273	96.7	(93.8 ; 98.5)	117/121	96.7	(91.8 ; 99.1)	0.01	(-3.48 ; 5.14)	Yes
PRN	263/273	96.3	(93.4 ; 98.2)	118/121	97.5	(92.9 ; 99.5)	-1.18	(-4.55 ; 3.67)	Yes
FIM	268/273	98.2	(95.8 ; 99.4)	118/121	97.5	(92.9 ; 99.5)	0.65	(-2.24 ; 5.32)	Yes

n: Number of subjects who achieve pertussis vaccine response.
N: number of subjects in per-protocol analysis set 3, for 2nd year of life vaccinations
Pertussis vaccine response for a subject with a pre-booster(4th) vaccinations < LLOQ, then post-booster(4th) vaccinations should be >= 4x the LLOQ;
95% CI of the single proportion calculated from the exact binomial method; 95% CI of the difference calculated from the Wilson Score method without continuity correction
Non-inferiority will be demonstrated if the lower limit of the 2-sided 95% CI is >-10% for all four antigens
Group 1b: MenACYW-TT at 2, 4, 6, and 15 to 18 months of age and routine vaccines at 2, 4, 6, 12 to 15 months of age
Group 2b: 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

Results

Death Narrative (1 subject in Group 1)

This case was reported by the Investigator concerning the 10 weeks-old-male subject who received MenACYW-TT and 6 days later experienced cardiac arrest with fatal outcome.

On the day of the event the subject was under his father care who placed crying bay in the swing, went to wash his hands and when returned, found the baby limb, not breathing and had turned white and then blue. The father gave a few mouth-to-mouth breaths, started chest compressions, and called 911, gave 2 rounds of Epinephrine prior to arrival to ED. The subject was admitted to the hospital where he received a total of 5 doses of epinephrine in ED from 09:41 to 10:03 a total of 22 minutes after arrival to ED. Subject had a history of vomiting with feeds, sometimes forceful, always NBNB (Non-blood non-bilious), no sweating or cyanosis with feeds. Subject had good gain weight, no prior cardiac history, no prior cardiac events. No family history of SCD (sudden cardiac death) or other cardiac issues. No fevers, URI (upper respiratory infection) symptoms. Received 2-month vaccines 4 days prior to ED visit. Subject weighed 6 kg on admission. General appearance unresponsive, limp. Glasgow coma scale 3. Pupil's field and dilated, no spontaneous movement. As per discharge summary, the arrest happened at home, so the down time was at least 30 minutes if not more. Initial pH was 6.5 with a base deficit of -25. They placed a 3.0 uncuffed ETT (endotracheal tube) with a large leak but were no able to upsize the tube to a 3.5 as it would not advance. However, this was all occurring during CPR. Head CT (Computerized tomogram) showed cerebral edema, with some subarachnoid hemorrhage and concern for a sinus venous thrombosis. He was given bicarbonate in the ED, started on a bicarbonate infusion, as well as an epinephrine infusion of 0.1. Access included 2 intraosseous lines and were able to place a peripheral intravenous. On arrival, he was being mechanically ventilated but had a very large leak around the endotracheal tube and needed to hold cricoid pressure to maintain ventilation. They exchanged the tube. His pupils were fixed, R was 5mm, and L was 3mm. He had a tight fontanelle which was bulging. He had no cough, no gag, no corneal reflexes, and no response to painful stimuli. His initial temperature was 33.1 on arrival and this exam remained consistent with a temperature of 35.3. He had coarse crackles bilaterally, no gallop rhythm. As per ophthalmology, identified retinal hemorrhages. He had a severe candida type rash under his chin and on his back and shoulder had bruising. He had no fractures on skeletal survey. His head CT was showed overall poor gray-white differentiation, which might be due to edema/ischemia versus technique. Additional findings concerning for a small amount of subarachnoid hemorrhage along the parietal convexities and possible cortical venous thrombosis along the right parietal convexity.

The baby was pronounced dead 2 days later. It was unknown if autopsy was done. Primary cause of death was cardiac arrest and secondary cause of death was unknown. No verbal autopsy was performed. Case is on hold with LAPD. The study was ended due to adverse event as the subject early terminated the study due to cardiac arrest.