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

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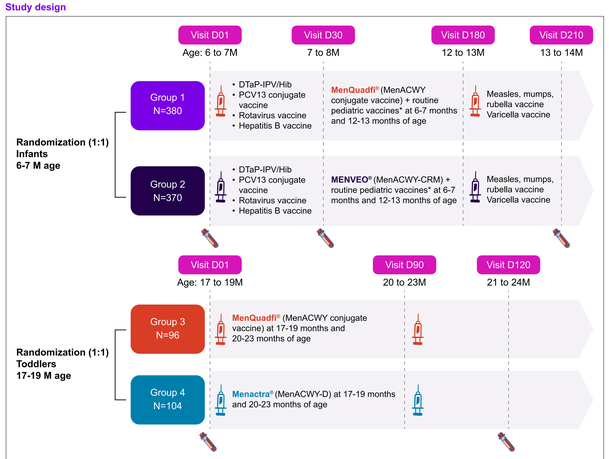
BACKGROUND

- MenQuadfi® (MenACWY conjugate vaccine) is currently licensed in the US for vaccination against invasive meningococcal disease (IMD) in individuals 2 years of age and older and is under development for use in infants as young as 6 weeks of age to provide protection against IMD caused by serogroups A, C, W and Y to all age groups
- This Phase III, randomized, parallel group, active-controlled study (NCT03691610) evaluated the safety and immunogenicity of MenACWY conjugate vaccine administered as a 2-dose schedule to infants ≥6 months of age

METHODS

Study design



*Routine pediatric vaccines administered: Pentacel® (DTaP-IPV//Hib) at 6 months of age; PREVNAR 13® (Pneumococcal 13-valent conjugate vaccine; PCV13) at 6, and 13 months of age; RotaTeq® (Rotavirus vaccine) at 6 months of age; ENGERIX-B® (Hepatitis B vaccine) at 6 months of age; M-M-R® II (Measles, mumps, and rubella vaccine) at 12 months of age; and VARIVAX® (Varicella vaccine) at 12 months of age
D: days; M: months

Main objectives

Primary objective (immunogenicity)
To demonstrate the non-inferiority of the vaccine seroresponse to meningococcal serogroups A, C, W, and Y following administration of 2 doses of MenACWY conjugate vaccine compared to 2 doses of MenACWY-CRM when given concomitantly with routine pediatric vaccines to infants and toddlers at 6 to 7 months of age and 12 to 13 months of age (Group 1 vs. Group 2)

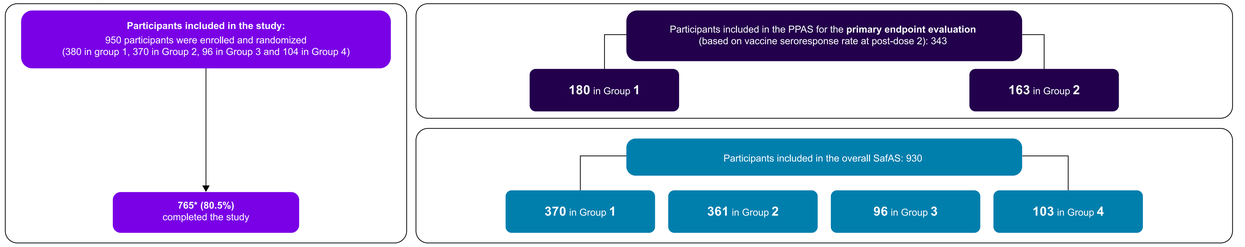
Key secondary objective (immunogenicity)
To demonstrate non-inferiority of seroprotection as defined as serum bactericidal assay using human complement (hSBA) titers ≥1:8 following the administration of 2 doses of MenACWY conjugate vaccine compared to 2 doses of MenACWY-CRM when given concomitantly with pediatric routine vaccines to infants and toddlers at 6 to 7 months of age and 12 to 13 months of age (Group 1 vs. Group 2)

Safety objective
To describe the safety profile of MenACWY conjugate vaccine, MenACWY-CRM and MenACWY-D when administered concomitantly with routine pediatric vaccines in healthy infants and toddlers (all four groups)

- **Safety endpoints:**
  - Immediate unsolicited adverse events (AE) and adverse reactions (AR) measured within 30 min post vaccinations
  - Solicited injection site & systemic AR measured within the 7 days post-vaccinations
  - Unsolicited AEs & AR measured within the 30d post vaccinations
  - Serious Adverse Events (SAEs) measured throughout the study duration

Gender: Among 950 participants, 452 (47.6%) were female
Race: 707 (74.4%) were White, 160 (16.8%) were Black or African American, 15 (1.6%) were Asian origin
Ethnicity: 396 (41.7%) were Hispanic or Latino
Descriptive immunogenicity assessment for groups 3 and 4 was done (data not shown)

Disposition & demographics



PPAS: Per-Protocol Analysis Set; SafAS: Safety Analysis Set

*High rate of discontinuation due to pandemic-related hesitancy to return to research sites

RESULTS:

Summary of immunogenicity findings (Figures 1-3)

- Seroresponses at day 30 following the first dose of MenACWY conjugate 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 (**Figure 3**)
- Six to 7 months following administration of a dose of MenACWY conjugate 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 (MoA), the hSBA GMTs were higher for all serogroups in participants administrated MenACWY conjugate 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 MenACWY conjugate vaccine administration compared to MenACWY-D

Summary of safety events after any vaccine injections (Table 1)

- One participant in Group 2 experienced an immediate unsolicited AE (head injury)
- A total of 6 participants (1.6%) in Group 1, 12 participants (3.3%) in Group 2, 1 participant (1.0%) in Group 3, and 4 participants (3.9%) in Group 4 reported SAEs during the study
  - There was 1 SAE (acute myeloid leukemia not related to the study vaccines), leading to study discontinuation in Group 2
- One participant (1.0%) in Group 4 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, 2 participants (0.6%) in Group 2, and 2 participants (1.9%) in Group 4 reported an AESI during the study. None of these AESI were related to the study vaccines
- No deaths were reported during the study

Safety

Table 1: Safety overview after any vaccine injections - overall safety analysis set for any dose

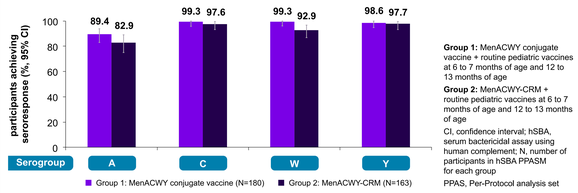
	Group 1 (N=370)			Group 2 (N=361)			Group 3 (N=96)			Group 4 (N=103)		
participants experiencing at least one	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**	**n/M**	**%**	**(95% CI)**
Within 30 mins after any vaccine injections												
Immediate unsolicited AE	0/370	0	(0; 1.0)	1/361	0.3	(0; 1.5)	0/96	0	(0; 3.8)	0/103	0	(0; 3.5)
Immediate unsolicited AR	0/370	0	(0; 1.0)	0/361	0	(0; 1.0)	0/96	0	(0; 3.8)	0/103	0	(0; 3.5)
Solicited injection site after injection of MenACWY or MenACWY-CRM or MenACWY-D	199/356	55.9	(50.6; 61.1)	180/342	52.6	(47.2; 58.0)	52/91	57.1	(46.3; 67.5)	48/100	48	(37.9; 58.2)
Solicited systemic reaction	235/356	66.0	(60.8; 70.9)	215/342	62.9	(57.5; 68.0)	55/91	60.4	(49.6; 70.5)	62/100	62.0	(51.7; 71.5)
Within 30 days after any vaccine injections												
Unsolicited AE	182/370	49.2	(44.0 54.4)	154/361	42.7	(37.5; 47.9)	36/96	37.5	(27.8; 48.0)	37/103	35.9	(26.7; 46.0)
Unsolicited AR	11/370	3.0	(1.5; 5.3)	9/361	2.5	(1.1; 4.7)	3/96	3.1	(0.6; 8.9)	4/103	3.9	(1.1; 9.6)
Unsolicited non-serious AE	182/370	49.2	(44.0; 54.4)	153/361	42.4	(37.2; 47.7)	36/96	37.5	(27.8; 48.0)	36/103	35.0	(25.8; 45.0)
Unsolicited non-serious AR	11/370	3.0	(1.5; 5.3)	9/361	2.5	(1.1; 4.7)	3/96	3.1	(0.6; 8.9)	3/106	2.9	(0.6; 8.3)
Unsolicited non-serious systemic AE	176/370	47.6	(42.4; 52.8)	150/361	41.6	(36.4; 46.8)	35/96	36.5	(26.9; 46.9)	34/103	33.0	(24.1; 43.0)
Unsolicited non-serious systemic AR	0/370	0	(0; 1.0)	0/361	0	(0; 1.0)	0/96	0	(0; 3.8)	0/103	0	(0; 3.5)
AE leading to study discontinuation	0/370	0	(0; 1.0)	1/361	0.3	(0; 1.5)	0/96	0	(0; 3.8)	0/103	0	(0; 3.5)
SAE	1/370	0.3	(0; 1.5)	2/361	0.6	(0.1; 2.0)	0/96	0	(0; 3.8)	2/103	1.9	(0.2; 6.8)
Death	0/370	0	(0; 1.0)	0/361	0	(0; 1.0)	0/96	0	(0; 3.8)	0/103	0	(0; 3.5)
AESI	0/370	0	(0; 1.0)	0/361	0	(0; 1.0)	0/96	0	(0; 3.8)	1/103	1.0	(0; 5.3)
MAAE	136/370	36.8	(31.8; 41.9)	117/361	32.4	(27.6; 37.5)	28/96	29.2	(20.3; 39.3)	28/103	27.2	(18.9; 36.8)

AE: adverse event; AESI: adverse event of special interest; AR: adverse reaction; CI: confidence interval; M: number of participants with available data for the relevant endpoint; MAAE: medically-attended adverse event; n: number of participants experiencing the endpoint listed in the first column; N: number of participants in overall safety analysis set for any dose
Percentages are based on M. "Immediate unsolicited AE" is collected only for immediate unsolicited systemic AEs. "Unsolicited AE" also includes immediate and serious unsolicited AEs. "Unsolicited non-serious AE" includes any unsolicited AE that is non-serious. Reactions related to IMP (MenACWY conjugate vaccine/MenACWY-CRM/MenACWY-D); Unsolicited injection site reactions related to NIMP (routine vaccines) are reported separately
Group 1: MenACWY conjugate 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; Group 3: MenACWY conjugate 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

Immunogenicity

The primary objective was met: The percentage of participants who achieved vaccine seroresponse* post-dose 2 at 12 – 13 months of age for meningococcal serogroups A, C, W, and Y in MenACWY vaccine group were non-inferior to the corresponding percentages in MenACWY-CRM Group

Figure 1: Non-inferiority of hSBA vaccine seroresponse rates 30 days after the second dose of MenACWY conjugate vaccine or MenACWY-CRM (Group 1 vs Group 2) – PPAS**

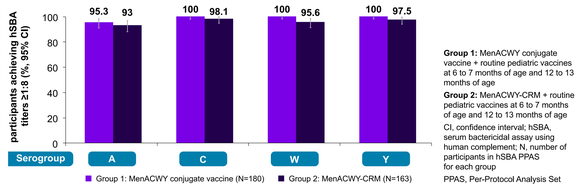


Group 1: MenACWY conjugate vaccine + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age
Group 2: MenACWY-CRM + routine pediatric vaccines at 6 to 7 months of age and 12 to 13 months of age
CI, confidence interval; hSBA, serum bactericidal assay using human complement; N, number of participants in hSBA PPASM for each group
PPAS, Per-Protocol analysis set

*hSBA vaccine seroresponse was defined as a post-vaccination titer ≥1:16 for participants with pre-vaccination hSBA titer <1:8, or a post-vaccination titer ≥4-fold increase from baseline for subject with pre-vaccination hSBA titer ≥1:8; **The overall non-inferiority is demonstrated if the lower limit of the 2-sided 95% CI is >-10% for all four serogroups. 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

Key secondary objective was met: Non-inferiority of the percentage of participants with hSBA titers to meningococcal serogroups A, C, W, and Y ≥1:8 following administration of 2 doses of MenACWY conjugate vaccine compared to 2 doses of MenACWY-CRM when given concomitantly with pediatric routine vaccines to infants and toddlers at 6 to 7 months of age and 12 to 13 months of age was demonstrated as the lower limit of the 2-sided 95% CI of the difference in hSBA response rates (antibody titers ≥1:8) were >-10% for all 4 serogroups

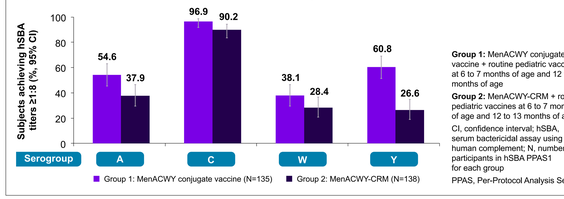
Figure 2: Non-inferiority of hSBA vaccine seroprotection* rates 30 days after the second dose of MenACWY conjugate vaccine or Menveo (Group 1 vs Group 2) – PPAS2



Group 1: MenACWY conjugate 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
CI, confidence interval; hSBA, serum bactericidal assay using human complement; N, number of participants in hSBA PPAS for each group
PPAS, Per-Protocol Analysis Set

*hSBA vaccine seroprotection for serogroups A, C, Y and W was defined as titers ≥1:8

Figure 3: Percentage of participants with hSBA titer ≥1:8 – 30 days post-vaccination at 6-7 months of age (PPAS1)



Group 1: MenACWY conjugate 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
CI, confidence interval; hSBA, serum bactericidal assay using human complement; N, number of participants in hSBA PPAS1 for each group
PPAS, Per-Protocol Analysis Set

CONCLUSION

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

DISCLOSURE OF CONFLICTS:
• BZ, MSD, OL, SB, JC, SG, and CR are employees of Sanofi and may hold company stocks and/or stock options. CD reports no conflicts of interest

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