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

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BACKGROUND

- **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 is also high 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, Y, and W.[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 children ≥2 years of age[7]
- In this modified double-blind, Phase-3 study (NCT03673462) conducted in the US and Puerto Rico, the safety of MenACYW-TT vs a quadrivalent meningococcal vaccine **MENVEO®** (MenACWY-CRM) was evaluated when **co-administered with routine pediatric vaccines** in healthy **infants** and **toddlers**

METHODS

Study objective

Primary objective

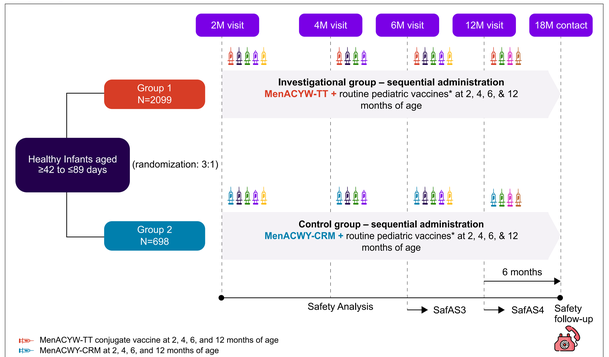
To describe the safety profile of **MenACYW-TT** and **MenACWY-CRM** when administered concomitantly with **routine pediatric vaccines in healthy infants and toddlers**:

- Immediate unsolicited systemic adverse events (AEs) within 30 minutes post-vaccination
- Solicited AEs collected during the first 7 days of vaccination
- Serious adverse events (SAEs) including adverse events of special interest (AESIs), and medically-attended adverse events (MAAEs) collected throughout the study, including the 6-month follow up period

Disposition & demographics

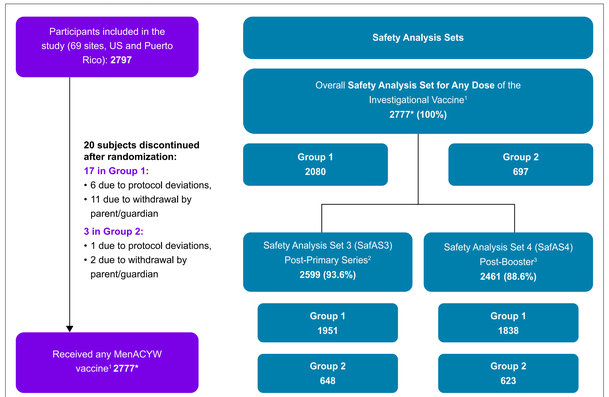
Gender: 1463 (52.3%) were male and 1334 (47.7%) were female
Race: 2299 (82.2%) were Caucasian, 277 (9.9%) were Black or African American, 131 (4.7%) were of mixed race, 40 (1.4%) were Asian, 14 (0.5%) were Native Hawaiian or Other Pacific Islander, and 13 (0.5%) did not report their race, 12 (0.4%) were of unknown race, and 8 (0.3%) were American Indian or Alaska Native
Ethnicity: 783 (27.3%) were Hispanic or Latino, 2025 (72.4%) were not Hispanic or Latino, and 9 (0.3%) did not report their ethnicity

Study design



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

Disposition & demographics *(Continued)*



*20 participants were excluded from the safety analysis set, because they did not receive any study vaccines
[1]Participants who received at least 1 dose of MenACYW-TT or MenACWY-CRM and for whom any safety data are available; [2]Participants who have received the study vaccine at around 6 months of age and have any safety data available (primary series); [3]Participants who have received the study vaccine at around 12 months of age and have any safety data available (booster)

RESULTS *(CONTINUED)*

Summary

- Most common non-serious unsolicited AEs were in the "**Infections and Infestations**" SOC
  - Respiratory and gastrointestinal infections were most commonly reported
- 129/2797 subjects reported SAEs, **none** were assessed to be related to study vaccines
  - 108/2080 (5.2%) SAEs in the MenACYW-TT group; 21/697 (3%) in the MenACWY-CRM group
- 20/2797 subjects reported 24 AESIs; **none** were assessed to be related to study vaccines
  - All AESIs were febrile and non-febrile seizures (Nervous system disorders SOC): 19 (0.9%) in the MenACYW-TT group and 1 (0.1%) in the MenACWY-CRM group
  - Out of the 24 instances of AESIs, confounding factors were identified in 21/24 (87.5%) of cases; 22/24 (92%) **did not meet** the **Brighton Collaboration case definition criteria**
- 12 discontinuations in total occurred throughout the study due to AEs
  - 7 subjects (all in Group 1) discontinued due to SAEs; 3 of these were due to death
  - None of SAE-related discontinuations or deaths were considered to be related to the study vaccine or study procedure by the primary investigator and sponsor

Brighton Collaboration is a Global Standard for Case Definitions (and Guidelines) for Adverse Events Following Immunization (AEFI) and adverse events of special interest (AESI). https://doi.org/10.1016/j.vaccine.2003.09.008
AEs, adverse events; AESIs, adverse events of special interest; SAEs, serious adverse events; SOC, system organ class

CONCLUSION

MenACYW-TT is safe when administered concomitantly with routine pediatric vaccines in healthy infants and toddlers beginning at 6 weeks of age. The safety profiles of both the MenACYW-TT and MenACWY-CRM groups were comparable for this age group

RESULTS

Safety assessment for any vaccine injections

Subjects experiencing at least one:	Group 1 (N = 2080) n/M	%	(95% CI)	Group 2 (N = 697) n/M	%	(95% CI)
Within 30 mins after any vaccine injections						
Immediate unsolicited AE	7/2080	0.3	(0.1 ; 0.7)	2/697	0.3	(0 ; 1.0)
Immediate unsolicited AR	3/2080	0.1	(0 ; 0.4)	1/697	0.1	(0 ; 0.8)
Solicited reaction from D0 to D7 within solicited period after any vaccine injections	1850/2021	91.5	(90.2 ; 92.7)	628/676	92.9	(90.7 ; 94.7)
Solicited injection site reaction	1715/2021	84.9	(83.2 ; 86.4)	572/676	84.6	(81.7 ; 87.3)
Solicited injection site after injection of MenACYW-TT/MenACWY-CRM	1596/2021	79.0	(77.1 ; 80.7)	525/676	77.7	(74.3 ; 80.8)
Solicited injection site after injection of PENTACEL®	1500/2017	74.4	(72.4 ; 76.3)	496/676	73.4	(69.9 ; 76.7)
Solicited injection site after injection of PREVNAR 13®	1559/2018	77.3	(75.4 ; 79.1)	531/676	78.6	(75.3 ; 81.6)
Solicited injection site after injection of ENGERIX-B®	1317/2013	65.4	(63.3 ; 67.5)	446/675	66.1	(62.4 ; 69.6)
Solicited injection site after injection of M-M-R® II	873/1756	49.7	(47.4 ; 52.1)	302/588	51.4	(47.2 ; 55.5)
Solicited injection site after injection of VARIVAX®	813/1758	46.2	(43.9 ; 48.6)	289/588	49.1	(45.0 ; 53.3)
Solicited systemic reaction	1759/2019	87.1	(85.6 ; 88.6)	596/676	88.2	(85.5 ; 90.5)
Unsolicited Events within 30 days after any vaccine injections						
Unsolicited non-serious AE	1347/2080	64.8	(62.7 ; 66.8)	437/697	62.7	(59.0 ; 66.3)
SAE	44/2080	2.1	(1.5 ; 2.8)	9/697	1.3	(0.6 ; 2.4)
Death	3/2080	0.1	(0 ; 0.4)	0/697	0	(0 ; 0.5)
AESI	5/2080	0.2	(0.1 ; 0.6)	0/697	0	(0 ; 0.5)
MAAE	1060/2080	51.0	(48.8 ; 53.1)	339/697	48.6	(44.9 ; 52.4)
Unsolicited Events during entire study period (including 6-month safety follow up)						
SAE	108/2080	5.2	(4.3 ; 6.2)	21/697	3.0	(1.9 ; 4.6)
Death	3/2080	0.1	(0 ; 0.4)	0/697	0	(0 ; 0.5)
AESI	19/2080	0.9	(0.6 ; 1.4)	1/697	0.1	(0 ; 0.8)
MAAE	1581/2080	76.0	(74.1 ; 77.8)	526/697	75.5	(72.1 ; 78.6)

Group 1: MenACYW-TT and routine pediatric vaccines administered at 2, 4, 6, and 12 months of age. **Group 2:** MenACWY-CRM vaccine and routine pediatric vaccines administered at 2, 4, 6, and 12 months of age. 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 who were randomized in assigned group, compliant with study protocol and had received at least one dose of study vaccines. Percentages are calculated based on M. "Immediate unsolicited AE" is collected only for immediate unsolicited systemic AEs. "Unsolicited Events within 30 days after any vaccine injection" includes immediate non-serious AEs and SAEs. "Unsolicited non-serious AE" includes any unsolicited AE that is not an SAE
AE, adverse event; AESI, adverse event of special interest; AR: adverse reaction; CI, confidence interval; D, day; MAAE, medically-attended adverse event; SAE, serious adverse event

Safety assessment after 6 months (post-primary series) – SAfAS3

Subjects experiencing at least one:	Group 1 (N=1951) n/M	%	(95% CI)	Group 2 (N=648) n/M	%	(95% CI)
Within 30 mins after any vaccine injections						
Immediate unsolicited AE	0/1951	0	(0 ; 0.2)	0/648	0	(0 ; 0.6)
Immediate unsolicited AR	0/1951	0	(0 ; 0.2)	0/648	0	(0 ; 0.6)
Solicited reaction from D0 to D7 within solicited period after any vaccine injections						
Solicited injection site reaction	1135/1797	63.2	(60.9 ; 65.4)	373/600	62.2	(58.2 ; 66.1)
Solicited injection site after injection of MenACYW-TT/MenACWY-CRM	974/1797	54.2	(51.9 ; 56.5)	310/599	51.8	(47.7 ; 55.8)
Solicited systemic reaction	1178/1796	65.6	(63.3 ; 67.8)	389/600	64.8	(60.9 ; 68.7)
Within 30 days after any vaccine injections						
Unsolicited AE	547/1951	28.0	(26.1 ; 30.1)	186/648	28.7	(25.2 ; 32.4)
Unsolicited non-serious AE	544/1951	27.9	(25.9 ; 29.9)	186/648	28.7	(25.2 ; 32.4)
Unsolicited non-serious systemic AE	475/1951	24.3	(22.5 ; 26.3)	164/648	25.3	(22.0 ; 28.8)
Unsolicited AR	48/1951	2.5	(1.8 ; 3.2)	16/648	2.5	(1.4 ; 4.0)
Unsolicited non-serious AR	48/1951	2.5	(1.8 ; 3.2)	16/648	2.5	(1.4 ; 4.0)
Unsolicited non-serious injection site AR	45/1951	2.3	(1.7 ; 3.1)	15/648	2.3	(1.3 ; 3.8)
Unsolicited non-serious systemic AR	4/1951	0.2	(0.1 ; 0.5)	1/648	0.2	(0 ; 0.9)
SAE	9/1951	0.5	(0.2 ; 0.9)	1/648	0.2	(0 ; 0.9)
Death	1/1951	<0.1	(0 ; 0.3)	0/648	0	(0 ; 0.6)
AESI	1/1951	<0.1	(0 ; 0.3)	0/648	0	(0 ; 0.6)
MAAE	392/1951	20.1	(18.3 ; 21.9)	134/648	20.7	(17.6 ; 24.0)
AE leading to study discontinuation	1/1951	<0.1	(0 ; 0.3)	0/648	0	(0 ; 0.6)

Group 1: MenACYW-TT and routine pediatric vaccines administered at 2, 4, 6, and 12 months of age; **Group 2:** MenACWY-CRM vaccine and routine pediatric vaccines administered at 2, 4, 6, and 12 months of age
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 who were randomized in assigned group, compliant with study protocol and had received at least one dose of study vaccines. Percentages are calculated based on M. "Immediate unsolicited AE" is collected only for immediate unsolicited systemic AEs."Unsolicited Events within 30 days after any vaccine injection" includes immediate non-serious AEs and SAEs. "Unsolicited non-serious AE" includes any unsolicited AE that is not an SAE
AE, adverse event; AESI, adverse event of special interest; AR: adverse reaction; CI, confidence interval; D, day; MAAE, medically-attended adverse event; SAE, serious adverse event

Safety assessment after 12 months (post-booster) – SAfAS4

Subjects experiencing at least one:	Group 1 (N=1951) n/M	%	(95% CI)	Group 2 (N=648) n/M	%	(95% CI)
Within 30 mins after any vaccine injections						
Immediate unsolicited AE	3/1838	0.2	(0 ; 0.5)	2/623	0.3	(0 ; 1.2)
Immediate unsolicited AR	2/1838	0.1	(0 ; 0.4)	1/623	0.2	(0 ; 0.9)
Solicited reaction from D0 to D7 within solicited period after any vaccine injections						
Solicited injection site reaction	1133/1768	64.1	(61.8 ; 66.3)	382/592	64.5	(60.5 ; 68.4)
Solicited injection site after injection of MenACYW-TT/MenACWY-CRM	948/1767	53.7	(51.3 ; 56.0)	326/592	55.1	(51.0 ; 59.1)
Solicited systemic reaction	1160/1767	65.6	(63.4 ; 67.9)	381/593	64.2	(60.2 ; 68.1)
Within 30 days after any vaccine injections						
Unsolicited AE	713/1838	38.8	(36.6 ; 41.1)	214/623	28.7	(30.6 ; 38.2)
Unsolicited non-serious AE	712/1838	38.7	(36.5 ; 41.0)	212/623	28.7	(30.3 ; 37.9)
Unsolicited non-serious systemic AE	621/1838	33.8	(31.6 ; 36.0)	191/623	25.3	(27.1 ; 34.4)
Unsolicited AR	87/1838	4.7	(3.8 ; 5.8)	30/623	2.5	(3.3 ; 6.8)
Unsolicited non-serious AR	87/1838	4.7	(3.8 ; 5.8)	30/623	2.5	(3.3 ; 6.8)
Unsolicited non-serious injection site AR	71/1838	3.9	(3.0 ; 4.8)	23/623	2.3	(2.4 ; 5.5)
Unsolicited non-serious systemic AR	16/1838	0.9	(0.5 ; 1.4)	7/623	0.2	(0.5 ; 2.3)
SAE	9/1838	0.5	(0.2 ; 0.9)	4/623	0.2	(0.2 ; 1.6)
Death	0/1838	0	(0 ; 0.2)	0/623	0	(0 ; 0.6)
AESI	3/1838	0.2	(0 ; 0.5)	0/623	0	(0 ; 0.6)
MAAE	447/1838	24.3	(22.4 ; 26.3)	129/623	20.7	(17.6 ; 24.1)
AE leading to study discontinuation	0/1838	0	(0 ; 0.2)	0/623	0	(0 ; 0.6)

Group 1: MenACYW-TT and routine pediatric vaccines administered at 2, 4, 6, and 12 months of age; **Group 2:** MenACWY-CRM vaccine and routine pediatric vaccines administered at 2, 4, 6, and 12 months of age
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 who were randomized in assigned group, compliant with study protocol and had received at least one dose of study vaccines. Percentages are calculated based on M. "Immediate unsolicited AE" is collected only for immediate unsolicited systemic AEs "Unsolicited Events within 30 days after any vaccine injection" includes immediate non-serious AEs and SAEs. "Unsolicited non-serious AE" includes any unsolicited AE that is not an SAE
AE, adverse event; AESI, adverse event of special interest; AR: adverse reaction; CI, confidence interval; D, day; MAAE, medically-attended adverse event; SAE, serious adverse event

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DISCLOSURE OF CONFLICTS

SG, MSD, BZ, LG, SB, OS, AH, OL and CR are employees of Sanofi and may hold company stocks and/or stock options. AM reports no conflicts of interest

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