Work Group Considerations Regarding MenQuadfi in Infants

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Advisory Committee on Immunization Practices

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Studies Reviewed

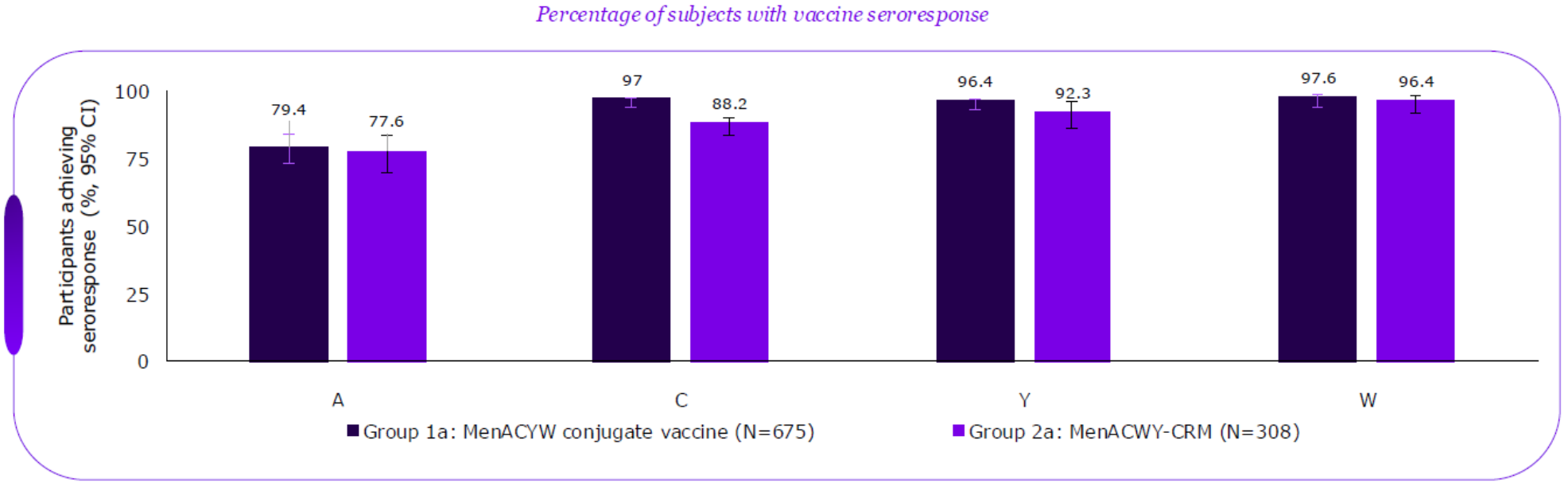
- Three Phase III studies in U.S. infants aged 6 weeks – 19 months
  - 4,321 infants enrolled in MenACWY-TT arm
    - 2 studies: 3+1 schedule (ages 2, 4, 6, 12 or 12–18 months)
    - 1 study: 1+1 schedule (age ≥6 months)
  - Comparator vaccine: 1,717 infants received MenACWY-CRM or MenACWY-D
- Vaccine co-administered with pediatric vaccines (6 arms)

Seroresponse: Met42

MET42 primary endpoint 1

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 Group 1a are **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 were higher than -10% for all 4 serogroups



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

Seroresponse: Met61

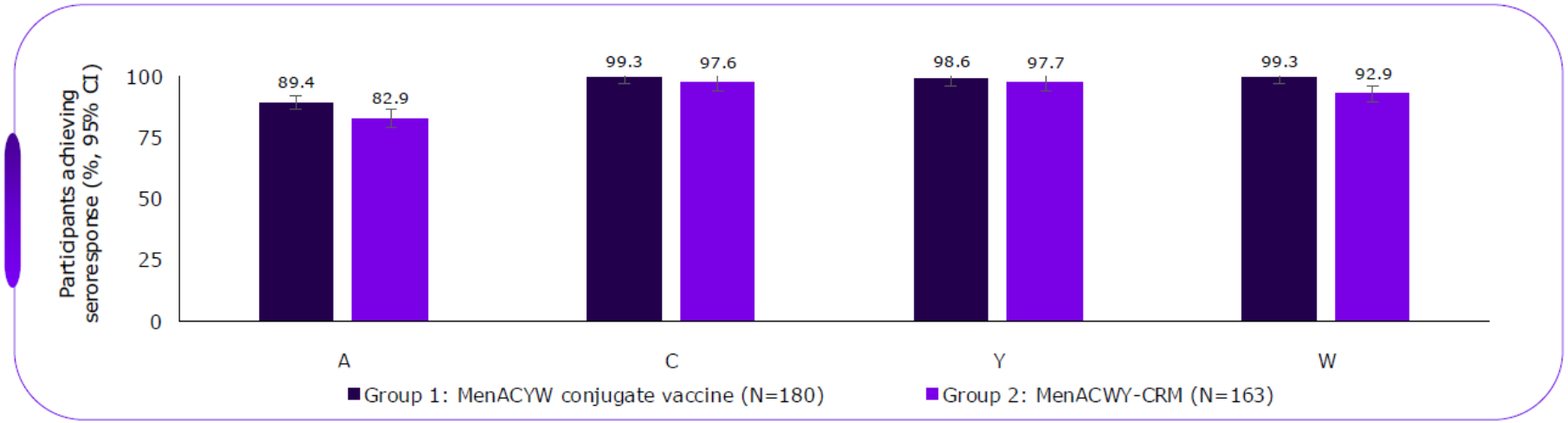
MET 61 primary endpoint 1

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

*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 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

Solicited Local and Systemic Adverse Reactions: Met42

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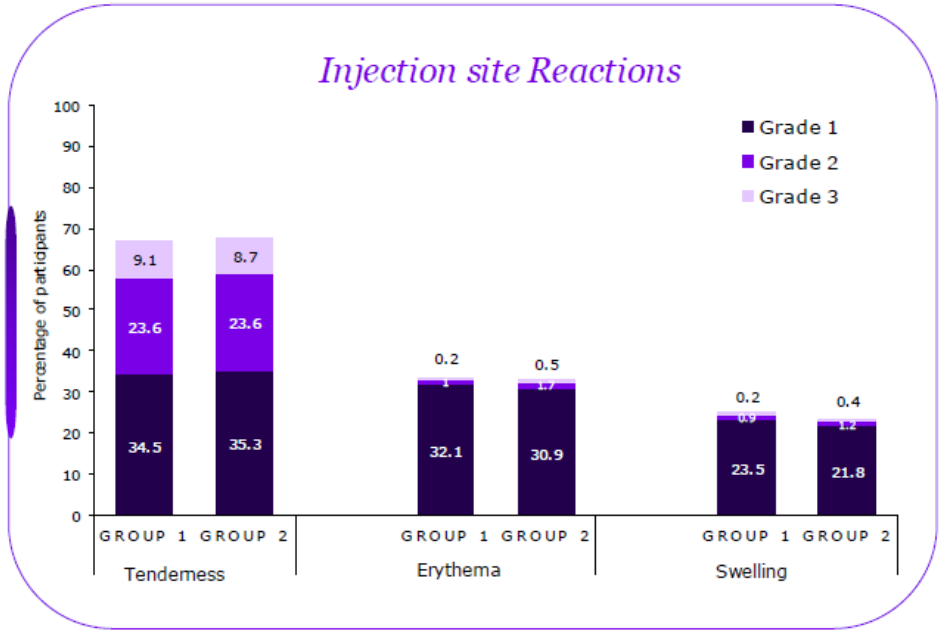
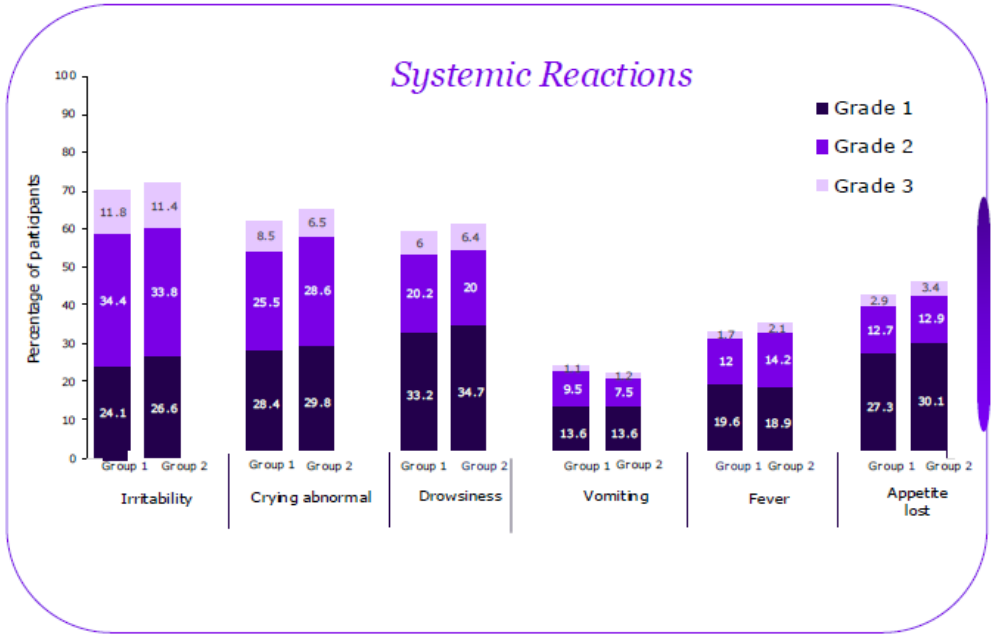
MET42: Solicited injection site & systemic reactions within 7 days after any dose





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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Solicited Local Adverse Reactions: Met61

Group 1=MenACWY-TT + routine pediatric vaccines at 6-7 months and 12-13 months

Group 2=MenACWY-CRM + routine pediatric vaccines at 6-7 months and 12-13 months

Group 3=MenACWY-TT at 17-19 months and 20-23 months

Group 4=MenACWY-D at 17-19 months and 20-23 months

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

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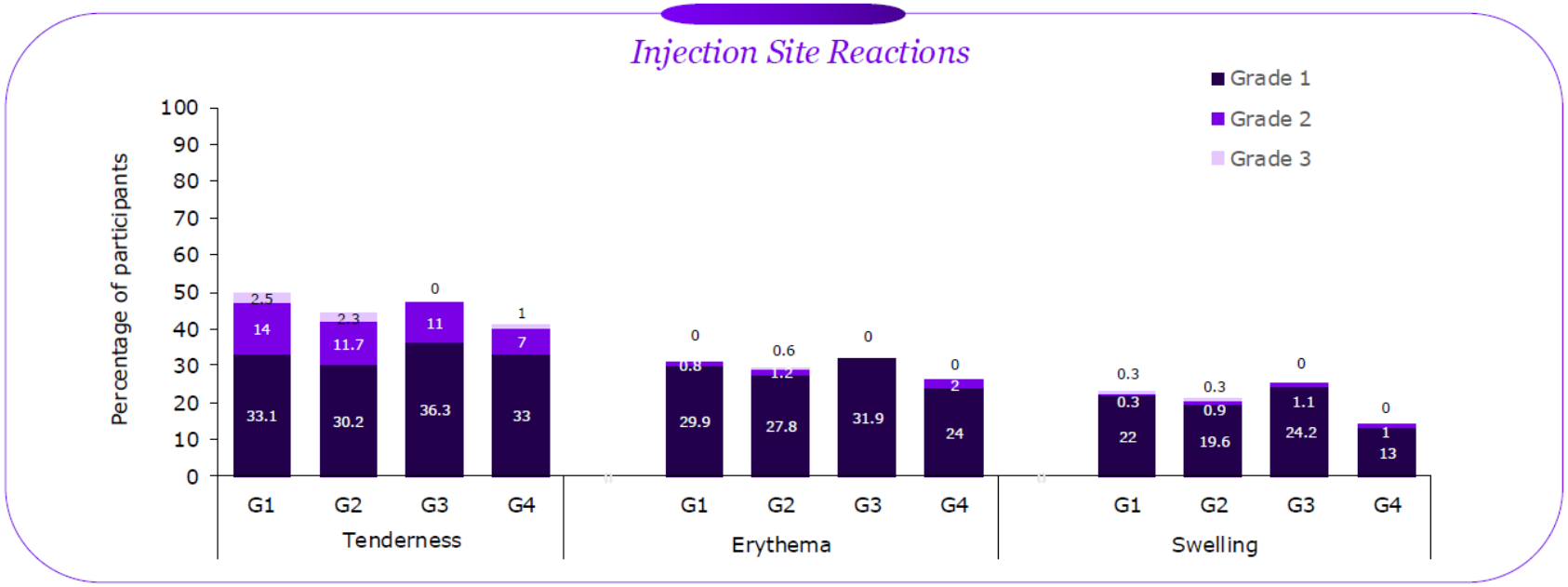

Majority of injection site reactions were Grade 1 (erythema and swelling) and Grade 1 & 2 (tenderness)

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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Solicited Systemic Adverse Reactions: Met61

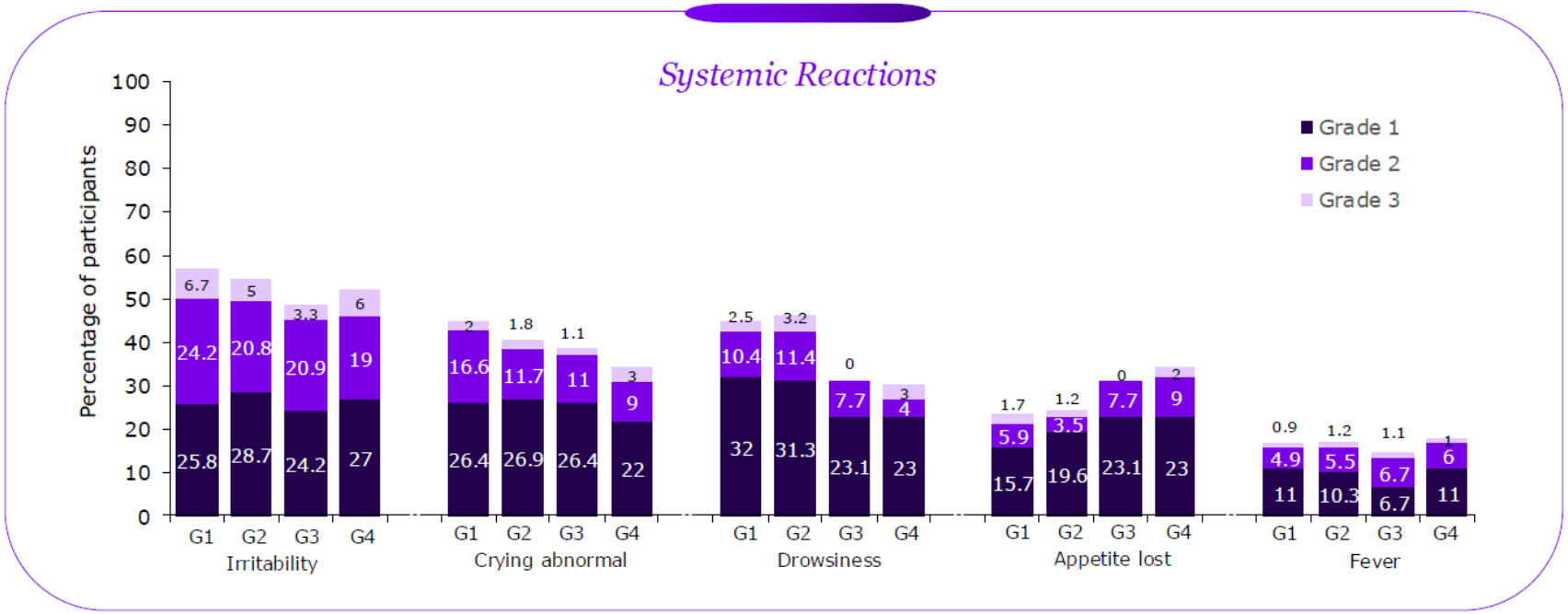
Group 1=MenACWY-TT + routine pediatric vaccines at 6-7 months and 12-13 months

Group 2=MenACWY-CRM + routine pediatric vaccines at 6-7 months and 12-13 months

Group 3=MenACWY-TT at 17-19 months and 20-23 months

Group 4=MenACWY-D at 17-19 months and 20-23 months

MET61: Solicited injection site & 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
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

SAEs, AESIs, and Unsolicited AEs

- Met41: Imbalance of febrile/non-febrile seizures
  - 19 subjects in intervention group (n=2080, 0.9%) vs. 1 in comparison group (n=697, 0.1%) with febrile or non-febrile seizures
  - All deemed not related to study vaccine by primary investigator and sponsor
- Met42: 1 febrile seizure who received study vaccine
  - Prior history of seizures/deemed related to study vaccine

SAE, serious adverse event; AESI, adverse event of special interest; AE, adverse event

SAEs, AESIs, and Unsolicited AEs, cont.

- 4 total deaths, all in intervention group and all deemed unrelated to study vaccine by primary investigator and sponsor
  - Met41:
    - Non-accidental injury of the head (30 days after vaccination)
    - Sudden unexplained death in infancy (24 days after vaccination)
    - Found by parent unresponsive in bed (4 days after vaccination)
  - Met42:
    - Cardiac arrest (6 days after vaccination)
  - Met61:
    - No deaths

SAE, serious adverse event; AESI, adverse event of special interest; AE, adverse event

Pooled Safety Analysis: Met41 and Met42

MET41 and MET42 pooled safety analysis

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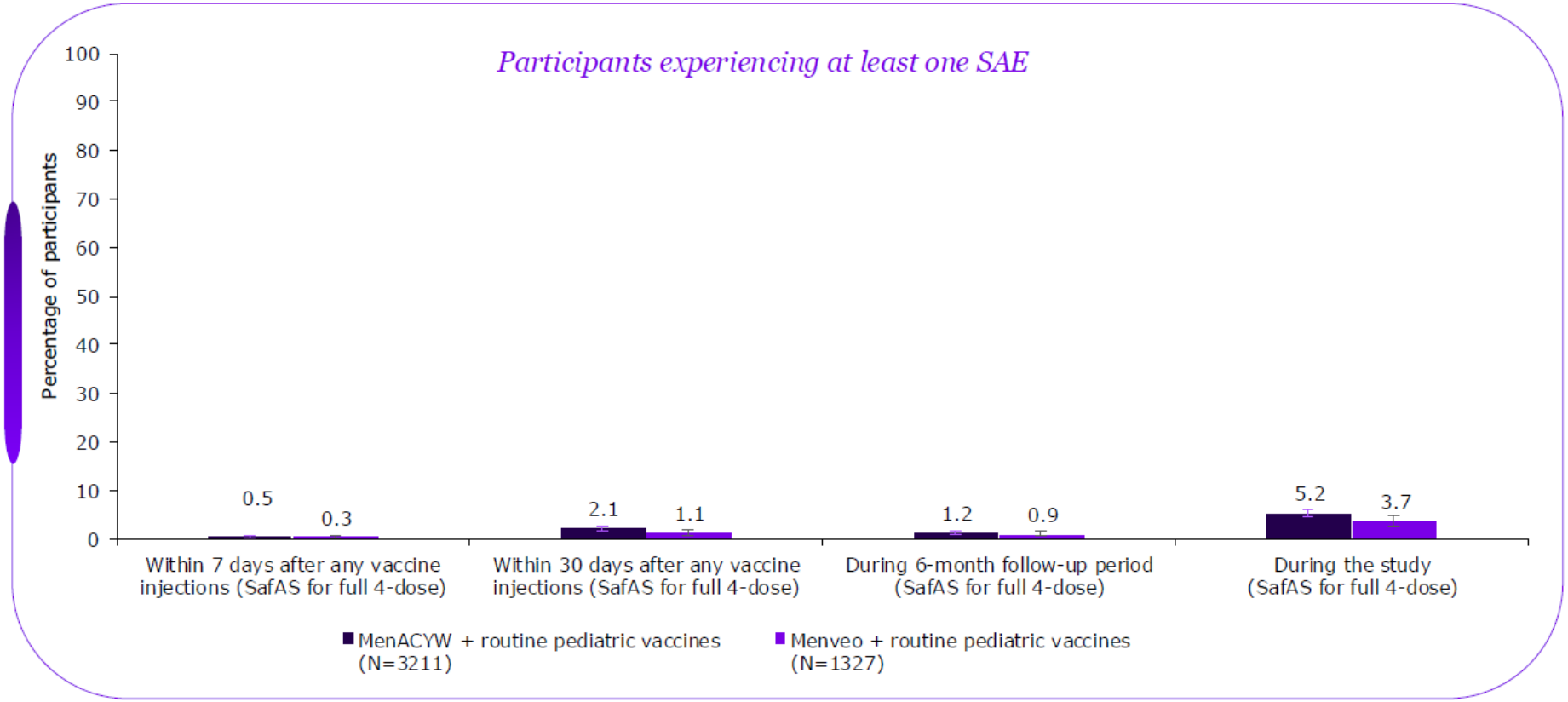

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1. Safety of a Quadrivalent Meningococcal Conjugate Vaccine Administered Concomitantly With Routine Pediatric Vaccines in Healthy Infants and Toddlers (MET41). ClinicalTrials.gov, Sanofi Pasteur, 14 Dec. 2023, https://clinicaltrials.gov/study/NCT03673462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

Summary

- Post-dose 4 seroresponse overall similar for MenQuadfi vs. comparator
  - Higher GMTs for Serogroup C among MenQuadfi recipients (vs. comparator)
- Safety
  - Solicited local and systemic reactions generally similar between study groups
    - Local reactions slightly greater for MenQuadfi in Met61
  - Among MenQuadfi recipients in Met41 and Met42, greater proportion of:
    - Febrile/non-febrile seizures
    - Serious Adverse Events
    - Deaths

Summary, cont.

- Results among healthy infants may not be representative of results for infants recommended for vaccine based on risk factors
  - Similar studies typically limited to healthy infants
- High attrition rates
  - Attributed to out-of-window visits, missed blood draws, COVID-19 pandemic
- Benefits of another vaccine option may outweigh risks

Acknowledgements

- Lucy McNamara
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