

Work Group Considerations Regarding MenQuadfi in Infants

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Advisory Committee on Immunization Practices

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U. S. Centers for Disease Control and Prevention.

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

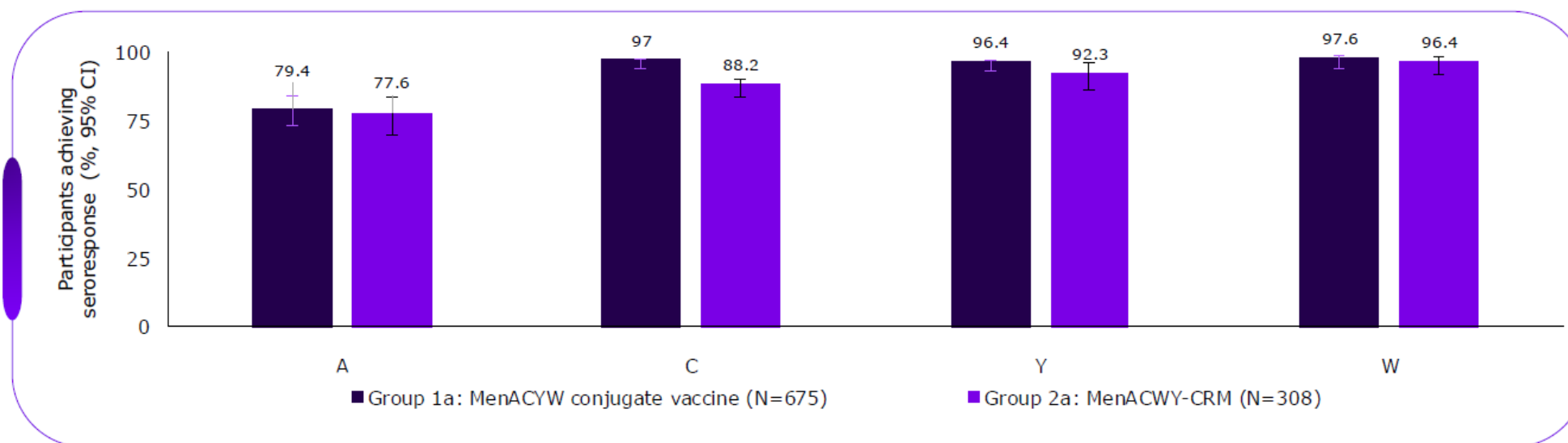
MET42 primary endpoint 1

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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

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 $\geq 1:16$
- For a subject with a pre-vaccination titer $\geq 1:8$, the post-vaccination titer had to be ≥ 4 -fold greater than the pre-vaccination titer

Seroresponse: Met61

MET 61 primary endpoint 1

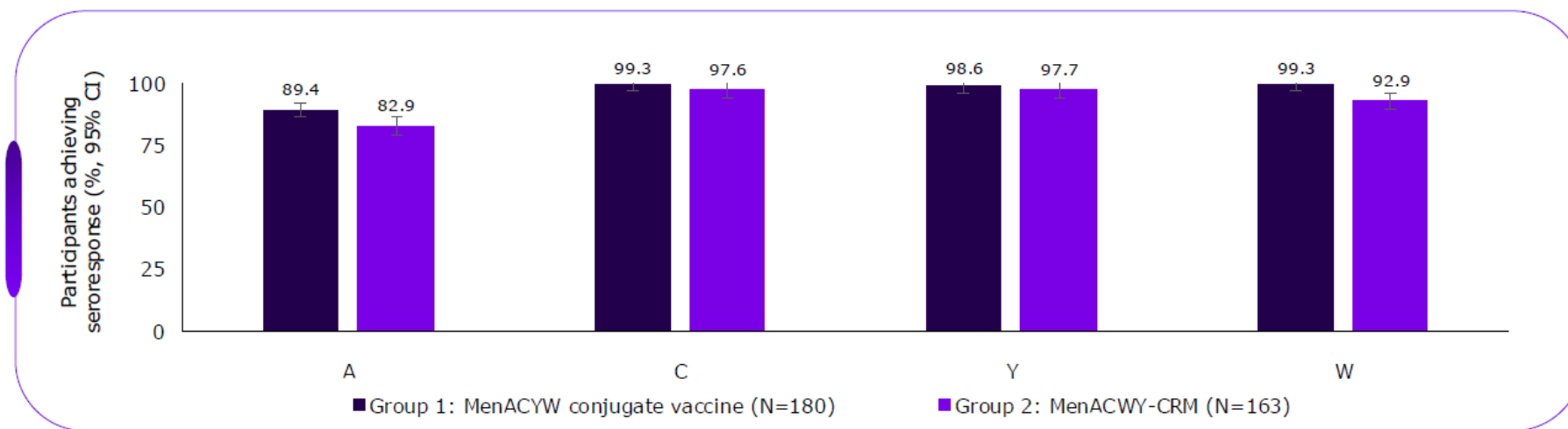
MET61: Post booster, MenACYW-TT seroresponse rates were high and comparable to those for MenACWY-CRM for all 4 serogroups

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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

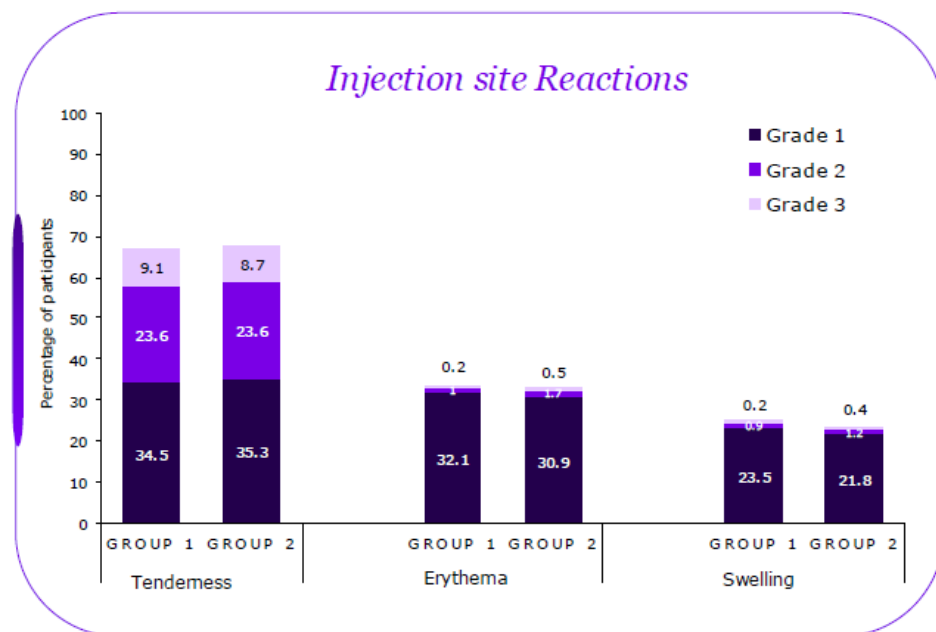
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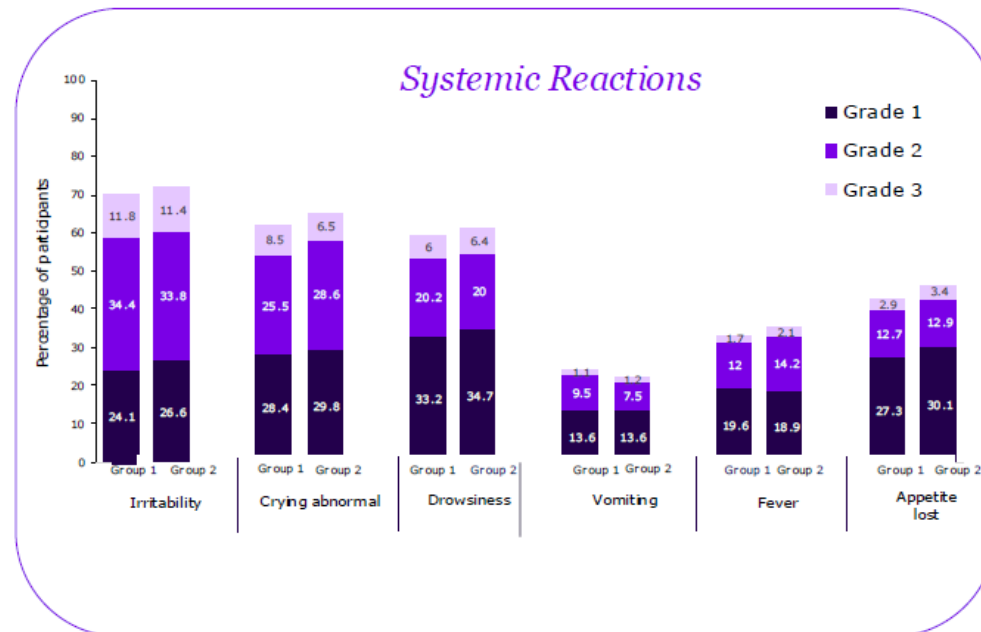
Solicited Local and Systemic Adverse Reactions: Met42

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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

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

Solicited Local Adverse Reactions: Met61

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

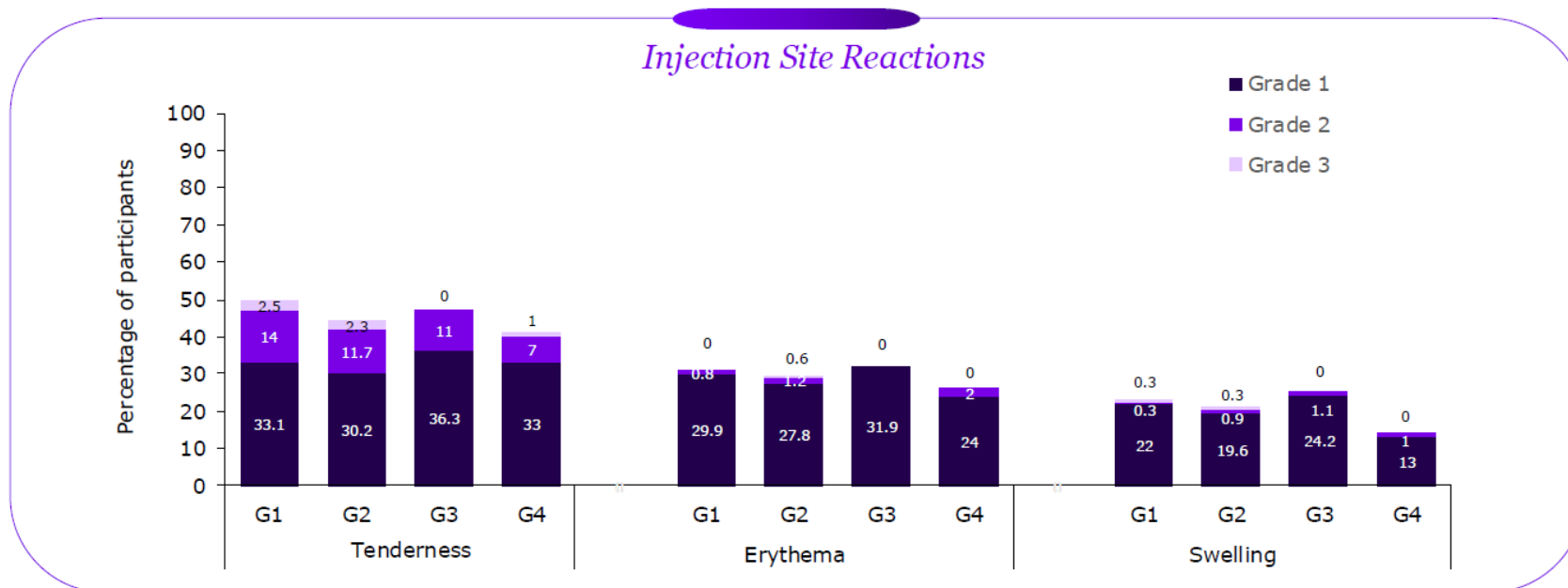
Group 2=MenACWY-CRM + routine pediatric vaccines at 6-7 months and 12-13 months

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): MenACWY-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): MenACWY-TT vaccine at 17 to 19 months of age and 20 to 23 months of age
 Group 4 (G4): MenACWY-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>

Solicited Systemic Adverse Reactions: Met61

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

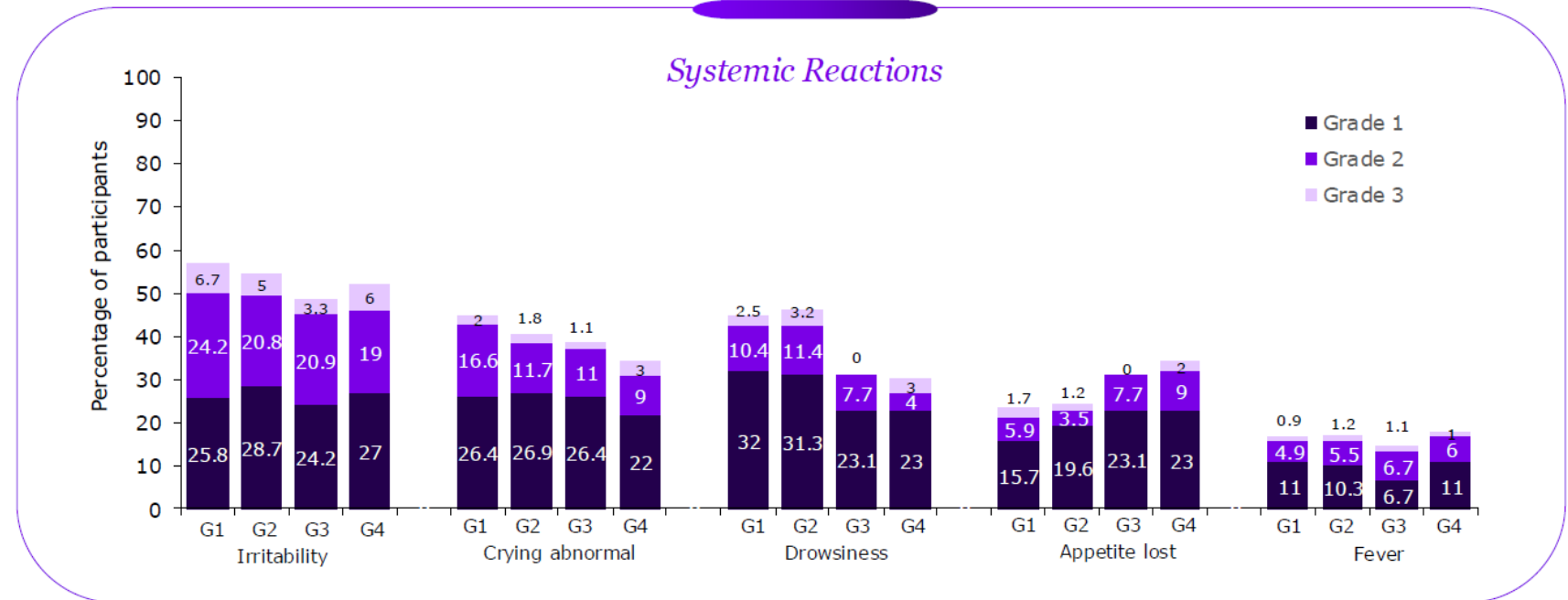
Group 2=MenACWY-CRM + routine pediatric vaccines at 6-7 months and 12-13 months

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

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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): MenACWY-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): MenACWY-TT vaccine at 17 to 19 months of age and 20 to 23 months of age
Group 4 (G4): MenACWY-D vaccine at 17 to 19 months of age and 20 to 23 months of age

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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

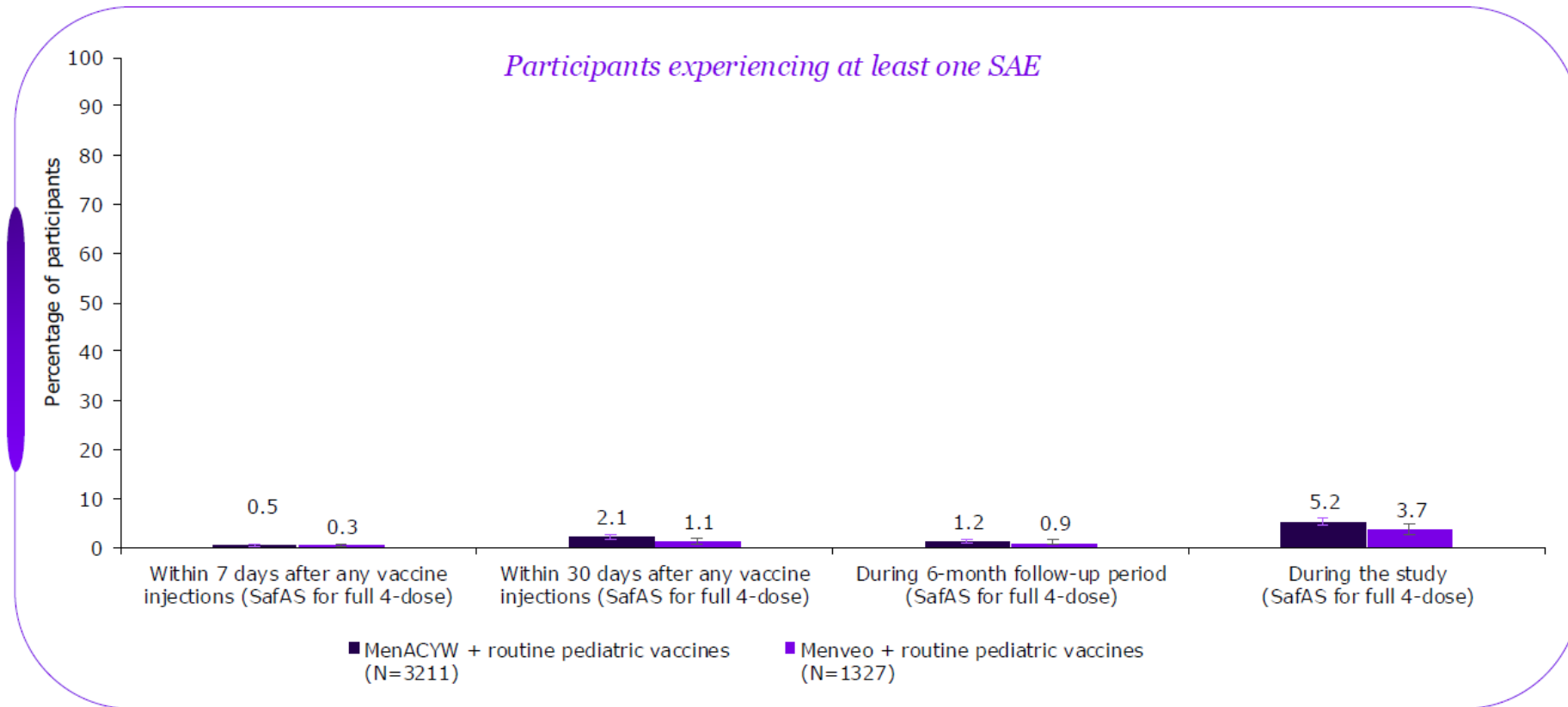
SAEs, AESIs, and Unsolicited AEs, cont.

- 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

Pooled Safety Analysis: Met41 and Met42

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MET41 and MET42 pooled safety analysis



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

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