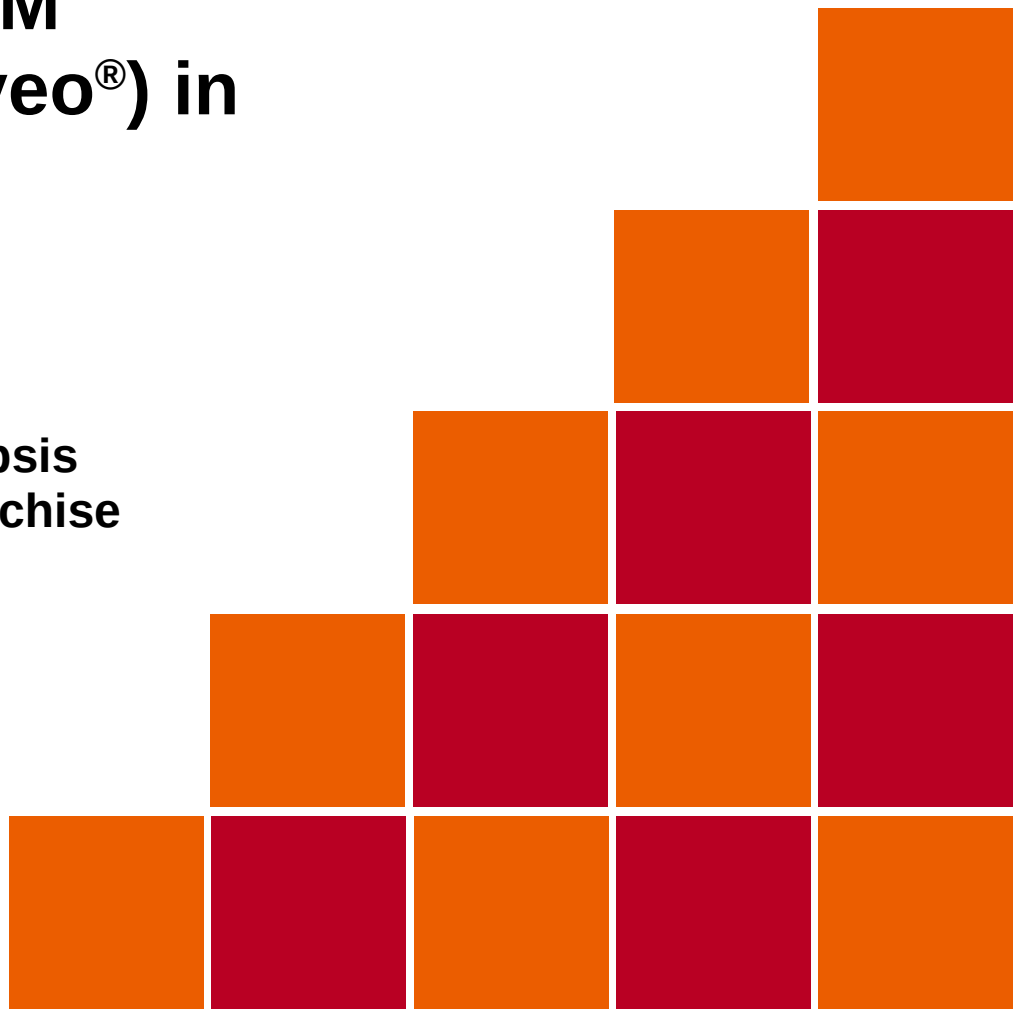
MenACWY-CRM Vaccine (Menveo®) in Infants

Peter Dull, MD

Head Meningitis & Sepsis Vaccines Clinical Franchise

Novartis Vaccines

October 23, 2013



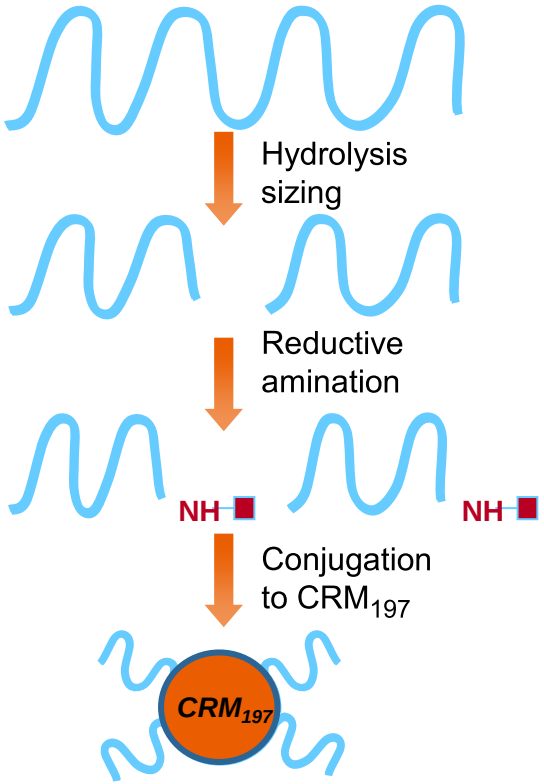
Agenda

- **Background and Overview**
- **MenACWY-CRM Phase 3 studies in infants**
  - Immunogenicity at 7, 12, and 13 months for 2, 4, 6, and 12 month dosing regimen
  - Concomitant vaccination with routine infant vaccines
  - Safety
- **MenACWY-CRM Phase 3 study in older infants**
  - Immunogenicity of a 7-9, 12 month schedule in infants
  - Concomitant MMRV vaccination at 12 months
  - Safety
- **MenACWY-CRM Phase 3b study - Persistence after infant series**

MenACWY-CRM Vaccine Description

MenACWY-CRM (Menveo©) is indicated for active immunization to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y and W-135. It is approved for use in persons 2 months through 55 years of age.

Glycoconjugation



Formulation

MenA-CRM: 10 μg/dose

MenC-CRM: 5 μg/dose

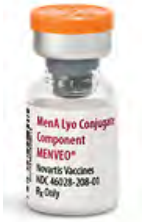
MenW-CRM: 5 μg/dose

MenY-CRM: 5 μg/dose

Adjuvant free

Preservative free

Presentation



MenA-CRM Conjugate
lyophilized (vial)

MenCWY-CRM Conjugate
liquid (vial)

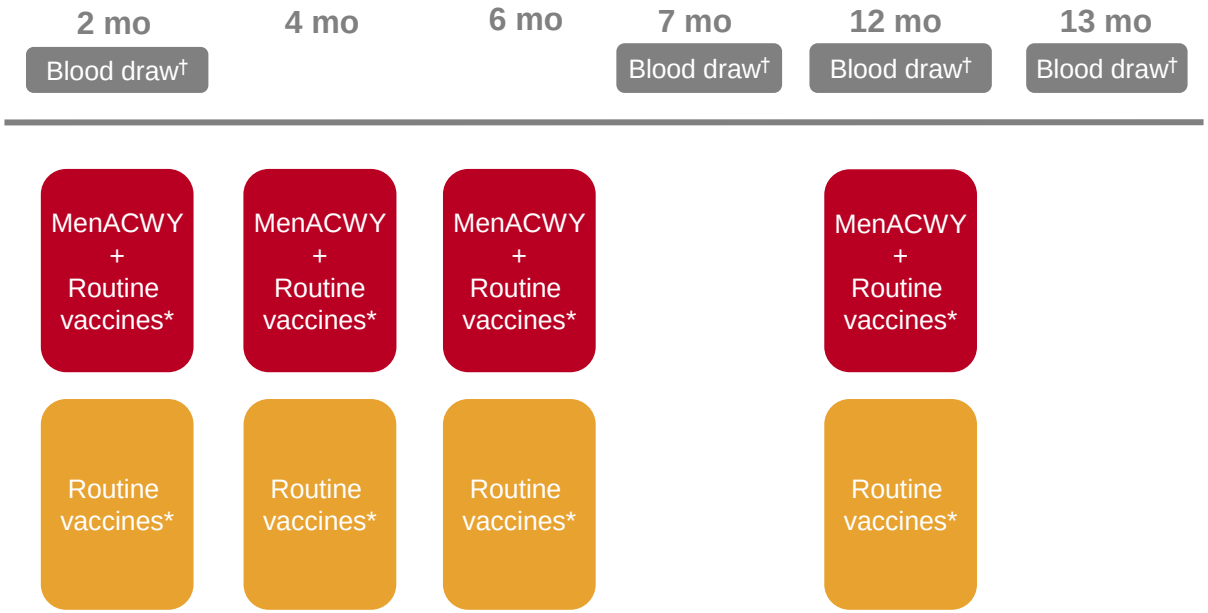
Clinical Development Overview - Key Studies in infants 2-23 months of age

Development Phase (Study #)	Total Population (Safety)	Total MenACWY Subjects	Primary & Secondary Objectives
Phase 2 (V59P5) Infants from 2 months of age	601	180	Dose- and dose-regimen finding
Phase 3 (V59P14) Infants from 2 months of age	4533	3021	Safety and Immuno; Co-administration with Pediarix-based routine vaccines
Phase 3b (V59P23) Infants from 2 months of age	7728	5760	Safety of 4-dose infant series
Phase 3 (V59_33) Infants from 2 months of age	525	255	Safety and Immuno; Co-administration with Pentacel-based routine vaccines
Phase 3 (V59P21) Older infants from 7 months of age	1603	1000	Safety and Immuno; Co-administration with MMRV

Overall, MenACWY-CRM Phase 2/3 safety database studies include 8745 infants vaccinated with 4-dose series and 1985 older infants vaccinated with 2-dose series

Phase 3 Results in Infants – Studies V59_33 and V59P23

Immunogenicity and Safety Trials - Study Design



Study Objectives

- **Adequacy of immune response following 4-dose series†;**
- **Assess safety and tolerability of MenACWY-CRM when given concomitantly with routine infant vaccines compared to routine vaccines alone**

*Routine vaccines include diphtheria-tetanus-acellular pertussis-inactivated poliovirus-*H. influenzae* type b combined vaccine (DTaP-IPV/Hib), 7-valent pneumococcal conjugate vaccine (PCV7), hepatitis B virus vaccine (HBV) and measles, mumps, and rubella vaccine (MMR) given in accordance with ACIP recommendations.

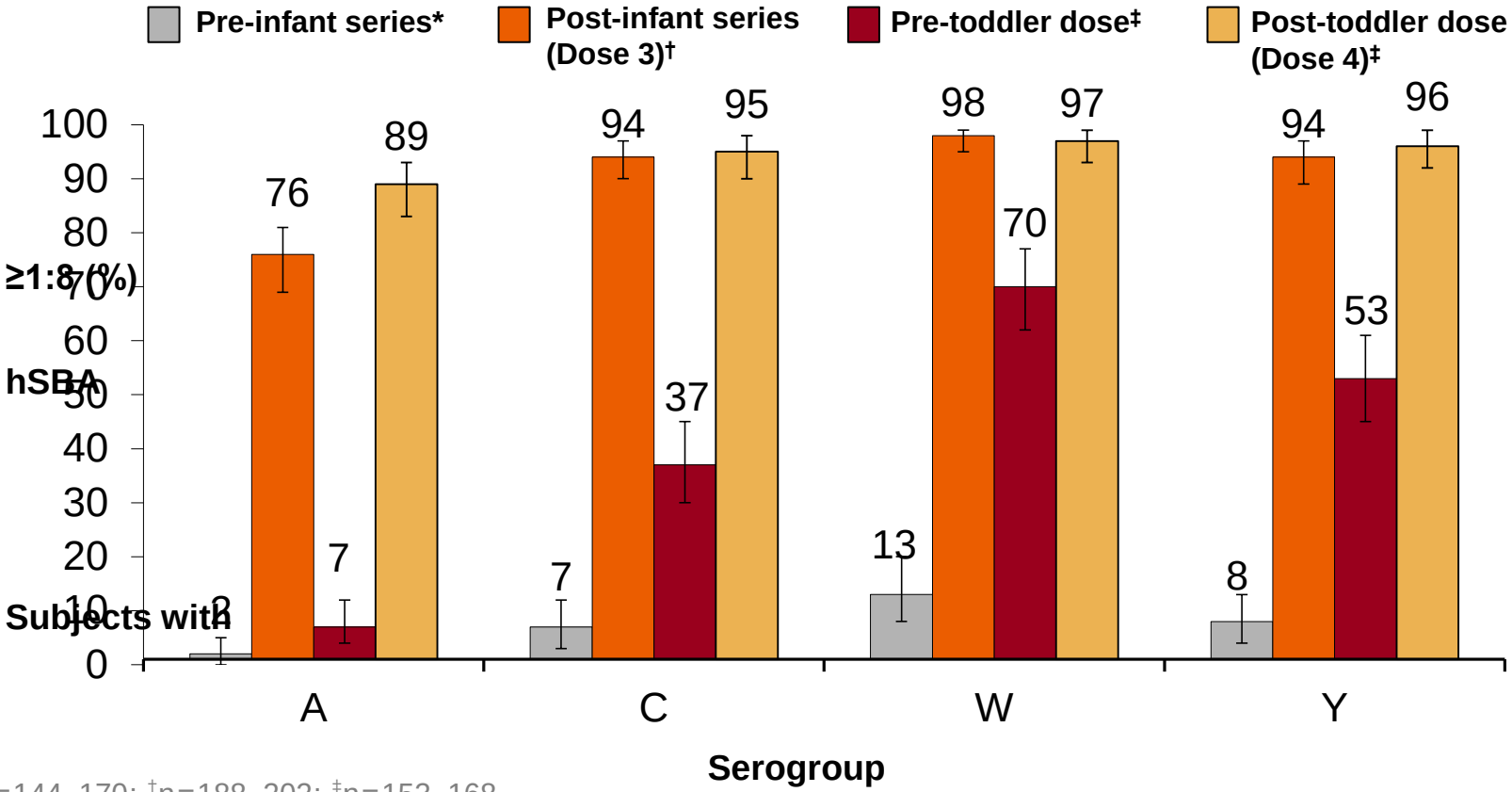
† Study V59_33 only

Clinicaltrials.gov Identifiers NCT01000311 (Study V59_33) and NCT00806195 (Study V59P23)

Phase 3 Immunogenicity in Infants – Study V59_33

Percentage of infants with hSBA ≥ 1:8 postvaccination with 4 doses of MenACWY-CRM concomitantly with routine vaccines

MenACWY-CRM given at 2, 4, 6 and 12 months of age
(Blood drawn at 2, 7, 12 and 13 months of age)



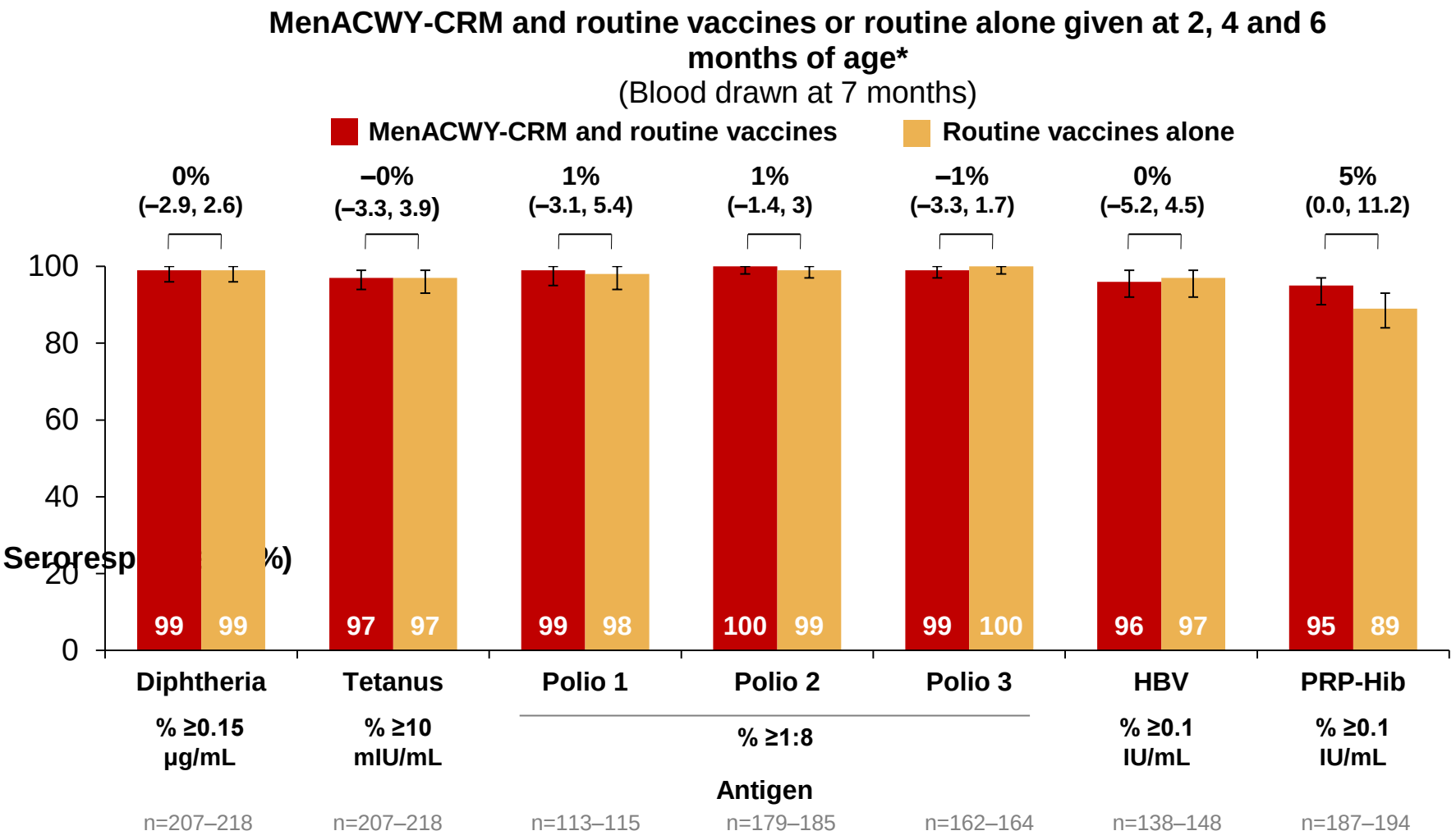
*n=144–170; †n=188–202; ‡n=153–168.

Routine vaccines: diphtheria-tetanus-acellular pertussis-inactivated poliovirus-*Haemophilus influenzae* type b combined vaccine (DTaP-IPV/Hib),7-valent pneumococcal conjugate vaccine (PCV7), hepatitis B virus vaccine (HBV) and measles, mumps, and rubella vaccine (MMR).

hSBA=human serum bactericidal assay

Nolan T, et al. Presented at the Infectious Diseases Society of America Annual Meeting; October 2012; San Diego, CA.
Clinicaltrials.gov Identifier NCT01000311

Phase 3 Immunogenicity in Infants – Study V59_33
Immunogenicity of routine vaccinations at 2, 4, and 6 months of age administered with or without MenACWY-CRM



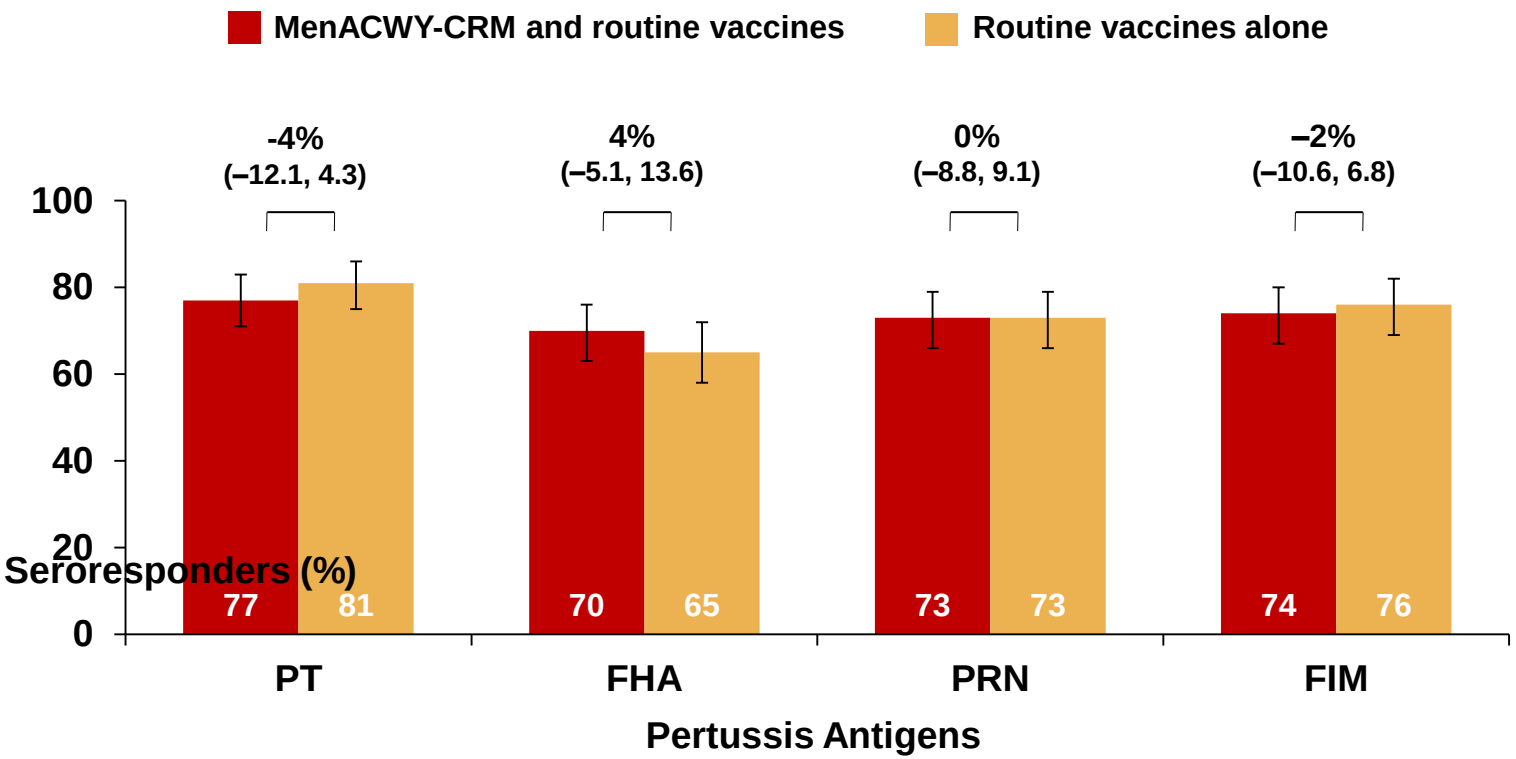
*Routine vaccines: diphtheria, tetanus, and pertussis; inactivated polio; *Haemophilus influenzae* type B; hepatitis B; pneumococcal protein conjugate;. PRP=polyribosylribitol phosphate; HBV=hepatitis B vaccine.

Nolan T, et al. Presented at the Infectious Diseases Society of America Annual Meeting; October 2012; San Diego, CA.

Clinicaltrials.gov Identifier NCT01000311

Phase 3 Immunogenicity in Infants – Study V59_33
Seroresponse to routine vaccinations at 2, 4, and 6 months of age administered with or without MenACWY-CRM

MenACWY-CRM and routine vaccines or routine alone given at 2, 4 and 6 months of age*
(Blood drawn at 7 months)



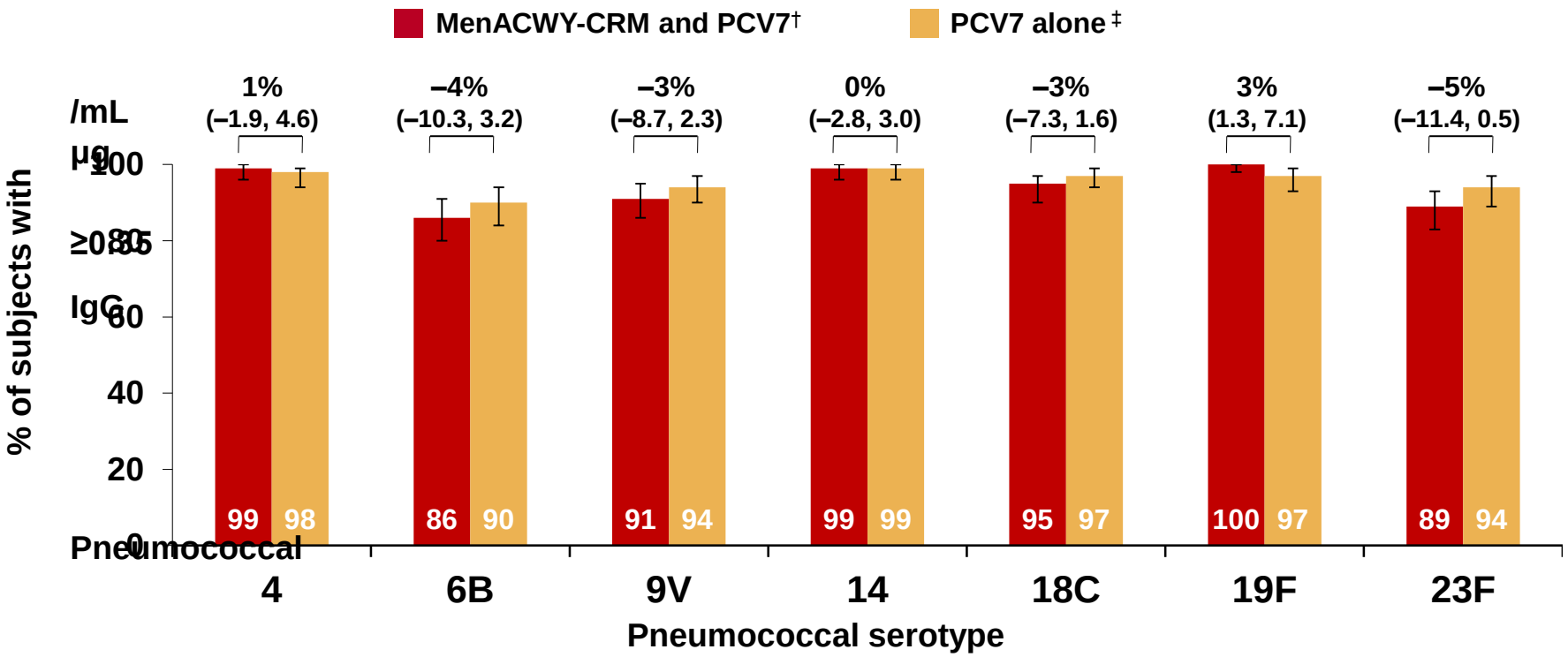
Post-hoc analysis accounting for group and center, non-inferiority was achieved for PT with a lower limit of 95%CI of -3.9%; FIM remained outside the limit with lower limit 95% CI of -10.2%.

*Routine vaccines: diphtheria, tetanus, and pertussis; inactivated polio; *Haemophilus influenzae* type B; hepatitis B; pneumococcal protein conjugate;. n=185-191

Nolan T, et al. Presented at the Infectious Diseases Society of America Annual Meeting; October 2012; San Diego, CA.
Clinicaltrials.gov Identifier NCT01000311

Phase 3 Immunogenicity in Infants – Study V59_33
Pneumococcal IgG responses after routine vaccinations at 2, 4, and 6 months of age administered with or without MenACWY-CRM

MenACWY-CRM and PCV7 or PCV7 alone given at 2, 4 and 6 months of age*
(Blood drawn at 7 months)

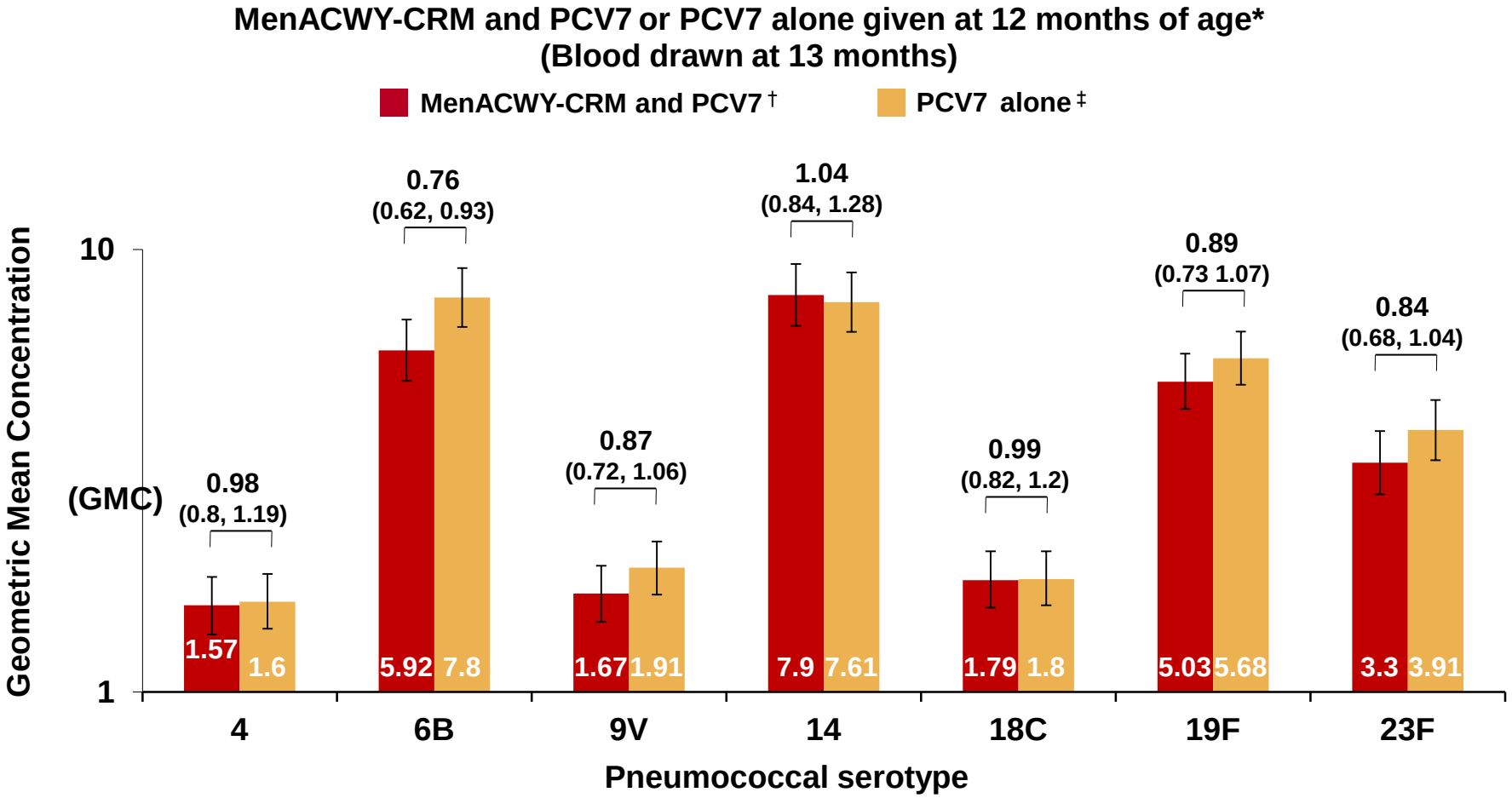


Post-hoc analysis accounting for group and center, non-inferiority was achieved for serotypes 6B and 23F with a lower limit of 95% CI of -1.8% and -2.3%, respectively.

*With other routine vaccines: diphtheria, tetanus, and pertussis; inactivated polio; *H. influenzae* type B; hepatitis B; †n=183; ‡n=178;
PCV=pneumococcal conjugate vaccine

Nolan T, et al. Presented at the Infectious Diseases Society of America Annual Meeting; October 2012; San Diego, CA.
Clinicaltrials.gov Identifier NCT01000311

Phase 3 Immunogenicity in Infants – Study V59_33
GMCs to pneumococcal antigens 1 month after the 12 month dose of routine vaccines administered with or without MenACWY-CRM

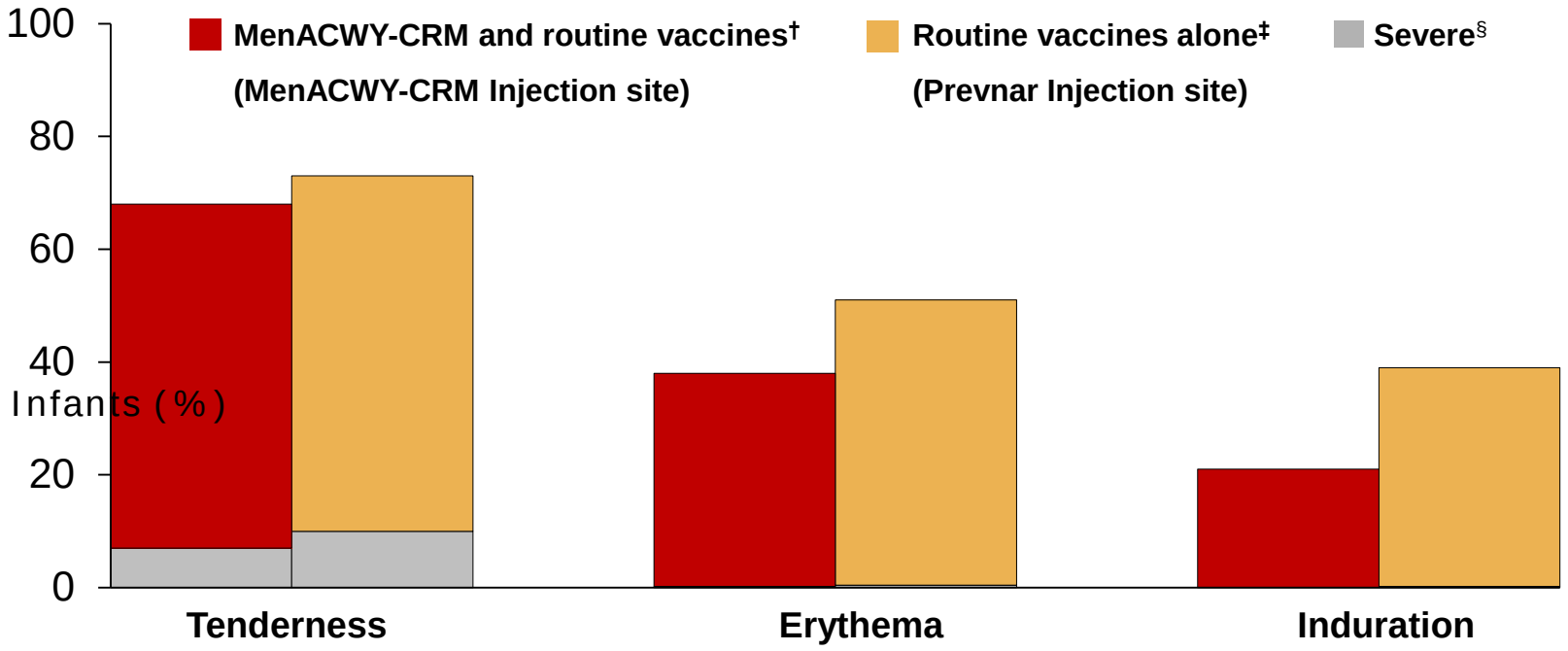


*With other routine vaccines: diphtheria, tetanus, and pertussis; inactivated polio; *Haemophilus influenzae* type B; hepatitis B; †n=161; ‡n=170; PCV=pneumococcal conjugate vaccine

Nolan T, et al. Presented at the Infectious Diseases Society of America Annual Meeting; October 2012; San Diego, CA. Clinicaltrials.gov Identifier NCT01000311

Phase 3b Safety in Infants – Study V59P23
Local Reactions After Any Infant Vaccination, by Severity

Percentage of subjects with at least 1 local reaction within 7 days after any vaccination with routine vaccines* either with or without MenACWY-CRM

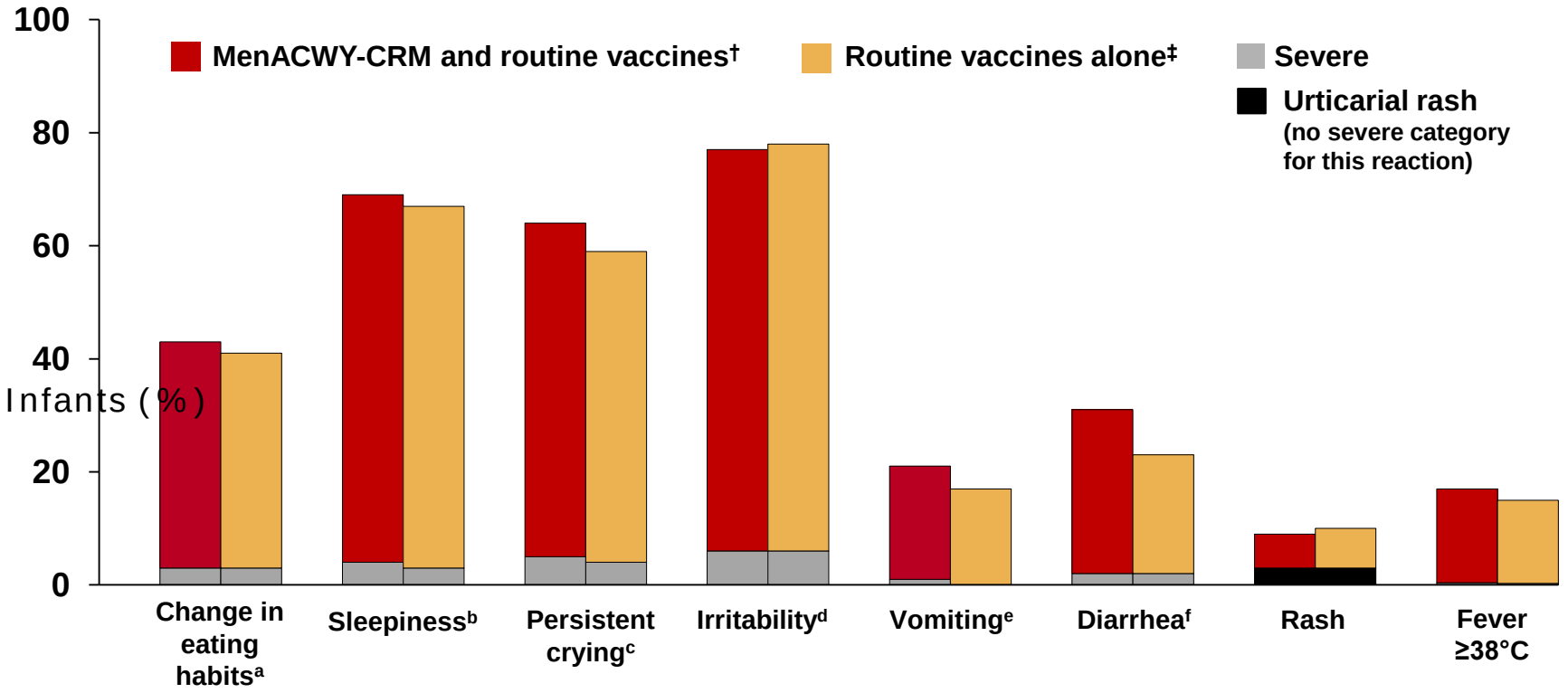


*Routine vaccines: diphtheria, tetanus, and pertussis; inactivated polio; *Haemophilus influenzae* type B; hepatitis B; pneumococcal protein conjugate;
†MenACWY-CRM was injected into the anterolateral area of the right thigh; n=1346-1348; ‡PCV7 was injected into the anterolateral area of the right thigh; n=460-461; §Tenderness, severe=cried when injected limb moved

Clinicaltrials.gov Identifier NCT00806195

Phase 3b Safety in Infants – Study V59P23
Systemic Reactions After Any Infant Vaccination, by Severity

Percentage of subjects with at least 1 systemic reaction within 7 days after vaccination with routine vaccines* either with or without MenACWY-CRM

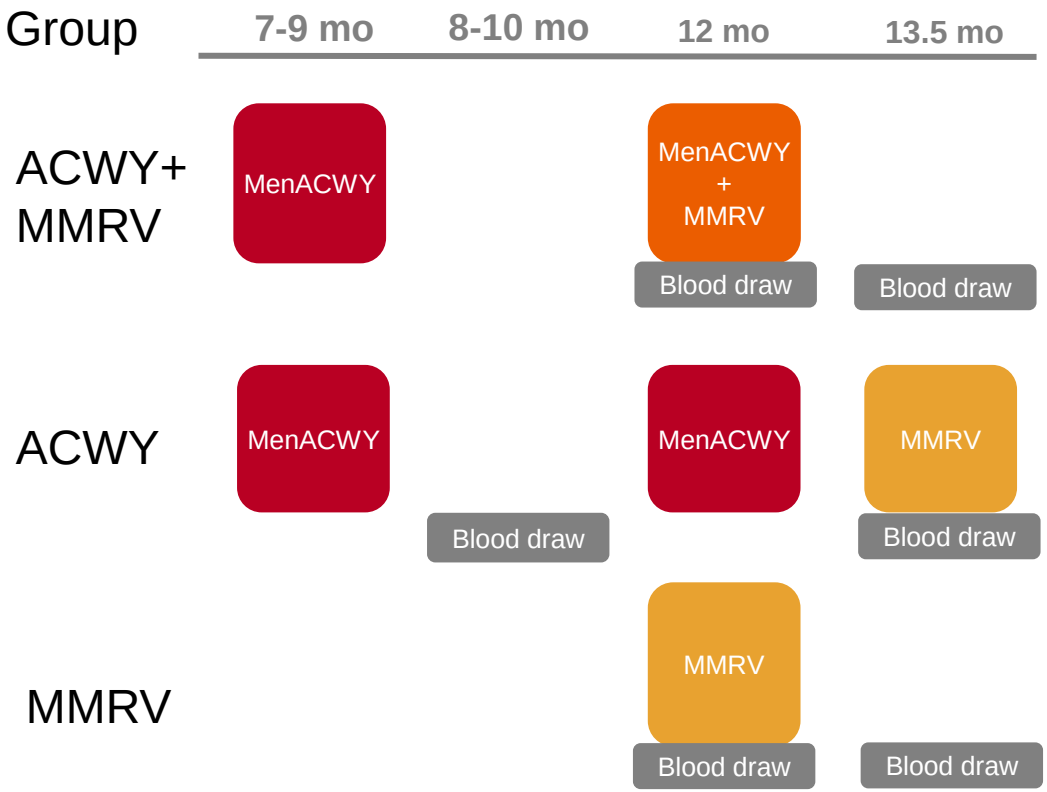


*Routine vaccines: diphtheria, tetanus, and pertussis; inactivated polio; *Haemophilus influenzae* type B; hepatitis B; pneumococcal protein conjugate; †n=1346-1348; ‡n=460-461

[a]Change in eating habits, severe=missed >2 feeds; [b]Sleepiness, severe=sleeps most of the time, hard to arouse; [c]Persistent crying, severe=≥3 hours; [d]Irratibility, severe=unable to console; [e]Vomiting, severe=little/no intake for more prolonged time; [f]Diarrhea, severe=≥6 liquid stools, no solid consistency

Clinicaltrials.gov Identifier NCT00806195

Phase 3 Data Older Infants – Study V59P21
Immunogenicity and Safety Study - Study Design



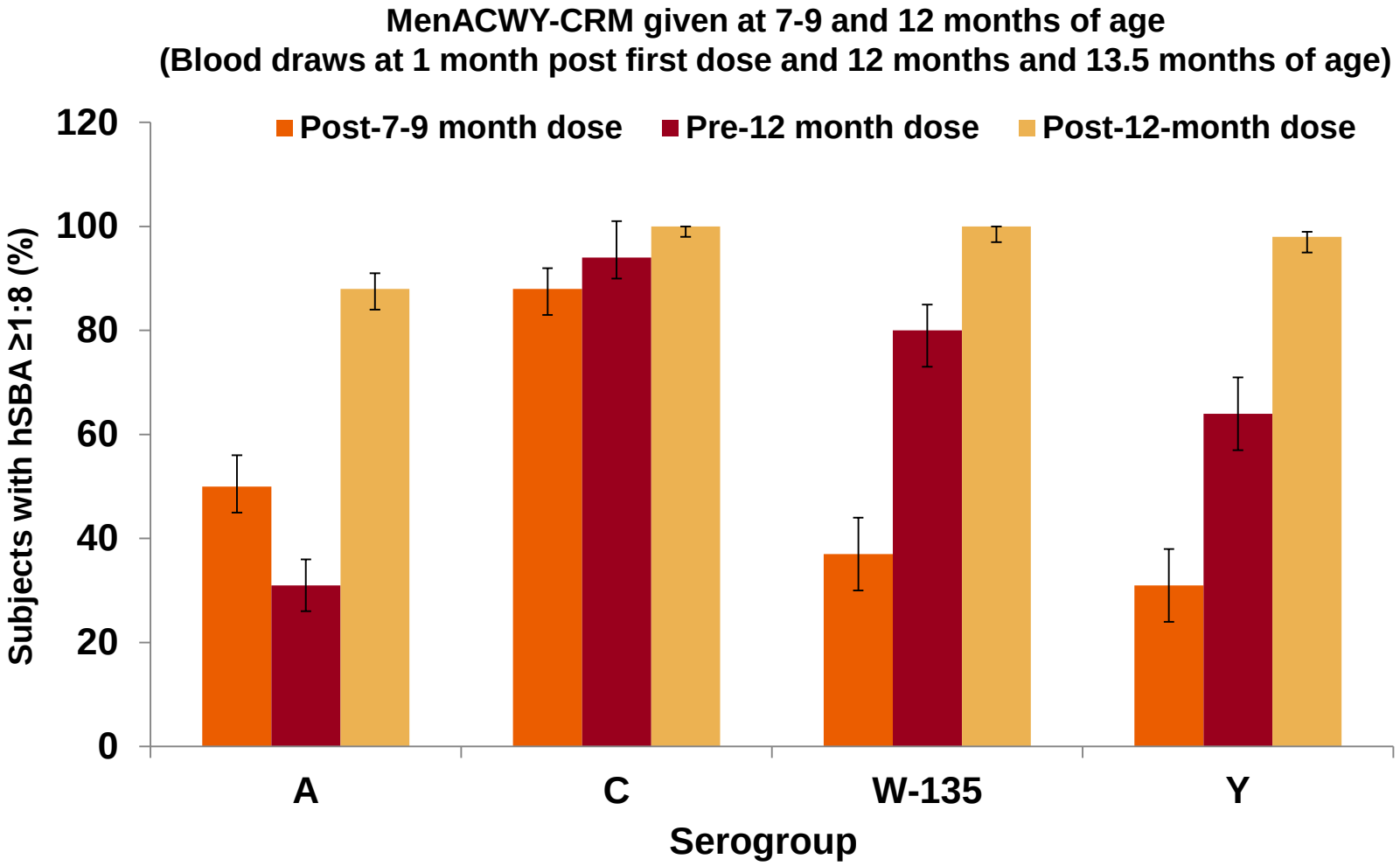
Study Objectives

- Immunogenicity of a 2 dose series of MenACWY-CRM
- Immune response to MMRV and MenACWY-CRM antigens when given concomitantly
- Safety and tolerability as measured by local and systemic reactions

Klein NP, et al. *Vaccine* 2012;30:3929-3936.
Clinicaltrials.gov Identifier NCT00626327

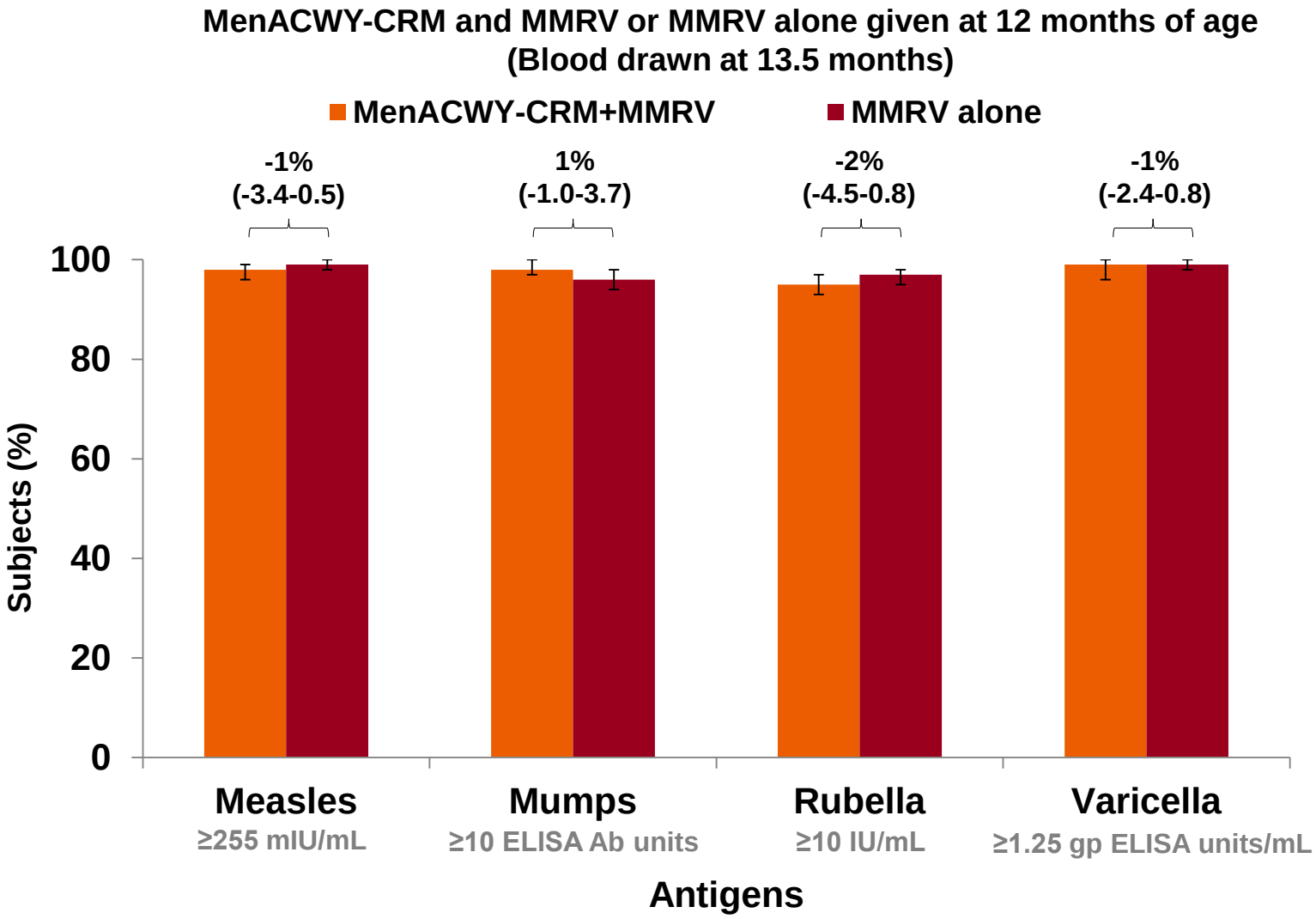
Phase 3 Immunogenicity in Infants – Study V59P21

hSBA ≥1:8 in Infants after 2 doses of MenACWY-CRM at 7-9 months of age and 12 months



hSBA=human serum bactericidal assay
Klein NP, et al. *Vaccine* 2012;30:3929-3936.
Clinicaltrials.gov Identifier NCT00626327

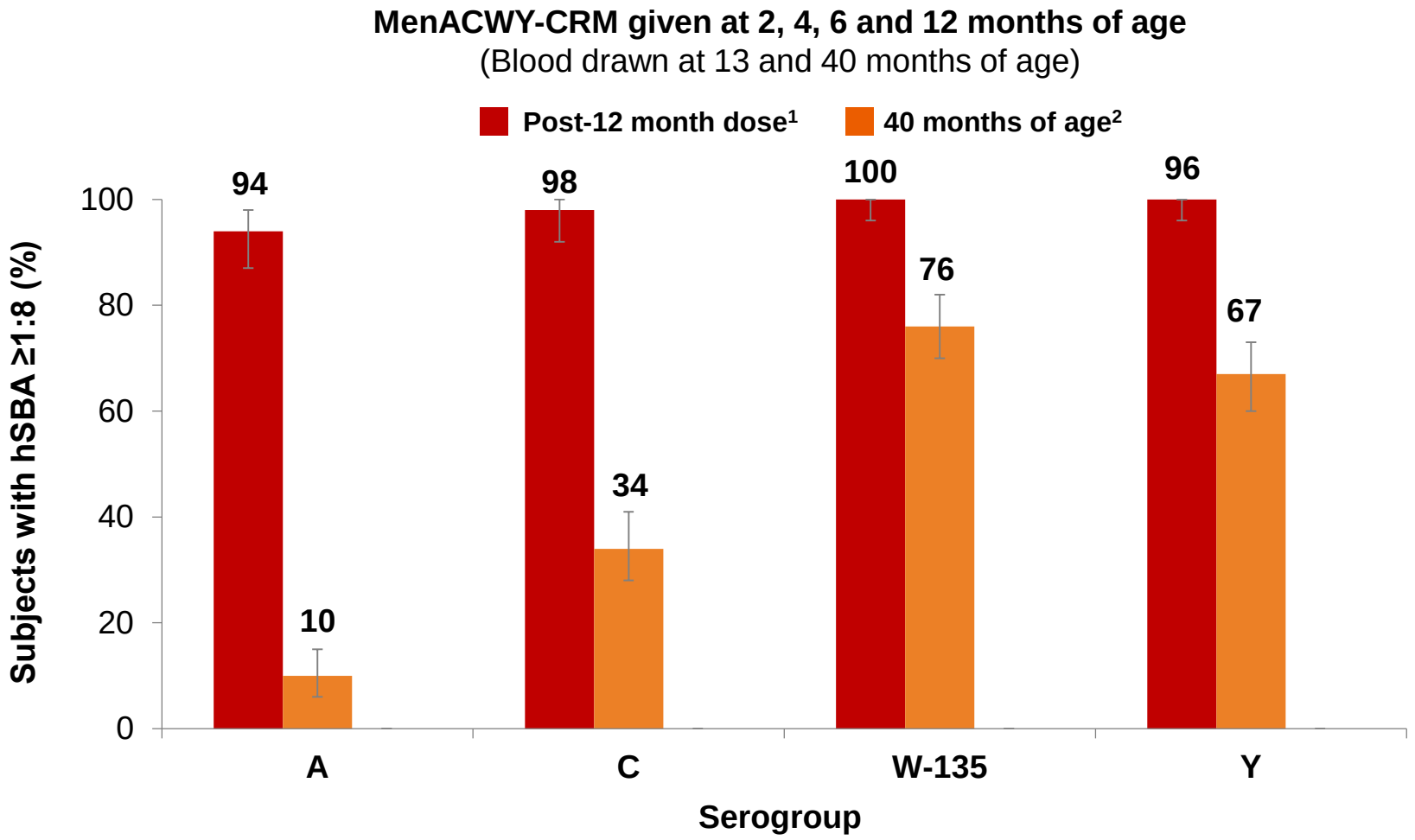
Phase 3 Immunogenicity in Infants – Study V59P21
Seroresponse to MMRV administered at 12 months of age with or without MenACWY-CRM



Klein NP, et al. *Vaccine* 2012;30:3929-3936.
Clinicaltrials.gov Identifier NCT00626327

Phase 3 Immunogenicity in Infants – Study V59P14E1

At 40 months of age: Percentage of Infants with hSBA ≥1:8 Postvaccination with MenACWY-CRM at 2, 4, 6, 12 months



hSBA=human serum bactericidal assay

1. Klein NP, et al. *Pediatr Infect Dis J.* 2012;31:64-71. 2. Data on file, Novartis Vaccines and Diagnostics.

Summary

- **MenACWY-CRM is well-tolerated and immunogenic in infants in a four dose series administered at 2, 4, 6, and 12 months**
  - No unexpected safety signals of concern observed
- **Similar immunogenicity of all concomitant vaccine antigens when administered with MenACWY-CRM**
  - Meets all non-inferiority across the 7 PCV serotypes at 13 months
- **MenACWY-CRM is well-tolerated and immunogenic when administered as a two dose series at 7 and 12 months**
  - No interference with MMRV observed
- **Persistence of hSBA evident at 40 months of age after infant series with further data at 60 months of age available in 2014**