20-valent Pneumococcal Conjugate Vaccine (PCV20) Phase 3 in Pediatrics

Wendy Watson, MD
Global Clinical Program Lead

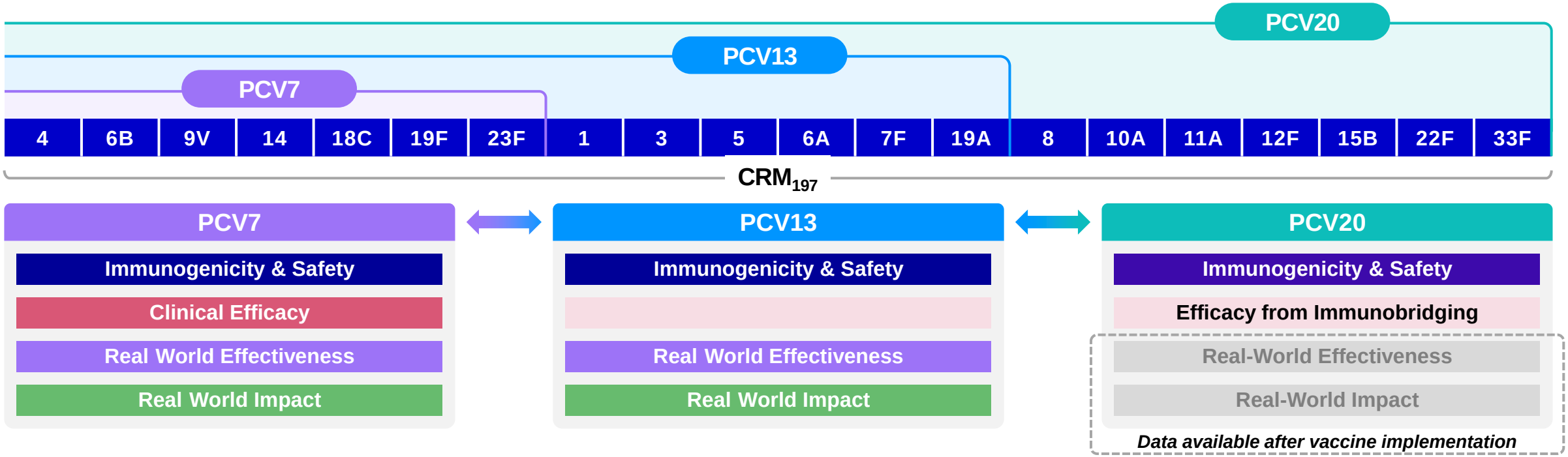
ACIP February 22, 2023

PCV20 is Built on the Established Platforms of PCV7 and PCV13

PCV20 Composition

- PCV20 builds on the 20-year legacy of PCVs and contains PCV13 components + conjugates for 7 additional serotypes to broaden disease coverage for pneumococcal disease in children
- The 7 additional conjugates were modelled on the PCV13 Pfizer platform

- Licensure based on satisfactory safety and immunogenicity compared to PCV13
- Totality of data to support comparability per regulatory agreement
- Seeking same indications as PCV13
- PCV20 in the pediatric program is the same vaccine currently approved, recommended, and administered in adults

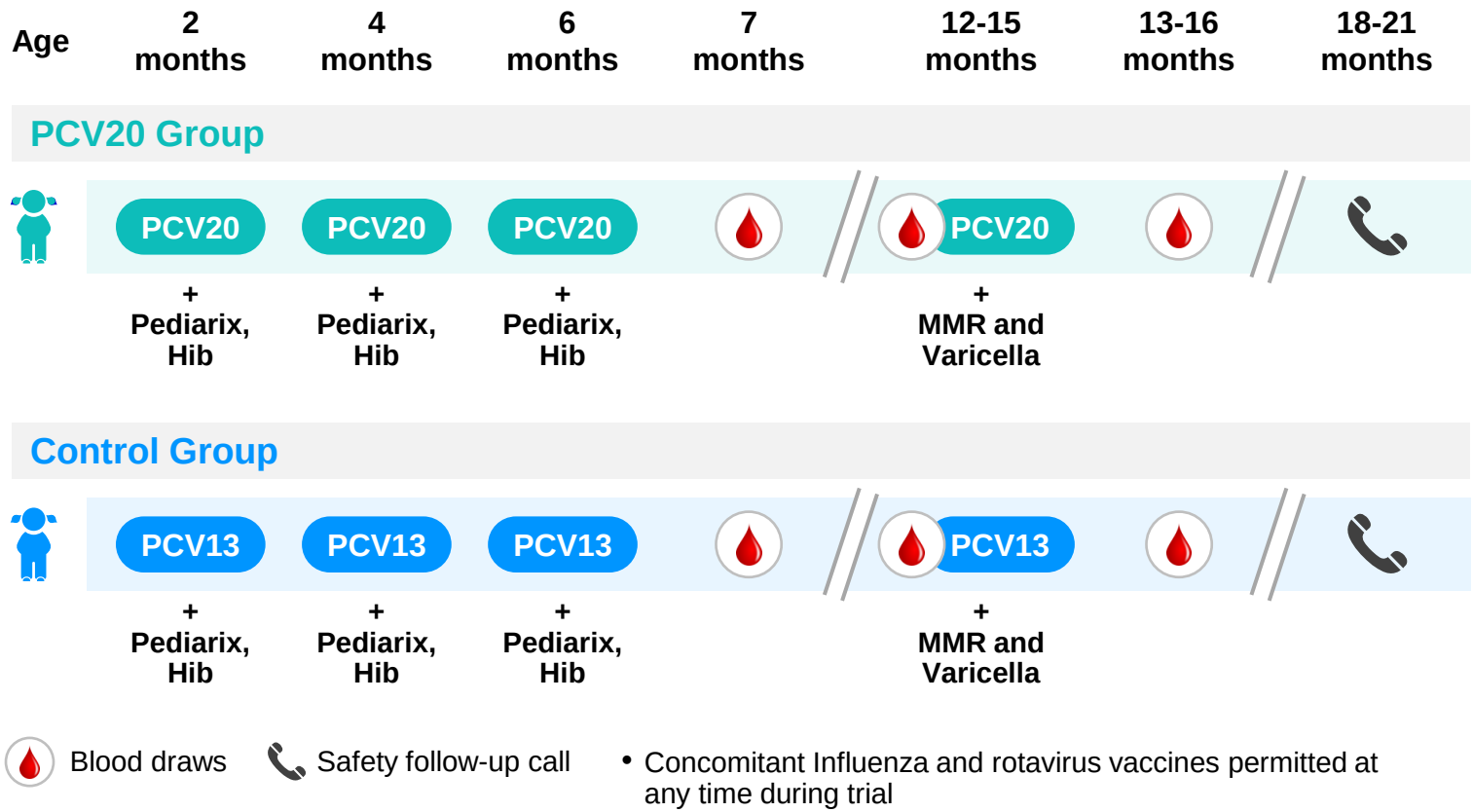


PCV20 Clinical Development Program

Phase 2	**Senders et al. 2021**	**2, 4, 6 and 12 months of age**	**460** Participants	**Demonstrate safety, tolerability, and immunogenicity of PCV20** • Concomitant administration with Pediarix • United States	IMMUNOGENICITY / SAFETY
Phase 3	**Pivotal Infant Study**	**2, 4, 6 and 12–15 months of age**	**1997** Participants	**Demonstrate noninferiority of immune response of PCV20 vs PCV13** • Concomitant administration with Pediarix, Hiberix, M-M-R II, Varivax • United States, Puerto Rico	IMMUNOGENICITY / SAFETY
Phase 3	**Pediatric Single Dose Study**	**Single dose (15 months–<18 years of age)**	**831** Participants	**Characterize safety and immunogenicity in children 15 months to 17 years of age** • United States	IMMUNOGENICITY / SAFETY
Phase 3	**Safety Study**	**2, 4, 6 and 12–15 months of age**	**1511** Participants	**Further characterize safety profile of PCV20** • Concomitant standard vaccines allowed • United States, Puerto Rico, Canada, Chile, Argentina, European Union	SAFETY

Study Design of Phase 3 Pivotal Study in Infants

Multicenter, Randomized, Double-blind Study in the US/Puerto Rico Study in Infants (92 sites, n=1997)



*N=number of participants in the specified age cohort. This value is the denominator for the percentage calculations.
†n=number of participants with the specified characteristic.

Similar Demographics of PCV20 and PCV13 Groups

	PCV20 N*=1001	PCV13 N*=987
Sex	**n† (%)**	**n† (%)**
Male	518 (51.7)	505 (51.2)
Race		
White	754 (75.3)	742 (75.2)
Black or African American	110 (11.0)	108 (10.9)
Asian	16 (1.6)	16 (1.6)
American Indian or Alaska Native	4 (0.4)	3 (0.3)
Native Hawaiian or other Pacific Islander	2 (0.2)	2 (0.2)
Multiracial	68 (6.8)	73 (7.4)
Ethnicity		
Hispanic/Latino	312 (31.2)	293 (29.7)
Non-Hispanic/ non-Latino	661 (66.0)	659 (66.8)

Pre-specified Immunogenicity Analyses

Importance of Multiple Immunologic Assessments to Infer Effectiveness

Primary Objectives	**Co-primary**: Noninferiority of IgG GMCs after toddler dose **Co-primary** Noninferiority of % of participants with IgG above predefined levels after infant series
Key Secondary Objective	Noninferiority of IgG GMC after infant series

Circulating IgG Antibody

- % above prespecified IgG level after toddler dose
- IgG GMCs and % above prespecified IgG for the 7 additional serotypes relative to the PCV13 group
- IgG Reverse Cumulative Distribution Curve (RCDC) after infant series and toddler dose

Functional Response

- OPA GMTs after infant series and toddler dose
- % with OPA titers ≥ LLOQ after infant series and toddler dose
- OPA titer RCDC after infant series and toddler dose

Memory Response

- Geometric fold-rises (GMFR) of IgG from after infant series to after the toddler dose
- GMFR of IgG from before to after the toddler dose
- GMFR of OPA from after infant series to after the toddler dose
- % with ≤ 4-fold rise in OPA titers from before to after the toddler dose

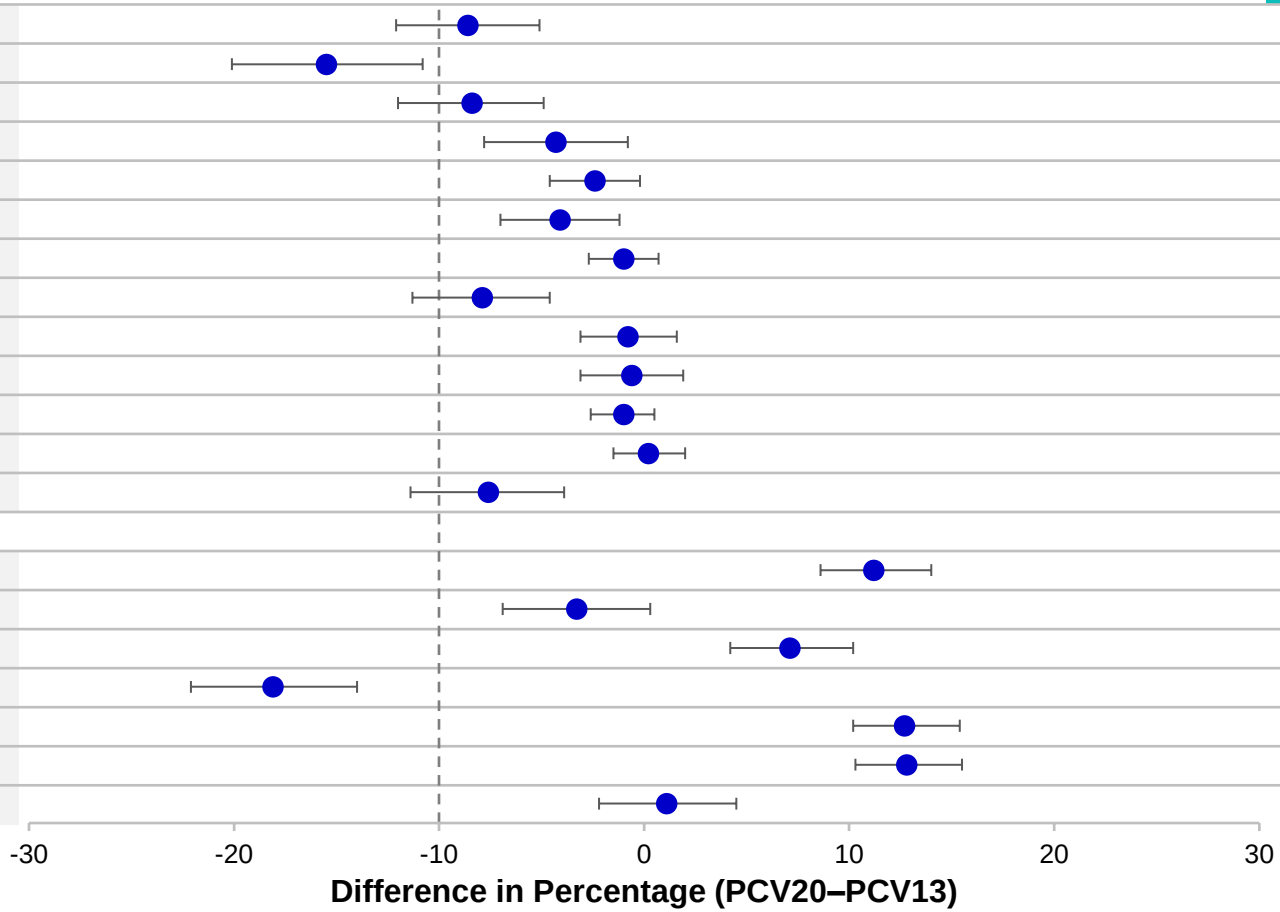
Additional Data

- Concomitant Vaccine Antigen GMCs and GMRs
- Comparison of % With Prespecified Antibody Levels for Concomitant Vaccine Antigens
- Explore cross protection to 6C and 15C

NI for GMC ratio (GMR) = the lower bound of 2-sided 95% CI for GMR (PCV20/PCV13) >0.5.
NI for difference in percentages of participants = the lower bound of 2-sided 95% CI for percent difference (PCV20-PCV13) > -10%.

Post Dose 3: Percentage with Predefined IgG Concentrations

14 Serotypes Met Noninferiority (Difference in %)

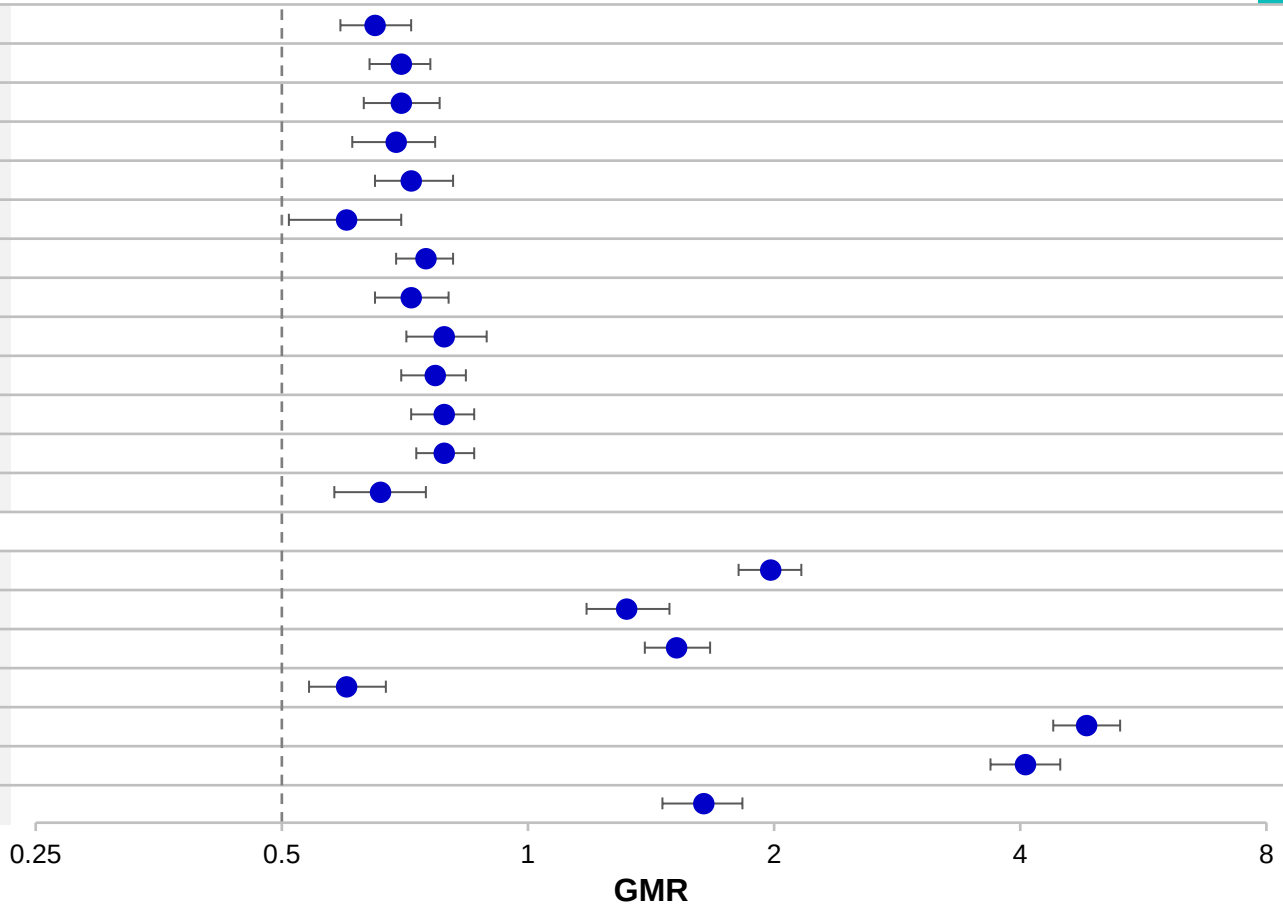


Serotype PCV13	PCV20 (%)	PCV13 (%)	Difference (%) (95% CI)
1	79.8	88.4	-8.6 (-12.1, -5.1)
3	52.1	67.6	-15.5 (-20.1, -10.8)
4	79.7	88.2	-8.4 (-12.0, -4.9)
5	82.5	86.8	-4.3 (-7.8, -0.8)
6A	93.5	95.9	-2.4 (-4.6, -0.2)
6B	88.3	92.4	-4.1 (-7.0, -1.2)
7F	96.6	97.6	-1.0 (-2.7, 0.7)
9V	81.9	89.8	-7.9 (-11.3, -4.6)
14	93.4	94.1	-0.8 (-3.1, 1.6)
18C	92.6	93.1	-0.6 (-3.1, 1.9)
19A	97.1	98.1	-1.0 (-2.6, 0.5)
19F	96.9	96.6	0.2 (-1.5, 2.0)
23F	77.9	85.5*	-7.6 (-11.4, -3.9)
7 Additional			
8	96.8	*85.5*	11.2 (8.6, 14.0)
10A	82.2	*85.5*	-3.3 (-6.9, 0.3)
11A	92.7	*85.5*	7.1 (4.2, 10.2)
12F	67.5	*85.5*	-18.1 (-22.1, -14.0)
15B	98.2	*85.5*	12.7 (10.2, 15.4)
22F	98.3	*85.5*	12.8 (10.3, 15.5)
33F	86.7	*85.5*	1.1 (-2.2, 4.5)

*The 7 additional serotypes are compared to the percentage for serotype 23F after Dose 3 (lowest in PCV13 group, excluding serotype 3).
Predefined IgG concentration – ≥0.35 µg/mL for all serotypes except ≥ 0.23 µg/mL, ≥0.10 µg/mL and ≥ 0.12 µg/mL for serotypes 5, 6B and 19A respectively.

Post Dose 3: IgG Concentration and Geometric Mean Ratio

All 20 Vaccine Serotypes Met Noninferiority



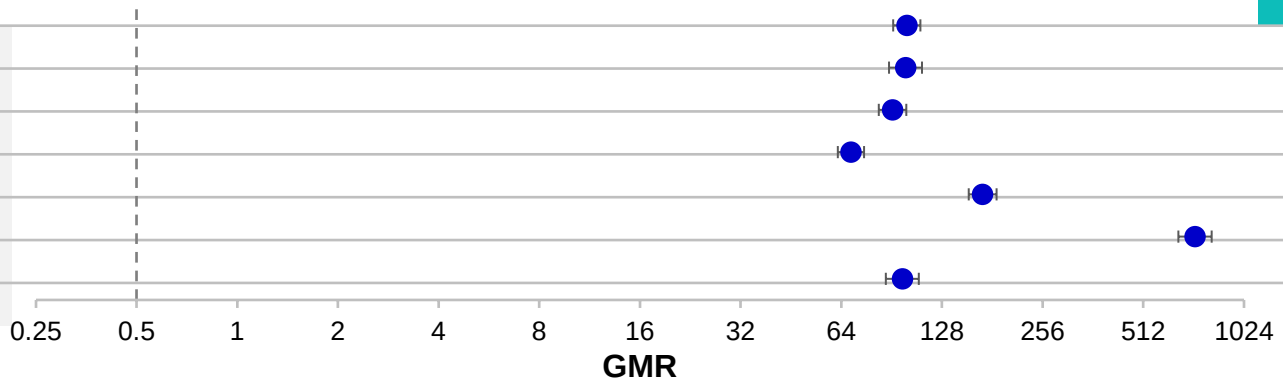
Serotype PCV13	PCV20 GMC	PCV13 GMC	GMR (95% CI)
1	0.74	1.14	0.65 (0.59, 0.72)
3	0.36	0.51	0.70 (0.64, 0.76)
4	0.75	1.08	0.70 (0.63, 0.78)
5	0.66	0.96	0.69 (0.61, 0.77)
6A	1.95	2.69	0.72 (0.65, 0.81)
6B	0.61	1.02	0.60 (0.51, 0.70)
7F	1.71	2.29	0.75 (0.69, 0.81)
9V	0.87	1.21	0.72 (0.65, 0.80)
14	2.16	2.72	0.79 (0.71, 0.89)
18C	1.31	1.71	0.77 (0.70, 0.84)
19A	0.72	0.91*	0.79 (0.72, 0.86)
19F	1.59	2.00	0.79 (0.73, 0.86)
23F	0.82	1.25	0.66 (0.58, 0.75)
7 Additional			
8	1.80	*0.91*	1.98 (1.81, 2.16)
10A	1.21	*0.91*	1.32 (1.18, 1.49)
11A	1.39	*0.91*	1.52 (1.39, 1.67)
12F	0.55	*0.91*	0.60 (0.54, 0.67)
15B	4.40	*0.91*	4.82 (4.39, 5.30)
22F	3.71	*0.91*	4.06 (3.68, 4.48)
33F	1.49	*0.91*	1.64 (1.46, 1.83)

* The 7 additional serotypes are compared to the GMC after Dose 3 for serotype 19A (lowest in PCV13 group, excluding serotype 3).

Post Dose 3: IgG Concentration and Geometric Mean Ratio

Statistically Significantly Higher Response when compared to actual PCV13 Response

Comparison of additional 7 serotypes to actual PCV13 IgG GMC, not lowest in PCV20 group

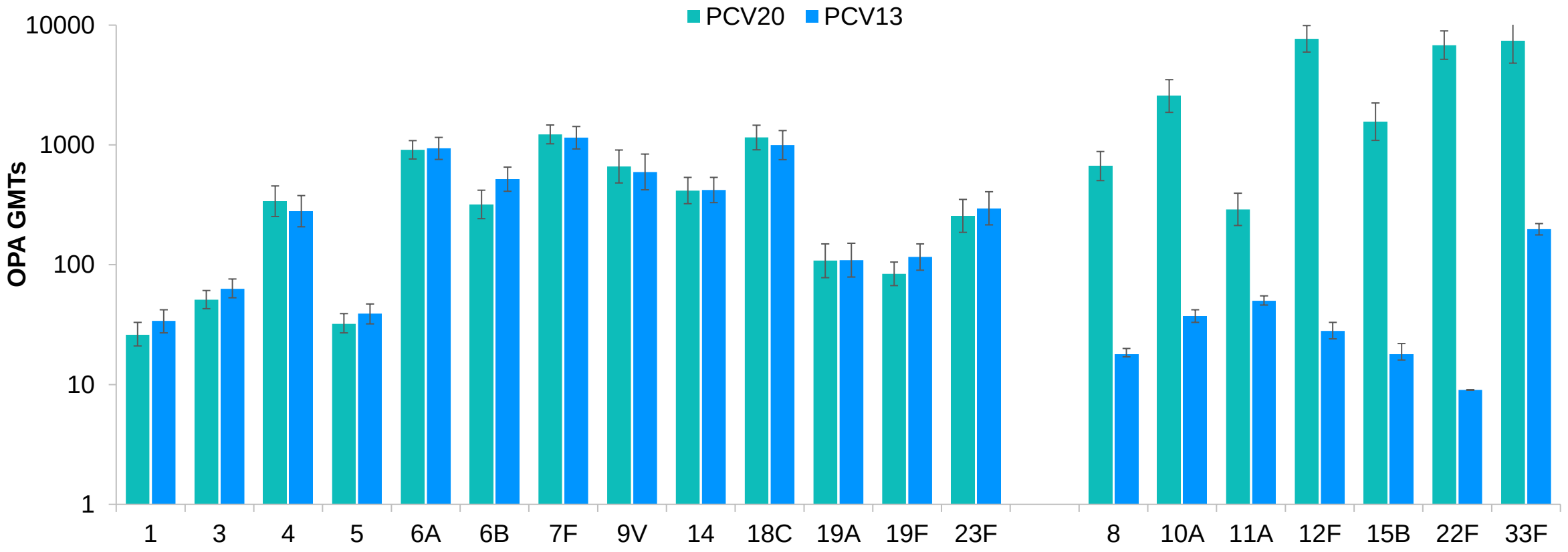


Serotype 7 Additional	PCV20 GMC	PCV13 GMC	GMR (95% CI)
8	1.80	*0.02*	100.54 (91.58, 110.38)
10A	1.21	*0.01*	99.64 (88.87, 111.70)
11A	1.39	*0.02*	91.03 (82.79, 100.09)
12F	0.55	*0.01*	68.42 (62.47, 74.94)
15B	4.40	*0.03*	169.40 (154.01, 186.33)
22F	3.71	*0.01*	730.84 (651.36, 820.01)
33F	1.49	*0.02*	97.45 (86.96, 109.21)

Post Dose 3: Comparison of PCV20 and PCV13 OPA GMTs

Functional Antibody Responses Were Similar Between PCV20 and PCV13 for Shared Serotypes

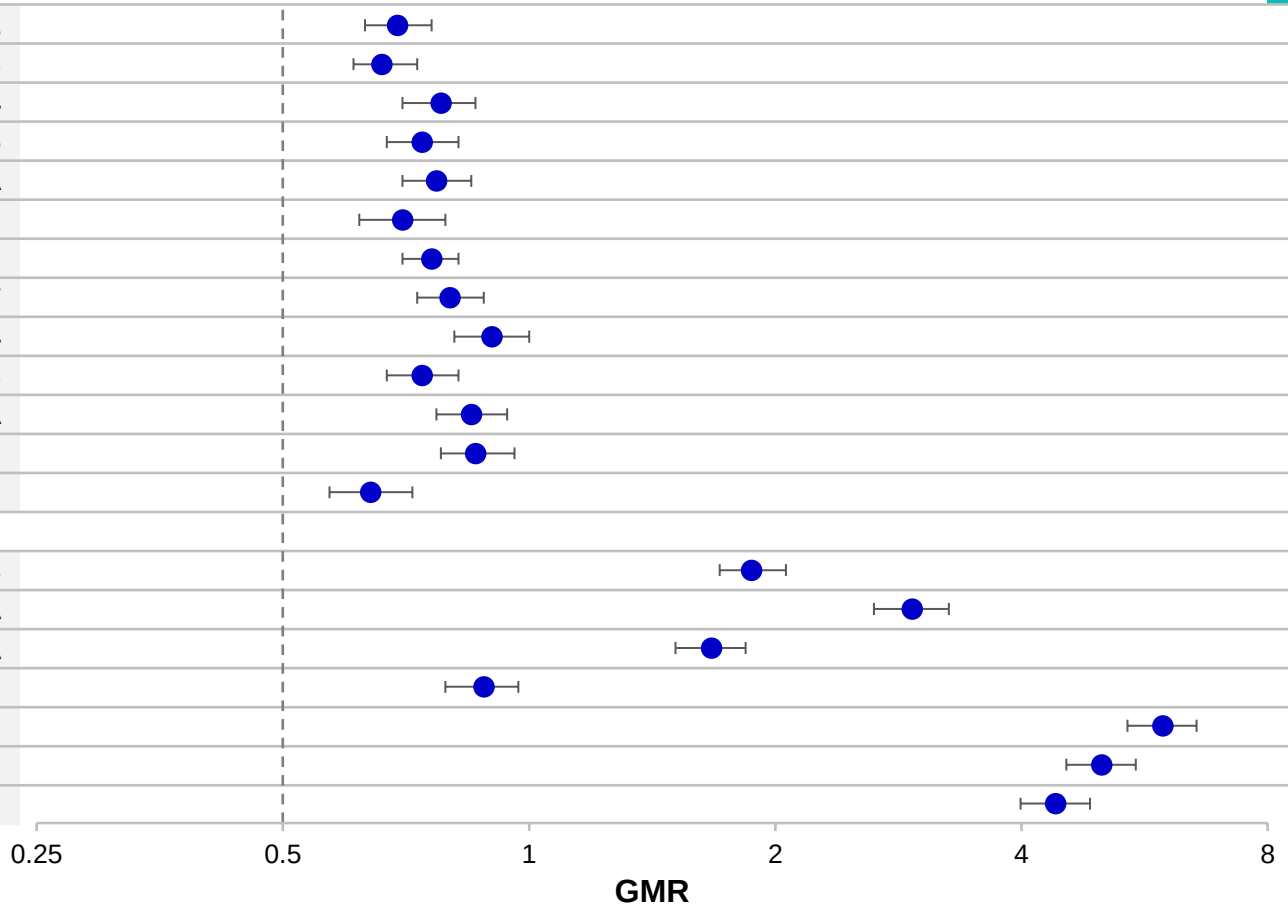
Post Dose 3



PCV20 (n= 80–105); PCV13 (n=77–113).

Post Dose 4: IgG Concentration and Geometric Mean Ratio

All 20 Vaccine Serotypes Met Noninferiority



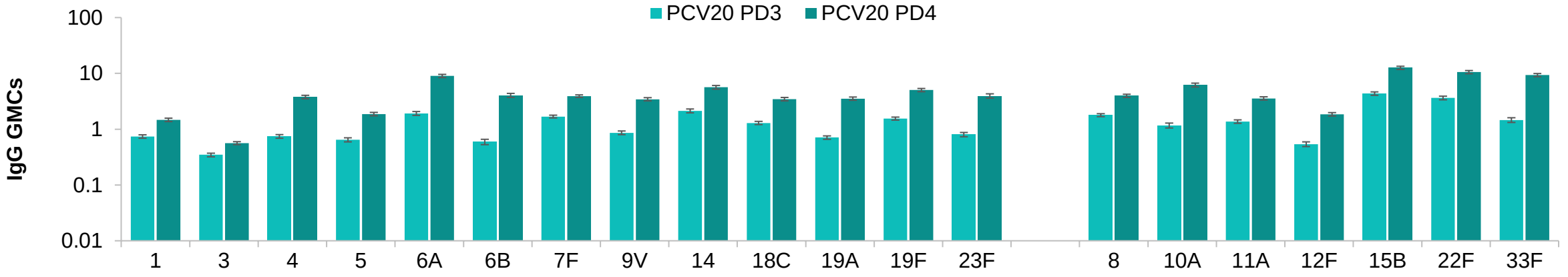
Serotype PCV13	PCV20 GMC	PCV13 GMC	GMR Ratio (95% CI)
1	1.47	2.12*	0.69 (0.63, 0.76)
3	0.56	0.85	0.66 (0.61, 0.73)
4	3.77	4.84	0.78 (0.70, 0.86)
5	1.87	2.51	0.74 (0.67, 0.82)
6A	9.01	11.69	0.77 (0.70, 0.85)
6B	4.01	5.74	0.70 (0.62, 0.79)
7F	3.91	5.18	0.76 (0.70, 0.82)
9V	3.44	4.30	0.80 (0.73, 0.88)
14	5.68	6.34	0.90 (0.81, 1.00)
18C	3.46	4.69	0.74 (0.67, 0.82)
19A	3.53	4.13	0.85 (0.77, 0.94)
19F	5.01	5.79	0.86 (0.78, 0.96)
23F	3.95	6.18	0.64 (0.57, 0.72)
7 Additional			
8	3.97	*2.12*	1.87 (1.71, 2.06)
10A	6.22	*2.12*	2.94 (2.64, 3.26)
11A	3.53	*2.12*	1.67 (1.51, 1.84)
12F	1.85	*2.12*	0.88 (0.79, 0.97)
15B	12.59	*2.12*	5.95 (5.39, 6.55)
22F	10.60	*2.12*	5.01 (4.54, 5.52)
33F	9.31	*2.12*	4.40 (3.99, 4.85)

* The 7 additional serotypes were compared to serotype 1 in the PCV13 group (lowest IgG GMC after Dose 4, excluding serotype 3).

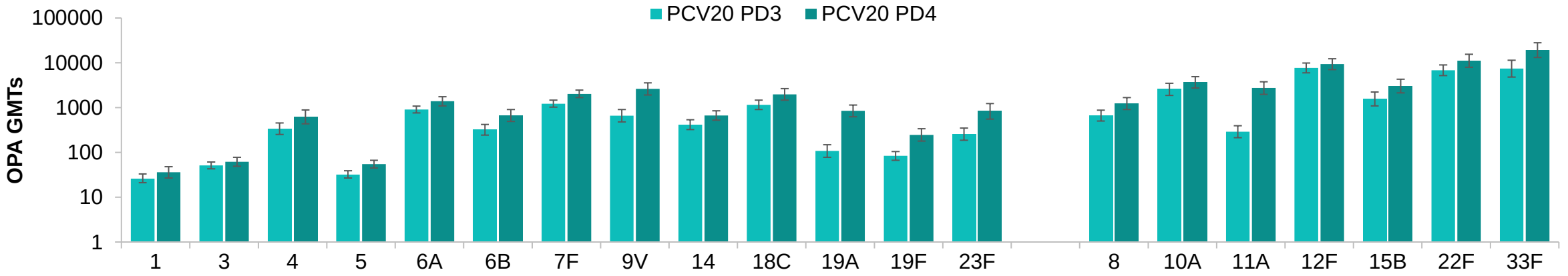
PD3 Compared to PD4: IgG and OPA Response to PCV20

Boosting Observed Across All 20 Serotypes Indicating Anamnestic Response/Memory

Post Dose 3 and Post Dose 4 IgG GMCs



Post Dose 3 and Pose Dose 4 OPA GMTs

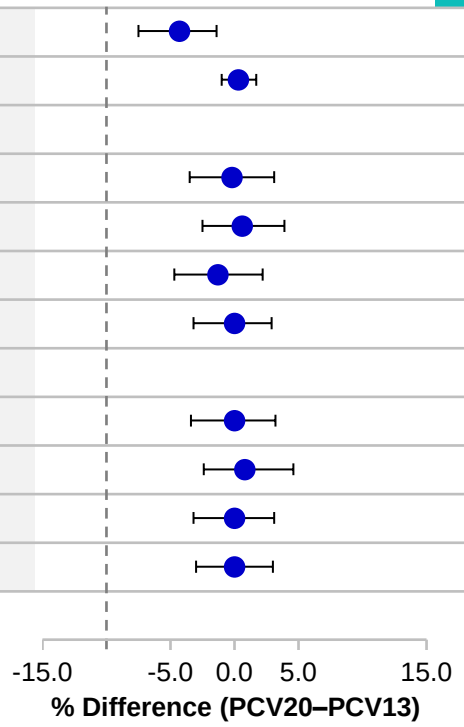


Concomitant Use: Responses to the Vaccines Were Similar When Given with PCV20 or PCV13 in the Infant Immunization Series

All Responses Met Noninferiority

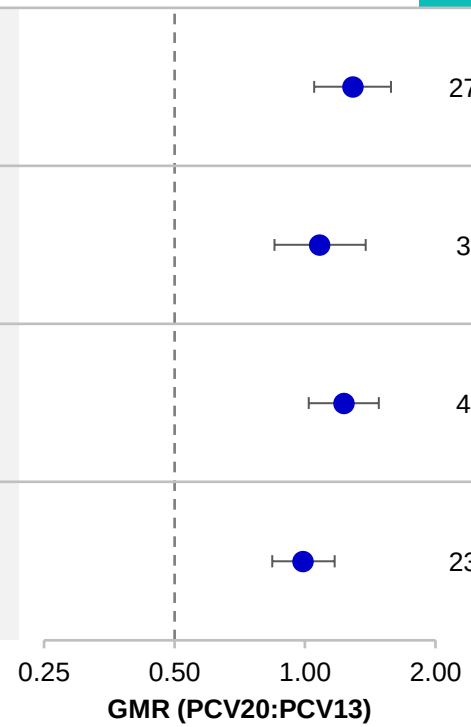
Post Dose 3: Pediarix and Hiberix®

Concomitant Vaccine Antigen	PCV20 (%)	PCV13 (%)	Difference (%) (95% CI)
Diphtheria	93.5	97.8	-4.3 (-7.5, -1.4)
Tetanus	99.7	99.4	0.3 (-1.0, 1.7)
Pertussis			
PT	94.9	95.0	-0.2 (-3.5, 3.1)
FHA	95.7	95.0	0.6 (-2.5, 3.9)
PRN	93.8	95.0	-1.3 (-4.7, 2.2)
HBsAg	100.0	100.0	0.0 (-3.2, 2.9)
Poliovirus			
Type 1	100.0	100.0	0.0 (-3.4, 3.2)
Type 2	100.0	99.2	0.8 (-2.4, 4.6)
Type 3	100.0	100.0	0.0 (-3.2, 3.1)
Hib	100.0	100.0	0.0 (-3.0, 3.0)



Post Dose 4: MMR ®II and Varivax®

Antigen (Units)	PCV20 GM	PCV13 GM	GMR (95% CI)
Measles (AU/mL)	277.74	215.41	1.29 (1.05, 1.58)
Mumps (AU/mL)	36.96	34.19	1.08 (0.85, 1.38)
Rubella (IU/mL)	49.63	40.44	1.23 (1.02, 1.48)
Varicella (mIU/mL)	233.05	234.78	0.99 (0.84, 1.17)

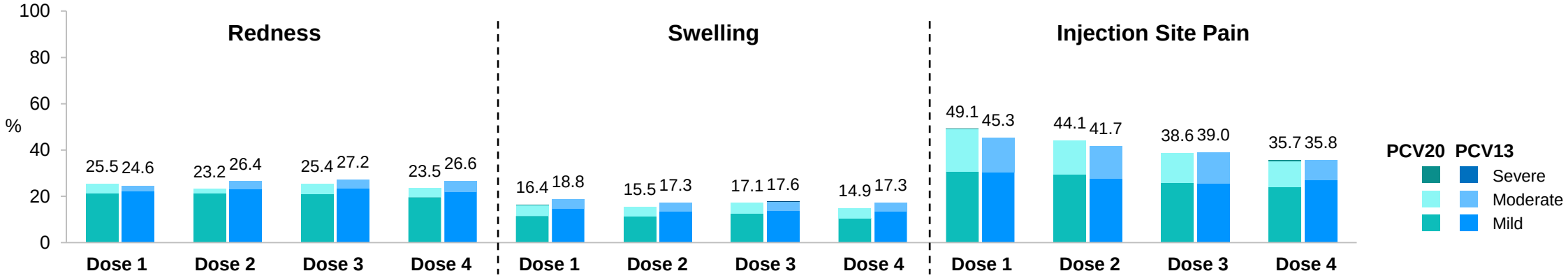


HBsAg = hepatitis B surface antigen; PT = pertussis toxoid, FHA =filamentous hemagglutinin (of *Bordetella pertussis*), PRN = pertactin (of *Bordetella pertussis*)

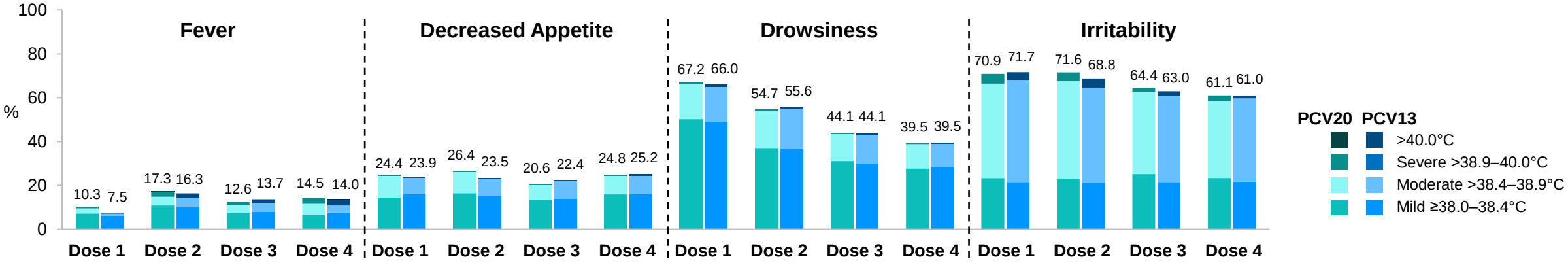
Solicited Reactions within 7 Days of Vaccination

Reactions Were Similar in Rate and Severity Across All 4 Doses

Local Reactions



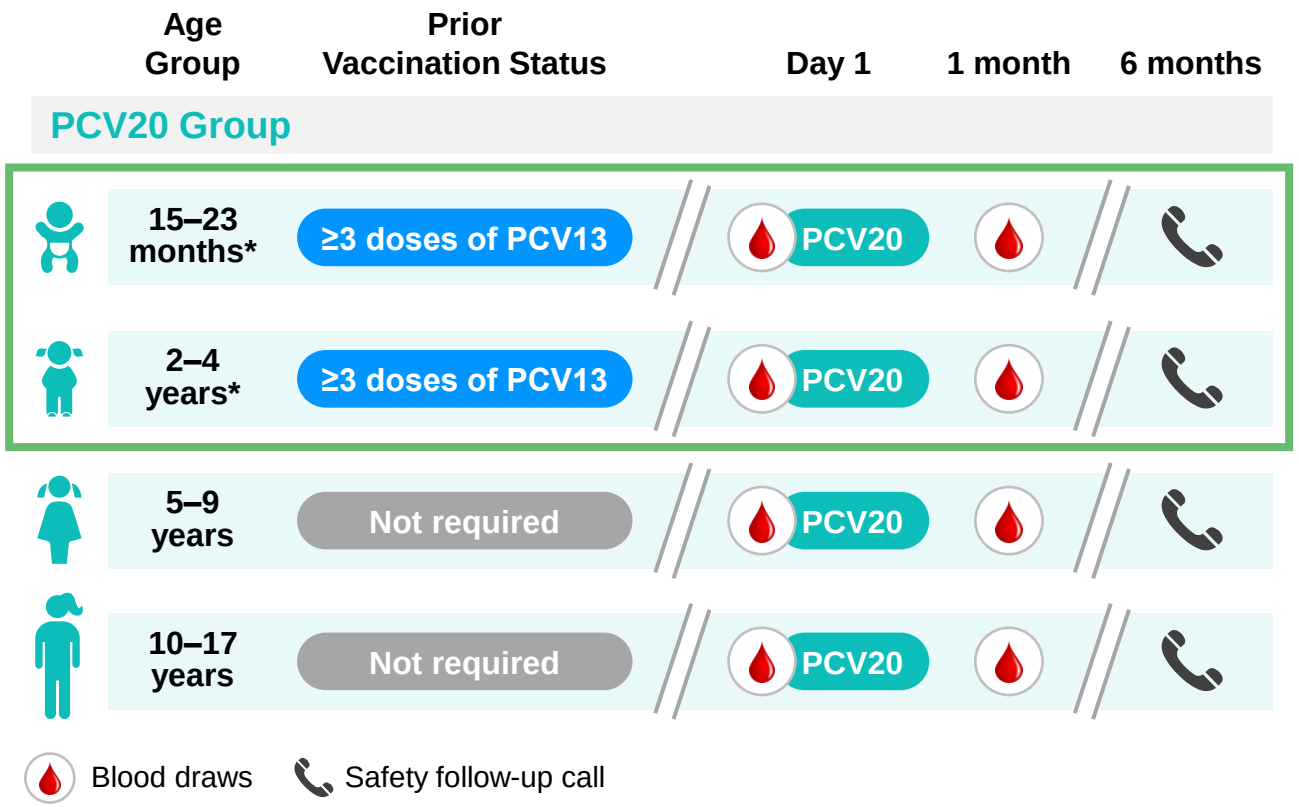
Systemic Reactions



PCV20: Dose 1=993, Dose 2=940, Dose 3=914, Dose 4=826. **PCV13:** Dose 1=974, Dose 2=924, Dose 3=901, Dose 4 =814.

Pediatric Single Dose Study Design and Demographics

Phase 3 Study



Demographic Characteristics – Safety Population

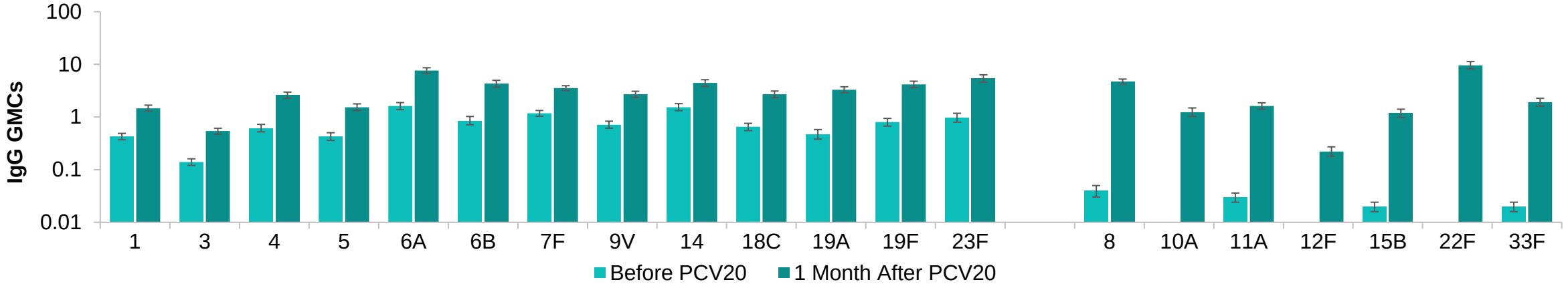
	15–23 mos N†=209	2–4 yrs N†=216	5–9 yrs N†=201	10–17 yrs N†=216
Sex	**n‡ (%)**	**n‡ (%)**	**n‡ (%)**	**n‡ (%)**
Male	117 (56.0)	106 (49.1)	108 (53.7)	115 (56.1)
Race				
White	168 (80.4)	173 (80.1)	174 (86.6)	178 (86.8)
Black or African American	26 (12.4)	26 (12.0)	22 (10.9)	17 (8.3)
Asian	3 (1.4)	0	0	0
American Indian or Alaska Native	0	1 (0.5)	0	0
Native Hawaiian or other Pacific Islander	0	0	0	1 (0.5)
Multiracial	10 (4.8)	13 (6.0)	5 (2.5)	9 (4.4)
Ethnicity				
Hispanic/Latino	35 (16.7)	45 (20.8)	31 (15.4)	43 (21.0)
Non-Hispanic/Latino	172 (82.3)	171 (79.2)	168 (83.6)	161 (78.5)

*Participants <5 years of age had confirmed receipt of >3 prior doses of PCV13.
† N=number of participants in the specified age cohort. This value is the denominator for the percentage calculations. ‡ n=number of participants with the specified characteristic.

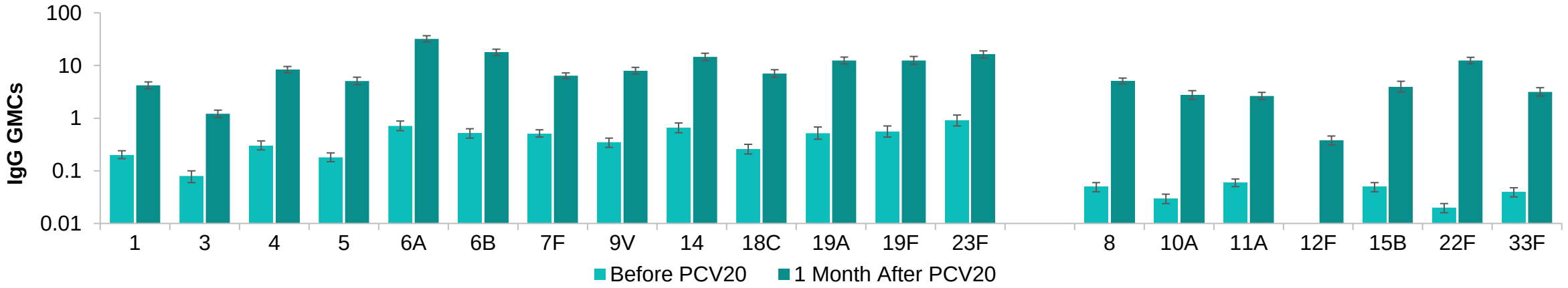
IgG GMC in Children Previously Vaccinated with PCV13

One Dose of PCV20 Elicited Responses to All Vaccine Serotypes

15 to <24 Months



2 to <5 Years



Overall Summary of Adverse Events in the US

PCV20 had no Related Serious Adverse Events or Deaths

	Age < 15 months		15 m - <18 yr
	PCV20 (N=1567)	**PCV13** (N=1376)	**PCV20** (N=831)
AEs	43.8%	46.3%	10.7%
Immediate AEs	0.1–0.2% /dose	0.1% /dose	0%
Related AE	1.1%	1.1%	0.1%
Severe AEs	1.4%	1.1%	0.2%
Serious AEs*	4.5%*	3.7%*	0.6%
Related SAEs	0	0	0
Deaths	0	0	0

*SAEs reported are in all sites, not just US (including Puerto Rico).
B7471003, B7471011, and B7471013 **(all sites)**: (PCV20 N=2232; PCV13 N=1717)

Summary of PCV20 Pediatric

- PCV20 is well tolerated with a safety profile similar to PCV13
- The totality of data shows PCV20 elicits immune responses to all 20 vaccine serotypes
- A single dose of PCV20 elicited a robust immune response to all 20 serotypes and was well tolerated in children 15 months to < 18 years of age, including those with prior PCV13
- PCV20 is compatible with routine pediatric vaccines
- PCV20 is currently under review by the FDA for use in pediatric population 6 weeks to <18 years of age with a target action date in April 2023

PCV20 has the potential to address a substantial burden of pneumococcal disease in children

Questions?