Persistence of Circulating Antibody Through 12 Months Following Vaccination With a 20-Valent Pneumococcal Conjugate Vaccine in Adults 60–64 Years of Age

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BACKGROUND

- *Streptococcus pneumoniae* infection, which causes invasive pneumococcal disease (IPD) as well as less serious conditions, continues to be a major cause of morbidity and mortality worldwide.[1,2]
- Introduction of pneumococcal vaccines such as the 13-valent pneumococcal conjugate vaccine (PCV13) resulted in considerable decreases in pneumococcal disease globally; however, disease due to non-PCV13 serotypes continues to cause substantial disease burden.[3,4]
- To expand serotype coverage beyond PCV13, a 20-valent PCV (PCV20) in development contains the components of PCV13 as well as polysaccharide conjugates for 7 additional serotypes (8, 10A, 11A, 12F, 15B, 22F, 33F).
  - A modeling analysis of adults based on 2017 US surveillance data showed that an additional 9900 IPD cases, 44,000 inpatient pneumonia cases, 52,000 outpatient pneumonia cases, and 4300 deaths were estimated to be caused by the 7 additional PCV20 serotypes.[5]
- In a phase 2 study evaluating PCV20 in adults 60–64 years of age, robust opsonic killing responses were reported for the 20 serotypes contained in PCV20 1 month after vaccination, with a safety profile comparable to other PCVs.[6]
  - The current study extends these results to describe the persistence of circulating antibody 12 months after PCV20.

OBJECTIVE

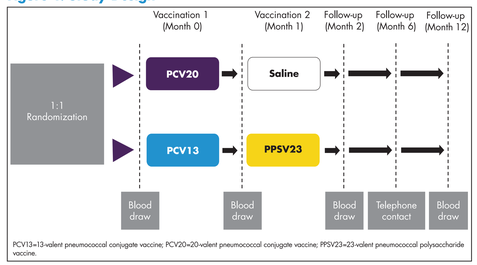
- To describe the immune response 12 months after PCV20 in adults 60–64 years of age

METHODS

Study Design and Subjects

- This was a phase 2, randomized, active-controlled, double-blind study of healthy adults, including those with stable preexisting disease, 60–64 years of age with no prior pneumococcal vaccination (NCT03313037; **Figure 1**).
  - Stable preexisting disease was defined as disease not requiring significant change in therapy or requiring hospitalization within 3 months before vaccine administration.

Figure 1. Study Design



PCV13=13-valent pneumococcal conjugate vaccine; PCV20=20-valent pneumococcal conjugate vaccine; PPSV23=23-valent pneumococcal polysaccharide vaccine.

Immunogenicity Evaluations

- Opsonophagocytic activity (OPA) titers for the PCV20 serotypes were determined in each blood sample collected.

METHODS (continued)

Statistical Analyses

- All analyses were descriptive, and there was no formal hypothesis testing between groups.
- OPA geometric mean titers (GMTs), OPA geometric mean fold rises (GMFRs), and their 95% CIs were obtained by taking the log transformation of titers, calculating the means and the 95% CIs (based on the *t*-distribution), and then exponentiating the means and CIs. OPA GMTs for each time point and GMFRs from before any vaccination (baseline) to 12 months after vaccination were summarized by serotype.
- The percentages of subjects with ≥4-fold rise in OPA titers from baseline to 12 months after vaccination were calculated for each serotype; 2-sided 95% CIs were obtained using the Clopper-Pearson method.

RESULTS

Subject Characteristics

- The study enrolled 222 subjects into the PCV20/saline group and 222 in the PCV13/PPSV23 group.
  - 202 subjects in the PCV20/saline group and 202 subjects in the PCV13/PPSV23 group completed the final study visit 12 months after the initial vaccination.
- Baseline demographics were similar between the vaccine groups **(Table 1)**.

Table 1. Subject Demographics[a]

Demographic	PCV20/Saline (n=210)	PCV13/PPSV23 (n=208)
Women, n (%)	111 (52.9)	126 (60.6)
Age, y[b]		
Mean (SD)	62.0 (1.4)	62.0 (1.4)
Median (range)	62 (60–64)	62 (60–64)
Race, n (%)		
White	164 (78.1)	154 (74.0)
Black or African American	33 (15.7)	43 (20.7)
Asian	7 (3.3)	7 (3.4)
American Indian or Alaskan Native	1 (0.5)	2 (1.0)
Multiracial	4 (1.9)	2 (1.0)
Not reported	1 (0.5)	0
Ethnicity, n (%)		
Hispanic/Latino	26 (12.4)	24 (11.5)
Non-Hispanic/Non-Latino	182 (86.7)	182 (87.5)
Unknown	2 (1.0)	2 (1.0)

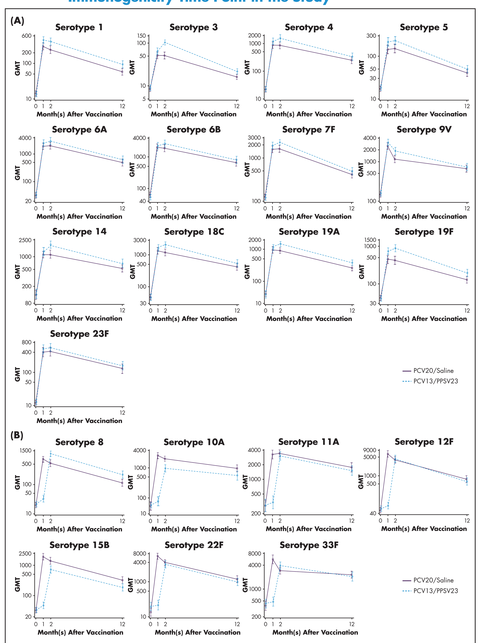
PCV13=13-valent pneumococcal conjugate vaccine; PCV20=20-valent pneumococcal conjugate vaccine; PPSV23=23-valent pneumococcal polysaccharide vaccine.
[a]Data are from the evaluable immunogenicity population, which included any subject who did not meet any exclusion and met all inclusion criteria; received the vaccine as randomized; had blood drawn within 27–49 days after Vaccination 1 or 2; had OPA titers for ≥1 serotype either 1 month after Vaccination 1 or 2; and had no major protocol deviations.
[b]At Vaccination 1.

Immunogenicity

- The OPA GMTs for the 13 serotypes matched to PCV13 (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) in the PCV20/saline group increased from before to 1 month after vaccination, then declined at the 12-month time point but remained elevated above baseline **(Figure 2A)**.
- This same pattern was observed for the OPA GMTs for the 7 additional serotypes **(Figure 2B)**.
- The OPA results for the 20 serotypes in the PCV13/PPSV23 group are also plotted.
  - Differences in the curves between the PCV20/saline group and the PCV13/PPSV23 should be interpreted with caution as 1) the PCV13/PPSV23 subjects received both PCV13 and PPSV23, 2) PCV13 and PPSV23 overlap in composition for 12 serotypes,[7] and 3) PPSV23 was given 1 month after the initial vaccination; therefore, the time point for the 7 additional serotypes is 11 months after PPSV23.
- OPA GMFRs from baseline to 12 months after PCV20 were 1.9–15.0 for the serotypes matched to PCV13, and were 5.6–15.6 for the 7 additional serotypes **(Table 2)**.
- Across all 20 serotypes, 25.1%–70.4% of subjects in the PCV20/saline group achieved ≥4-fold rise in OPA titers above baseline at 12 months after initial vaccination **(Figure 3)**.

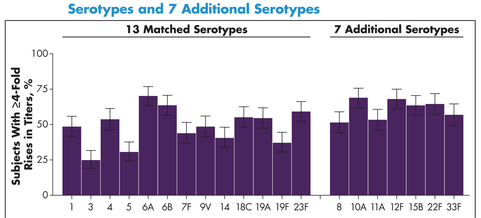
RESULTS (continued)

Figure 2. Pneumococcal OPA GMT Antibody Response Curves for (A) PCV13 Serotypes and (B) 7 Additional Serotypes at Each Immunogenicity Time Point in the Study



GMT=geometric mean titer; LLOQ= lower limit of quantitation; OPA=opsonophagocytic activity; PCV13=13-valent pneumococcal conjugate vaccine; PCV20=20-valent pneumococcal conjugate vaccine; PPSV23=23-valent pneumococcal polysaccharide vaccine.
Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis. The 9V serotype data at 1 month after vaccination are retest data. OPA for the PCV20 serotypes 12 months after vaccination was determined in blood samples obtained at the 12-month follow-up visit, occurring 12 months after PCV20 in the PCV20/saline group, 12 months after PCV13 in the PCV13/PPSV23 group, and 11 months after PPSV23 in the PCV13/PPSV23 group.

Figure 3. Percentages of Subjects With ≥4-Fold Rises in OPA Titers From Baseline to 12 Months After PCV20 for PCV13 Serotypes and 7 Additional Serotypes



LLOQ= lower limit of quantitation; OPA=opsonophagocytic activity; PCV13=13-valent pneumococcal conjugate vaccine; PCV20=20-valent pneumococcal conjugate vaccine.
Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis. OPA for the PCV20 serotypes 12 months after vaccination was determined in blood samples obtained at the 12-month follow-up visit, occurring 12 months after PCV20 in the PCV20/saline group.

Table 2. OPA GMFRs 12 Months After PCV20 Administration Compared With Baseline

Serotype[a]	Time Point[b,c]	Value (95% CI)
13 Matched Serotypes		
1	Baseline OPA GMT	14 (12.4, 16.1)
	12 Month OPA GMT	58 (45.7, 72.6)
	GMFR	**4.1 (3.32, 5.03)**
3	Baseline OPA GMT	8 (7.4, 9.2)
	12 Month OPA GMT	16 (13.9, 18.7)
	GMFR	**1.9 (1.70, 2.24)**
4	Baseline OPA GMT	23 (17.6, 29.3)
	12 Month OPA GMT	225 (163.4, 309.2)
	GMFR	**9.9 (7.17, 13.65)**
5	Baseline OPA GMT	17 (16.0, 18.8)
	12 Month OPA GMT	41 (34.2, 49.2)
	GMFR	**2.4 (1.99, 2.81)**
6A	Baseline OPA GMT	32 (26.9, 38.9)
	12 Month OPA GMT	483 (369.5, 631.8)
	GMFR	**15.0 (11.36, 19.68)**
6B	Baseline OPA GMT	62 (49.1, 78.6)
	12 Month OPA GMT	652 (496.9, 856.1)
	GMFR	**10.5 (8.09, 13.64)**
7F	Baseline OPA GMT	122 (102.2, 145.2)
	12 Month OPA GMT	395 (328.2, 475.4)
	GMFR	**3.2 (2.68, 3.93)**
9V	Baseline OPA GMT	150 (124.2, 181.2)
	12 Month OPA GMT	659 (540.1, 803.5)
	GMFR	**4.4 (3.65, 5.29)**
14	Baseline OPA GMT	119 (91.5, 154.6)
	12 Month OPA GMT	502 (400.5, 629.1)
	GMFR	**4.2 (3.27, 5.45)**
18C	Baseline OPA GMT	49 (38.4, 63.3)
	12 Month OPA GMT	399 (304.3, 522.6)
	GMFR	**8.1 (6.00, 10.91)**
19A	Baseline OPA GMT	40 (31.9, 49.5)
	12 Month OPA GMT	256 (209.1, 313.8)
	GMFR	**6.5 (5.14, 8.10)**
19F	Baseline OPA GMT	38 (33.1, 44.0)
	12 Month OPA GMT	127 (99.8, 160.4)
	GMFR	**3.3 (2.63, 4.17)**
23F	Baseline OPA GMT	12 (10.2, 14.9)
	12 Month OPA GMT	127 (92.2, 175.8)
	GMFR	**10.3 (7.68, 13.92)**
7 Additional Serotypes		
8	Baseline OPA GMT	19 (15.5, 23.8)
	12 Month OPA GMT	108 (83.2, 139.9)
	GMFR	**5.6 (4.22, 7.49)**
10A	Baseline OPA GMT	59 (42.2, 82.1)
	12 Month OPA GMT	917 (691.4, 1215.7)
	GMFR	**15.6 (11.07, 21.92)**
11A	Baseline OPA GMT	273 (205.1, 362.0)
	12 Month OPA GMT	1699 (1350.1, 2138.9)
	GMFR	**6.2 (4.85, 8.02)**
12F	Baseline OPA GMT	53 (42.2, 66.1)
	12 Month OPA GMT	674 (502.6, 903.6)
	GMFR	**12.8 (9.37, 17.37)**
15B	Baseline OPA GMT	31 (26.0, 37.8)
	12 Month OPA GMT	302 (225.4, 406.0)
	GMFR	**9.6 (7.23, 12.88)**
22F	Baseline OPA GMT	108 (78.0, 150.8)
	12 Month OPA GMT	1218 (908.0, 1633.5)
	GMFR	**1.2 (8.20, 15.39)**
33F	Baseline OPA GMT	347 (260.2, 462.4)
	12 Month OPA GMT	2191 (1742.7, 2753.8)
	GMFR	**6.3 (4.78, 8.33)**

GMFR=geometric mean fold rise; GMT=geometric mean titer; LLOQ=lower limit of quantitation; OPA=opsonophagocytic activity; PCV20=20-valent pneumococcal conjugate vaccine.
[a]Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.
[b]GMTs were calculated using all subjects with available data for the specified time point. GMFRs were calculated for all subjects with available data from both before and 12 months after vaccination. OPA for the PCV20 serotypes 12 months after vaccination was determined in blood samples obtained at the 12-month follow-up visit, occurring 12 months after PCV20 in the PCV20/saline group.
[c]GMFR n=165–198.

CONCLUSIONS

- **Increases in circulating antibody induced by PCV20 persisted throughout 12 months after vaccination in healthy adults 60–64 years of age.**
- **For all serotypes included in PCV20, pneumococcal OPA GMTs increased substantially 1 month after vaccination then declined but remained elevated above baseline at 12 months.**
  - A similar pattern was observed in the PCV13 clinical program.
- **The pattern of antibody decline at 12 months after vaccination was also observed in a PCV13 efficacy study conducted in ≥65 year olds,[8] but efficacy against vaccine-type pneumonia did not decline through 4 years of follow-up.[9]**
  - The efficacy data indicate that the unique attributes of conjugate vaccines, including T–cell-mediated responses and induction of immunologic memory,[8] enable these vaccines to induce long-term protection against invasive and noninvasive disease that does not exclusively rely on circulating antibody levels.
- **This and the important immunologic properties of PCVs support the potential of PCV20 to expand serotype coverage and further reduce pneumococcal disease among older adults.**

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FUNDING AND ACKNOWLEDGMENTS

This study was sponsored by Pfizer Inc. Medical writing support was provided by Kate Russin, PhD, of ICON plc (North Wales, PA) and was funded by Pfizer Inc.

DISCLOSURES

D Hurley and C Griffin were investigators on Pfizer Inc–sponsored studies. All other authors are employees or former employees of Pfizer Inc and may hold stock or stock options.

Presented at IDWeek 2020, October 21–25, 2020; Virtual Event