A phase 2, randomized, double-blind study to evaluate the safety, tolerability, and immunogenicity of a 21-valent pneumococcal conjugate vaccine (V116) in adults ≥50 years

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Introduction

Burden of disease due to *S. pneumo* in older adults remains high

- The introduction of pneumococcal conjugate vaccines (PCV) has significantly decreased disease incidence in pediatrics and changed epidemiology in adults
- Major serotypes that cause pneumococcal disease currently differ between adults and children
- Burden of invasive pneumococcal disease (IPD) is currently higher in adults than in children
- **A vaccine including serotypes that are not in any currently licensed vaccines and are associated with higher burden of disease in adults has the potential to significantly reduce adult residual disease burden**

Methods

Figure 1. V116 is an investigational 21-valent PCV with 8 unique serotypes

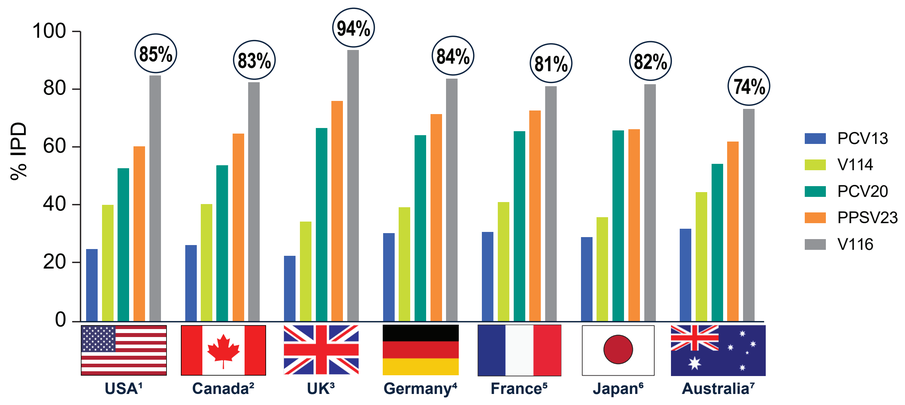
Serotype composition																														
PCV7	4	6B	9V	14	18C	19F	23F																							
PCV13	4	6B	9V	14	18C	19F	23F	1	3	5	6A	7F	19A																	
V114	4	6B	9V	14	18C	19F	23F	1	3	5	6A	7F	19A	22F	33F															
PPSV23	4	6B	9V	14	18C	19F	23F	1	3	5		7F	19A	22F	33F	2	8	9N	10A	11A	12F	15B	17F	20						
PCV20	4	6B	9V	14	18C	19F	23F	1	3	5	6A	7F	19A	22F	33F		8		10A	11A	12F	15B								
V116									3		6A	7F	19A	22F	33F		8	9N	10A	11A	12F		17F	20	15A	15C[a]	16F	23A	23B	24F	31	35B

[a]15C is denoted here to represent the serotype protection proposed with deOAc15B as the molecular structures for deOAc15B and 15C are similar.

- Designed to provide significantly broader disease coverage by targeting residual pneumococcal disease in adults
- Contains 8 unique serotypes not currently in any licensed pneumococcal vaccine

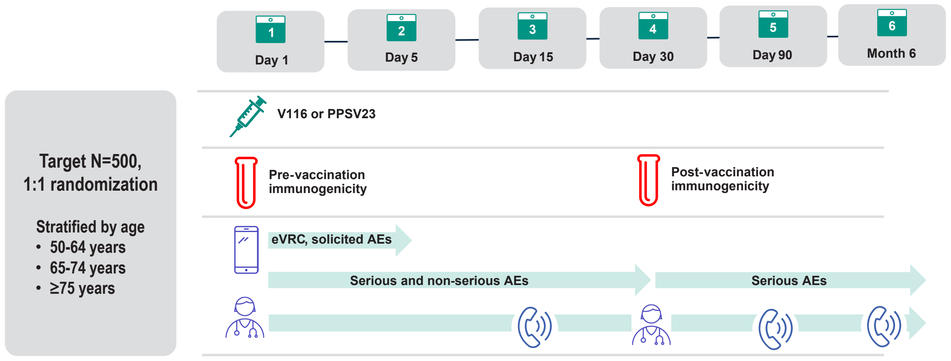
Figure 2. Serotypes in V116 are responsible for 74%-94% of IPD in adults ≥65 years

Invasive pneumococcal disease (IPD) coverage in adults ≥65* by country and vaccine



1. US Centers for Disease Control and Prevention, IPD serotype data 2019, as compiled from data provided through Active Bacterial Core surveillance (ABCs).
2. Canada - National Laboratory Surveillance of Invasive Streptococcal Disease in Canada, Annual Summary 2018. https://www.canada.ca/en/public-health/services/publications/drugs-health-products/national-laboratory-surveillance-invasive-streptococcal-disease-canada-annual-summary-2018.html. Accessed 5/23/2022.
3. UK - PHE Surveillance Report 2017/2018.
4. Germany – data is for ages 60+ years of age; IPD surveillance report by Mark Van der Linden 2018-2019.
5. France – CNRP 2018 report.
6. Japan - Infectious Agents Surveillance Report (IASR) 2018.
7. Australia - Enhanced Invasive Pneumococcal Disease Surveillance Working Group (Communicable Diseases Network Australia), 2018.

Figure 3. V116 Phase 2 study design



- This study enrolled pneumococcal vaccine-naïve adults ≥50 years of age in good general health, with or without stable chronic medical conditions

Figure 4. V116 Phase 2 study objectives

Safety

- Solicited injection-site events (days 1-5): Erythema, swelling, injection-site pain
- Solicited systemic events (days 1-5): Fatigue, myalgia, headache, arthralgia
- Serious vaccine-related events (days 1-180)

Primary immunogenicity

To demonstrate noninferiority of V116 to PPSV23 for the 12 common serotypes
- OPA GMT (day 30): 0.33 noninferiority margin[a]

To demonstrate superiority of V116 to PPSV23 for the 9 unique serotypes
- OPA GMT (day 30): 1.0 superiority margin[a]

[a]Immunogenicity assessments are based on the lower bound of the 2-sided 95% confidence interval.
OPA GMT, opsonophagocytic antibody geometric mean titers.

Results

Table 1. Baseline characteristics

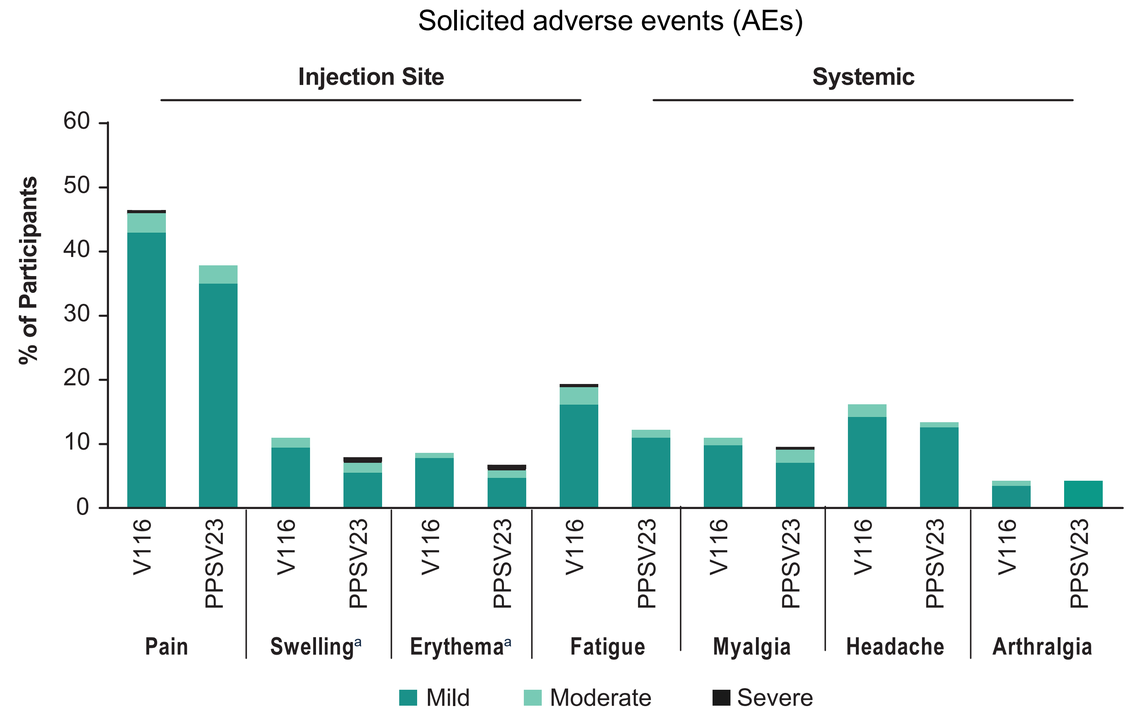
All vaccinated participants	V116 N=254	PPSV23 N=254
Gender		
Female	55.9%	54.7%
Age (years)		
Mean (min to max)	61 (50 to 87)	61 (50 to 88)
50 to 64	71.3%	70.9%
65 to 74	23.2%	23.6%
≥75	5.5%	5.5%
Race		
White	88.2%	85.8%
Black or African American	9.8%	11.8%
Asian	0.8%	1.2%
Other[a]	1.2%	1.2%
Ethnicity		
Hispanic or Latino	42.1%	41.7%

[a]Race category of Other includes American Indian or Alaska Native, Multiple, and Native Hawaiian or Other Pacific Islander.

Table 2. Participant disposition

All randomized participants	V114 N=254	PPSV23 N=256
	n (%)	n (%)
Vaccinated	254 (100)	254 (99.2)
Trial disposition		
Completed	244 (96.1)	247 (96.5)
Discontinued	10 (3.9)	9 (3.5)
Death	1 (0.4)	0 (0.0)
Lost to follow-up	7 (2.8)	5 (2.0)
Withdrawal by participant	2 (0.8)	4 (1.6)

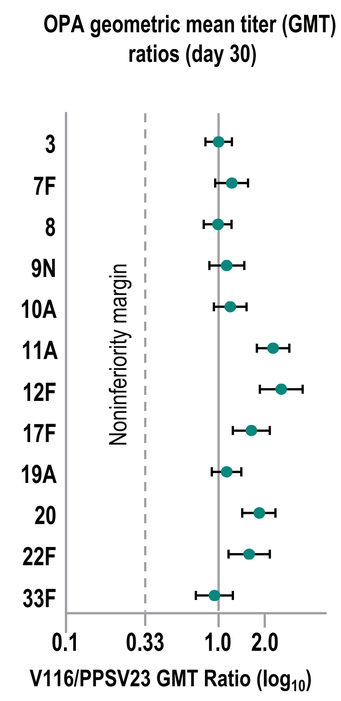
Figure 5. V116 is well tolerated in adults ≥50 years of age with a safety profile generally comparable to PPSV23



[a]For solicited injection-site erythema and injection-site swelling, mild ≥0 to ≤5 cm, moderate ≥5 to ≤10 cm, and severe ≥10 cm.

- 66.5% of V116 and 59.4% of PPSV23 recipients reported ≥1 AE
- No vaccine-related serious adverse events (SAE) were reported
- 1 death occurred in the V116 group due to COVID-19; assessed as not related to vaccine
- Majority of AEs in both groups were mild in severity, and of short duration (≤3 days)

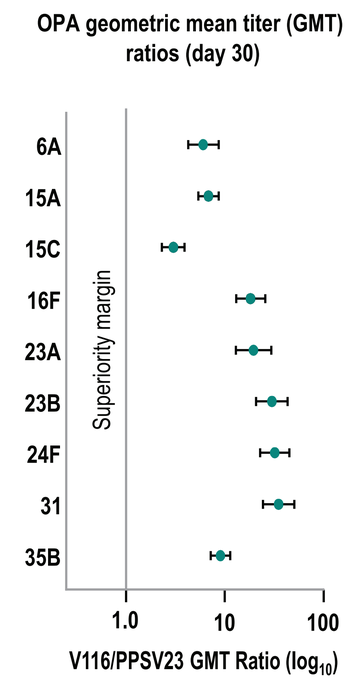
Figure 6. V116 is noninferior to PPSV23 for the 12 common serotypes



Serotype	V116 (n=252) GMT	PPSV23 (n=254) GMT	GMT ratio (95% CI)
3	226.3	226.2	1.00 (0.82, 1.22)
7F	3535.4	2906.8	1.22 (0.95, 1.56)
8	1504.7	1526.8	0.99 (0.80, 1.21)
9N	10327.2	9106.3	1.13 (0.87, 1.47)
10A	6062.2	5092.1	1.19 (0.93, 1.52)
11A	2840.4	1252.3	2.27 (1.78, 2.90)
12F	2549.5	991.1	2.57 (1.86, 3.55)
17F	18394.1	11249.9	1.64 (1.24, 2.16)
19A	2388.1	2116.1	1.13 (0.90, 1.41)
20	9305.3	5068.0	1.84 (1.43, 2.36)
22F	8213.6	5192.2	1.58 (1.16, 2.16)
33F	28129.2	29974.6	0.94 (0.71, 1.24)

OPA, opsonophagocytic antibody.

Figure 7. V116 is noninferior to PPSV23 for the 9 unique serotypes



Serotype	V116 (n=252) GMT	PPSV23 (n=254) GMT	GMT ratio (95% CI)
6A	2757.6	457.0	6.03 (4.23, 8.62)
15A	11640.0	1711.4	6.80 (5.37, 8.62)
15C	12611.8	4200.7	3.00 (2.31, 3.90)
16F	9820.7	539.2	18.21 (12.98, 25.57)
23A	11554.5	593.9	19.45 (12.87, 29.40)
23B	3137.2	105.0	29.88 (20.72, 43.09)
24F	7640.8	238.7	32.02 (22.83, 44.89)
31	4462.0	127.8	34.90 (24.25, 50.23)
35B	15704.7	1745.2	9.00 (7.19, 11.26)

OPA, opsonophagocytic antibody.

Conclusions

In adults ≥50 years of age

- V116 is well tolerated with an overall safety profile generally comparable to PPSV23 and consistent with reported data for licensed PCVs
- OPA GMT responses in the V116 group at day 30 are:
  - Noninferior to PPSV23 for the 12 common serotypes
  - Superior to PPSV23 for the 9 serotypes unique to V116
- The results of this study support the continued development of V116 for the prevention of pneumococcal disease in adults
- **V116 has the potential to address the unmet medical need due to the residual pneumococcal disease burden in adults**

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