A phase 3 study to evaluate the safety, tolerability, and immunogenicity of V116, a pneumococcal conjugate vaccine designed for adults (STRIDE-3)

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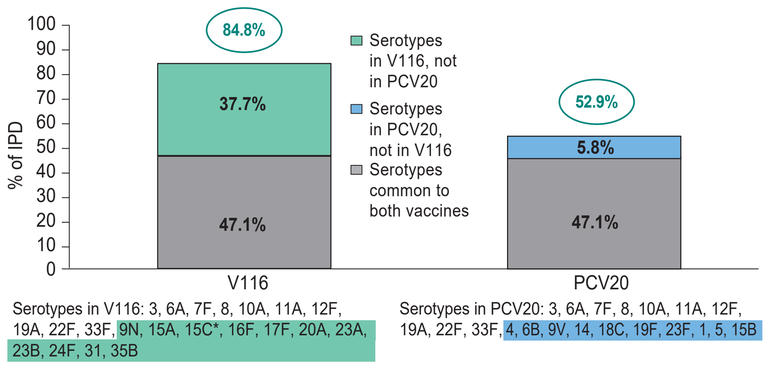
Background

- The introduction of pneumococcal conjugate vaccines (PCV) into pediatric immunization programs resulted in a decrease in the overall incidence of pneumococcal disease[1]
  - Substantial decreases were observed in children under 5 years
  - More modest decreases were seen in adults
- A burden of pneumococcal disease in adults remains, and is currently higher than in children[1]
- V116, a PCV designed specifically for adults:
  - Was developed, in part, based on available global epidemiology data in adults in regions with well-established pediatric vaccination programs
  - Has the potential to significantly reduce residual adult pneumococcal disease

Serotypes in V116 are responsible for the majority of residual invasive pneumococcal disease (IPD) in adults

Figure 1. Percent of IPD coverage in US, 2019, adults aged 65 and older[2]



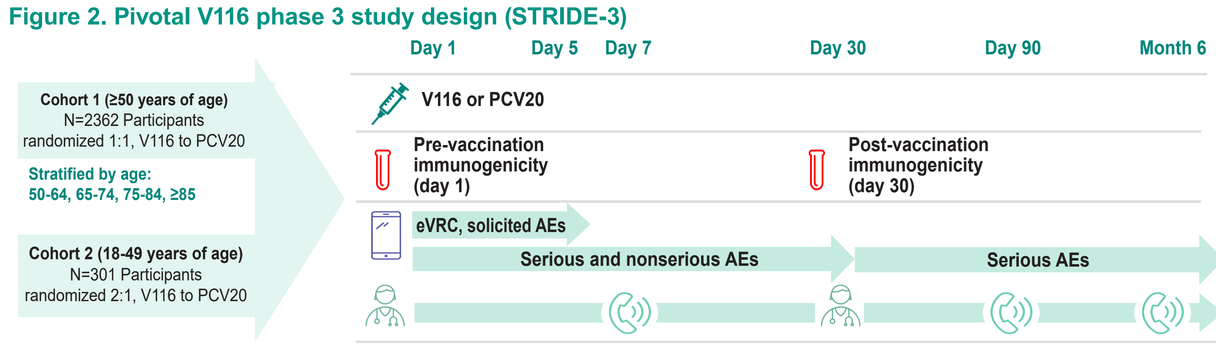
Serotypes in V116: 3, 6A, 7F, 8, 10A, 11A, 12F, 19A, 22F, 33F, 9N, 15A, 15C*, 16F, 17F, 20A, 23A, 23B, 24F, 31, 35B

Serotypes in PCV20: 3, 6A, 7F, 8, 10A, 11A, 12F, 19A, 22F, 33F, 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 15B

*V116 contains deOAc15B pneumococcal polysaccharide, which has a similar molecular structure as 15C (referred to as 15C hereafter); antibodies to 15C are assessed in this study.

Methods

Figure 2. Pivotal V116 phase 3 study design (STRIDE-3)



This global study enrolled pneumococcal vaccine-naïve adults in good general health with or without stable chronic medical conditions

Study objectives and methods

Primary immunogenicity

In adults ≥50 years:

Demonstrate that V116 is noninferior to PCV20 for 10 common serotypes

Lower bound of the 2-sided 95% CI of the OPA GMT ratio (V116/PCV20) to be >0.5[a]

Demonstrate that V116 is superior to PCV20 for 11 unique serotypes

Lower bound of the 2-sided 95% CI of the OPA GMT ratio (V116/PCV20) to be >2.0[a]

2-sided 95% CI of the differences (V116 – PCV20) between the proportions of participants with a ≥4-fold rise to be >10%[b]

In adults 18-49 years:

Demonstrate V116 immunobridges to adults 50-64 years of age for 21 serotypes in V116

Lower bound of the 2-sided 95% CI of the OPA GMT ratio (V116 18-49 years/116 50-64 years) to be >0.5[c]

Primary safety

To evaluate the safety and tolerability of V116 as assessed by the proportion of participants with adverse events (AEs)

Solicited injection-site events days 1-5 postvaccination: erythema, swelling, injection-site pain

Solicited systemic events days 1-5 postvaccination: headache, myalgia, fatigue

Serious vaccine-related events through the duration of participation in the study

OPA GMT, opsonophagocytic antibody geometric mean titers. Immunogenicity analyses were performed using the Per-protocol Population (all randomized participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoints). Safety analyses were conducted using the "All participants as treated" population, which consists of randomized participants who received study intervention.

[a]Prevaccination on day 1 to day 30 postvaccination using the constrained longitudinal data analysis method[3].
[b]Geometric mean fold rise prevaccination on day 1 to day 30, difference calculated using the stratified M&N method[4].
[c]Prevaccination on day 1 to day 30 postvaccination using the longitudinal data analysis method[3].

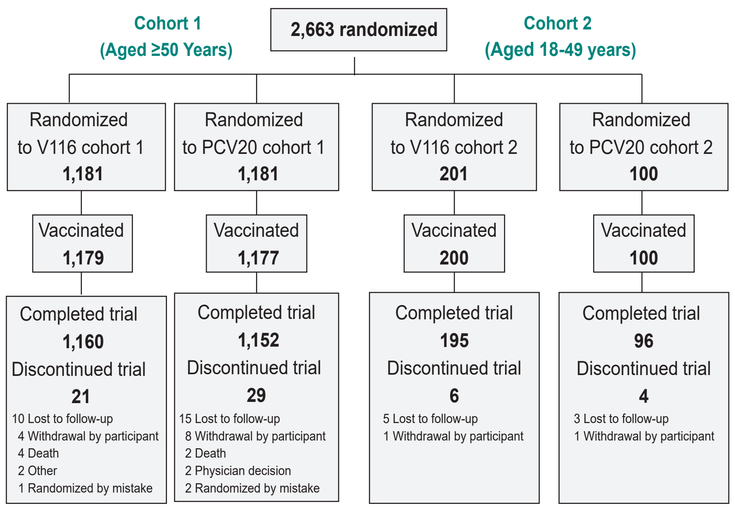
Results

Table 1. Baseline characteristics

	Cohort 1 (aged ≥50 years)		Cohort 2 (aged 18-49 years)	
	V116, N=1,179	PCV20, N=1,177	V116, N=200	PCV20, N=100
Sex				
Female	687 (58.3)	670 (56.9)	137 (68.5)	64 (64.0)
Age (years)				
Median (min to max)	65 (50-91)	65 (50-97)	36 (18-49)	34 (18-49)
18-49, n (%)	0 (0)	0 (0)	200 (100)	100 (100)
50-64, n (%)	589 (50.0)	587 (49.9)	0 (0)	0 (0)
65-74, n (%)	464 (39.4)	464 (39.4)	0 (0)	0 (0)
75-84, n (%)	112 (9.5)	113 (9.6)	0 (0)	0 (0)
≥85, n (%)	14 (1.2)	13 (1.1)	0 (0)	0 (0)
Race				
White	867 (73.5)	844 (71.7)	139 (69.5)	62 (62.0)
Asian	148 (12.6)	168 (14.3)	38 (19.0)	15 (15.0)
Black or African American	116 (9.8)	115 (9.8)	13 (6.5)	14 (14.0)
Multiple	26 (2.2)	30 (2.5)	9 (4.5)	6 (6.0)
Native Hawaiian or Pacific Islander	17 (1.4)	16 (1.4)	1 (0.5)	2 (2.0)
American Indian or Alaskan Native	4 (0.3)	4 (0.3)	0 (0)	1 (1.0)
Ethnicity				
Hispanic or Latino	259 (22.0)	242 (20.6)	58 (29.0)	24 (24.0)
Pneumococcal risk factors				
1 risk factor	347 (29.4)	328 (27.9)	45 (22.5)	18 (18.0)
2 or more risk factors	100 (8.5)	81 (6.9)	3 (1.5)	1 (1.0)

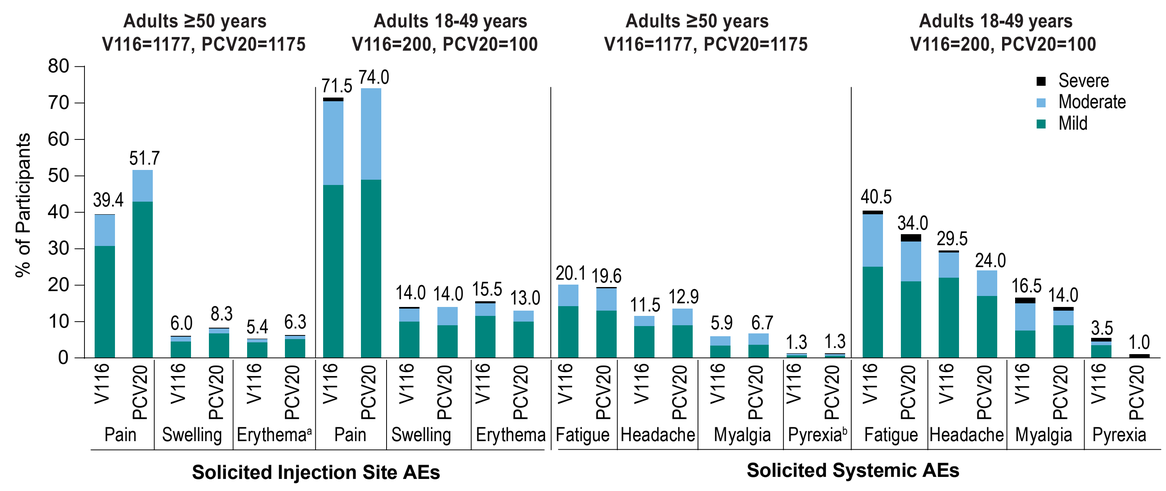
Risk factors include prespecified medical history conditions based on broad category from terms (alcoholism, chronic heart disease, chronic kidney disease, chronic liver disease, chronic lung disease, diabetes, smoking) in MedDRA version 26.0 .Smoking includes only current smokers. One participant data (0.1%) for Race was missing in the V116 Cohort 1 group. All vaccinated participants population.

Figure 3. Participant disposition



Two participants were randomized into the study twice. Each individual received a dose of PCV20 at the first study site and a dose of V116 at the second study site, accounting for 4 allocation numbers. These are reflected as "Discontinued due to other" under V116 cohort 1. These individuals were excluded from the safety population ("All participants as treated") and the per-protocol population.

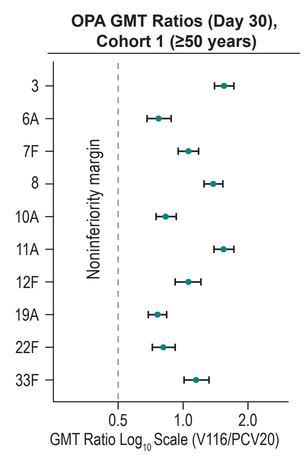
Figure 4. Safety summary



- 61.7% of V116 and 67.2% of PCV20 recipients reported ≥1 AE
- SAEs were low overall (1.5% in V116 and 2.1% in PCV20); none were vaccine related
- There were 6 deaths (all reported in cohort 1, adults ≥50 years); none were related to study treatment

[a]One report of erythema each in the PCV20 and V116 groups, cohort 1, were of unknown intensity.
[b]One report of pyrexia in the V116 group, cohort 2, was reported as grade 4 (life-threatening), but the investigator considered the value to be erroneous based on the clinical assessment of the participant. Body temperature was collected days 1-5; temperature of ≥100.4ºF was classified as pyrexia.

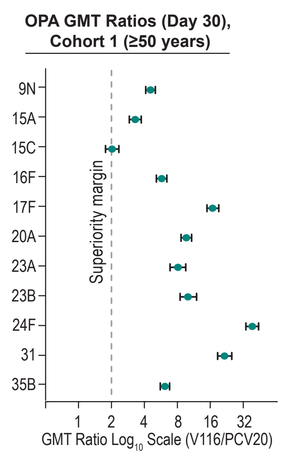
Figure 5. Noninferiority testing for common serotypes; OPA GMT analysis at day 30



Serotype	V116 N=1179 GMT	PCV20 N=1177 GMT	GMT ratio (95% CI)
3	274.0	176.7	1.55 (1.40, 1.72)
6A	2302.0	2972.5	0.77 (0.68, 0.88)
7F	3637.4	3429.9	1.06 (0.95, 1.18)
8	2501.3	1811.1	1.38 (1.25, 1.53)
10A	3893.4	4678.0	0.83 (0.75, 0.93)
11A	3232.6	2092.8	1.54 (1.39, 1.72)
12F	2641.2	2499.6	1.06 (0.92, 1.21)
19A	2136.1	2817.8	0.76 (0.69, 0.84)
22F	3874.5	4770.1	0.81 (0.72, 0.92)
33F	13558.9	11742.1	1.15 (1.01, 1.32)

N=number of participants randomized and vaccinated.

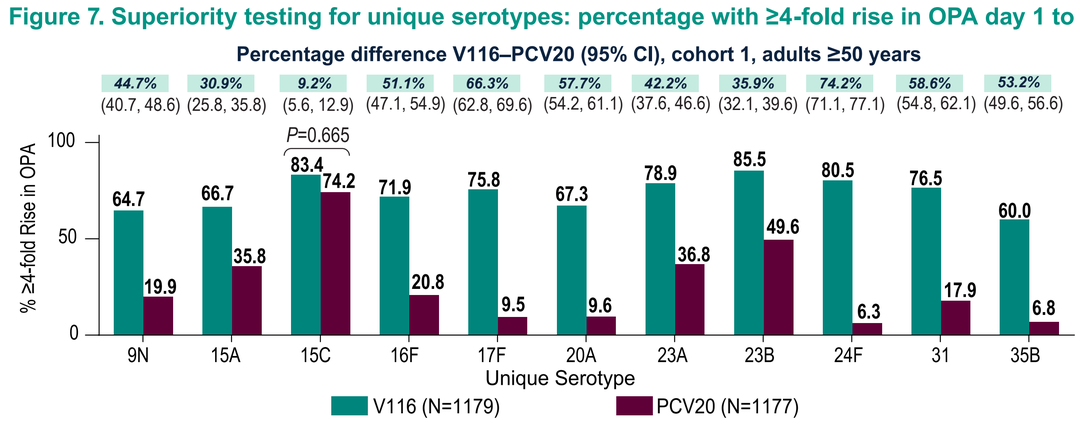
Figure 6. Superiority testing for unique serotypes; OPA GMT analysis at day 30



Serotype	V116 N=1179 GMT	PCV20 N=1177 GMT	GMT ratio (95% CI)
9N	7470.7	1640.4	4.55 (4.12, 5.04)
15A	5237.2	1589.0	3.30 (2.91, 3.74)
15C	4216.2	2072.3	2.03 (1.77, 2.34)
16F	4868.2	846.3	5.75 (5.16, 6.41)
17F	7764.9	460.4	16.86 (14.90, 19.09)
20A	6099.2	631.1	9.66 (8.66, 10.79)
23A	3737.2	461.5	8.10 (6.86, 9.55)
23B	1082.5	107.3	10.09 (8.48, 12.00)
24F	2728.6	70.5	38.71 (33.87, 44.25)
31	3132.5	144.4	21.69 (18.68, 25.18)
35B	8527.8	1383.0	6.17 (5.59, 6.80)

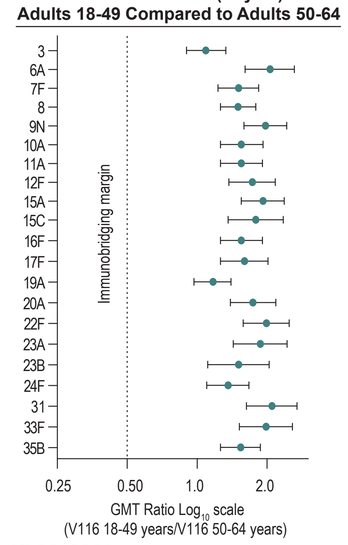
N=number of participants randomized and vaccinated.

Figure 7. Superiority testing for unique serotypes: percentage with ≥4-fold rise in OPA day 1 to day 30



The *P*-values for serotypes 9N, 15A, 16F, 17F, 20A, 23A, 23B, 24F, 31 and 35B were *P*<0.001. N=number of participants randomized and vaccinated.

Figure 8. Immunobridging testing for adults aged 18-49 years compared to ages 50-64 years



Serotype	GMT V116 (18-49 yrs, N=200)	GMT V116 (50-64 yrs, N=589)	GMT ratio (95% CI)
3	308.6	282.7	1.09 (0.90, 1.33)
6A	5289.6	2572.9	2.06 (1.61, 2.62)
7F	6447.2	4278.8	1.51 (1.23, 1.84)
8	4516.0	3004.7	1.50 (1.26, 1.79)
9N	17,283.2	8791.4	1.97 (1.59, 2.43)
10A	6808.1	4382.6	1.55 (1.26, 1.92)
11A	5871.6	3785.8	1.55 (1.26, 1.91)
12F	6150.4	3561.2	1.73 (1.37, 2.17)
15A	11,319.2	5901.2	1.92 (1.55, 2.37)
15C	10,194.0	5708.0	1.79 (1.36, 2.35)
16F	8877.0	5720.0	1.55 (1.26, 1.91)
17F	16,070.6	10,068.0	1.60 (1.26, 2.02)
19A	2773.2	2374.6	1.17 (0.97, 1.40)
20A	13,150.0	7562.7	1.74 (1.39, 2.18)
22F	9299.6	4683.6	1.99 (1.58, 2.49)
23A	8848.7	4739.5	1.87 (1.43, 2.44)
23B	2140.1	1420.9	1.51 (1.11, 2.04)
24F	4137.6	3047.2	1.36 (1.10, 1.67)
31	8005.6	3820.7	2.10 (1.63, 2.69)
33F	34,805.5	17,607.4	1.98 (1.52, 2.57)
35B	13,933.4	9053.9	1.54 (1.26, 1.87)

N=number of participants randomized and vaccinated.

Conclusions

Safety

- V116 is well tolerated with an overall safety profile generally comparable to PCV20 and consistent with reported data for licensed pneumococcal vaccines

Immunogenicity

In adults 50 years of age and older, OPA GMT responses in the V116 group at day 30 are:

- Noninferior to PCV20 for the 10 common serotypes
- Superior to PCV20 for 10 of the 11 serotypes unique to V116 (all except 15C)
  - Assessment of immune responses for serotype 15C in V116 impacted by responses to 15C observed in the PCV20 group, attributed, likely, to cross-reactive immune responses to serotype 15B
  - V116 induced robust functional immune responses to 15C
- V116 immunobridged immune responses in recipients aged 18-49 years compared to aged 50-64 years
- **This pivotal study supports the use of V116 as a novel population-specific PCV for the prevention of PD in adults**

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