2.7.4.7　付録

2.7.4.7.1　海外第Ⅰ／Ⅱ相試験（001試験）

付録 2.7.4-1　有害事象の要約（APaT 集団）（001 試験　第Ⅱ相パート）

Adverse Event Summary
(All Participants as Treated Population)
(Phase 2)

	V116		PPSV23		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	254		254		508	
with one or more adverse events	169	(66.5)	151	(59.4)	320	(63.0)
injection-site	131	(51.6)	104	(40.9)	235	(46.3)
systemic	113	(44.5)	111	(43.7)	224	(44.1)
with no adverse event	85	(33.5)	103	(40.6)	188	(37.0)
with vaccine-related[a] adverse events	157	(61.8)	129	(50.8)	286	(56.3)
injection-site	131	(51.6)	104	(40.9)	235	(46.3)
systemic	87	(34.3)	68	(26.8)	155	(30.5)
with serious adverse events	4	(1.6)	3	(1.2)	7	(1.4)
with serious vaccine-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)
who died	1	(0.4)	0	(0.0)	1	(0.2)

[a] Determined by the investigator to be related to the vaccine.

Nonserious adverse events were collected from Day 1 to Day 30 following vaccination, and serious adverse events were collected from Day 1 through the duration of participation in the study.

All injection site adverse events are considered vaccine related.

Unsolicited adverse events were collected from Day 1 to Day 30 following vaccination.

PPSV23=PNEUMOVAX™23.

Source:　[P001V116: adam-adsl; adaece]

付録 2.7.4-2　事前に規定した注射部位の有害事象（0%超）（APaT 集団）（001 試験　第Ⅱ相パート）

Analysis of Participants With Solicited Injection Site Adverse Events
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Phase 2 - Day 1 to Day 5 Postvaccination)

	V116		PPSV23		Difference in % vs PPSV23
	n	(%)	n	(%)	Estimate (95% CI)[a]
Participants in population	254		254		
with one or more Solicited Injection Site adverse events	130	(51.2)	104	(40.9)	10.2 (1.6, 18.8)
with no Solicited Injection Site adverse events	124	(48.8)	150	(59.1)	-10.2 (-18.8, -1.6)
一般・全身障害および投与部位の状態	**130**	**(51.2)**	**104**	**(40.9)**	**10.2 (1.6, 18.8)**
注射部位紅斑	22	(8.7)	17	(6.7)	2.0 (-2.8, 6.8)
注射部位疼痛	118	(46.5)	96	(37.8)	8.7 (0.1, 17.1)
注射部位腫脹	28	(11.0)	20	(7.9)	3.1 (-2.0, 8.4)

[a] Based on Miettinen & Nurminen method.

Every participant is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

MedDRA version 24.0 was used in the reporting of this study.

PPSV23=PNEUMOVAX™23

Source:　[P001V116: adam-adsl; adaece]

付録 2.7.4-3　事前に規定した全身性の有害事象（0%超）（APaT 集団）
（001 試験　第Ⅱ相パート）

Analysis of Participants With Solicited Systemic Adverse Events
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Phase 2 - Day 1 to Day 5 Postvaccination)

	V116		PPSV23		Difference in % vs PPSV23
	n	(%)	n	(%)	Estimate (95% CI)[a]
Participants in population	254		254		
with one or more Solicited Systemic adverse events	88	(34.6)	75	(29.5)	5.1 (-3.0, 13.2)
with no Solicited Systemic adverse events	166	(65.4)	179	(70.5)	-5.1 (-13.2, 3.0)
一般・全身障害および投与部位の状態	**49**	**(19.3)**	**31**	**(12.2)**	**7.1 (0.8, 13.5)**
疲労	49	(19.3)	31	(12.2)	7.1 (0.8, 13.5)
筋骨格系および結合組織障害	**34**	**(13.4)**	**31**	**(12.2)**	**1.2 (-4.7, 7.1)**
関節痛	11	(4.3)	11	(4.3)	0.0 (-3.8, 3.8)
筋肉痛	28	(11.0)	24	(9.4)	1.6 (-3.8, 7.0)
神経系障害	**43**	**(16.9)**	**34**	**(13.4)**	**3.5 (-2.7, 9.9)**
頭痛	43	(16.9)	34	(13.4)	3.5 (-2.7, 9.9)

[a] Based on Miettinen & Nurminen method.

Every participant is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

MedDRA version 24.0 was used in the reporting of this study.

PPSV23=PNEUMOVAX™23

Source:　[P001V116: adam-adsl; adaece]

2.7.4.7.2　国内第Ⅰ相試験（002試験）

付録 2.7.4-4　試験の内訳（002 試験）

Disposition of Participants
(All Randomized Participants Population)

	pPCV		PPSV23		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	51		51		102	
Trial Disposition						
Completed	51	(100.0)	51	(100.0)	102	(100.0)

Each participant is counted once for Trial Disposition based on the latest corresponding disposition record.
Completed indicates that the participants have completed the study.
pPCV= polyvalent pneumococcal conjugate vaccine; PPSV23=PNEUMOVAX™23.

Source:　[P002V116: adam-adsl]

付録 2.7.4-5 人口統計学的特性（APaT 集団）（002 試験）

Participant Characteristics
(All Randomized Participants Population)

	pPCV		PPSV23		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	51		51		102	
Sex						
Male	23	(45.1)	27	(52.9)	50	(49.0)
Female	28	(54.9)	24	(47.1)	52	(51.0)
Age (Years)						
20 to 29	1	(2.0)	3	(5.9)	4	(3.9)
30 to 39	6	(11.8)	0	(0.0)	6	(5.9)
40 to 49	2	(3.9)	4	(7.8)	6	(5.9)
50 to 59	3	(5.9)	5	(9.8)	8	(7.8)
60 to 64	5	(9.8)	5	(9.8)	10	(9.8)
>= 65	34	(66.7)	34	(66.7)	68	(66.7)
Mean	63.1		64.0		63.6	
SD	13.7		12.7		13.2	
Median	66.0		66.0		66.0	
Range	29 to 83		27 to 82		27 to 83	
Race						
Asian	51	(100.0)	51	(100.0)	102	(100.0)
Ethnicity						
Not Hispanic Or Latino	51	(100.0)	51	(100.0)	102	(100.0)

pPCV= polyvalent pneumococcal conjugate vaccine; PPSV23=PNEUMOVAX™23. SD=Standard Deviation.

Source: [P002V116: adam-adsl]

付録 2.7.4-6　重症度別の有害事象（0%超）（APaT 集団）（002 試験）

Participants With Adverse Events by Maximum Intensity
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)

	Intensity Grading	pPCV		PPSV23		Total	
		n	(%)	n	(%)	n	(%)
Participants in population with follow-up		51		51		102	
with one or more adverse events	Total	34	(66.7)	35	(68.6)	69	(67.6)
	Mild	26	(51.0)	29	(56.9)	55	(53.9)
	Moderate	8	(15.7)	6	(11.8)	14	(13.7)
胃腸障害							
腹部不快感	Total	0	(0.0)	1	(2.0)	1	(1.0)
	Moderate	0	(0.0)	1	(2.0)	1	(1.0)
腹痛	Total	0	(0.0)	1	(2.0)	1	(1.0)
	Mild	0	(0.0)	1	(2.0)	1	(1.0)
口内炎	Total	1	(2.0)	0	(0.0)	1	(1.0)
	Mild	1	(2.0)	0	(0.0)	1	(1.0)
一般・全身障害および投与部位の状態							
疲労[a]	Total	7	(13.7)	5	(9.8)	12	(11.8)
	Mild	7	(13.7)	4	(7.8)	11	(10.8)
	Moderate	0	(0.0)	1	(2.0)	1	(1.0)
注射部位内出血	Total	1	(2.0)	1	(2.0)	2	(2.0)
	Mild	1	(2.0)	1	(2.0)	2	(2.0)
注射部位紅斑[a]	Total	4	(7.8)	0	(0.0)	4	(3.9)
	Mild	3	(5.9)	0	(0.0)	3	(2.9)
	Moderate	1	(2.0)	0	(0.0)	1	(1.0)
注射部位知覚低下	Total	1	(2.0)	0	(0.0)	1	(1.0)
	Moderate	1	(2.0)	0	(0.0)	1	(1.0)

Participants With Adverse Events by Maximum Intensity
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)

	Intensity Grading	pPCV		PPSV23		Total	
		n	(%)	n	(%)	n	(%)
注射部位疼痛[a]	Total	30	(58.8)	34	(66.7)	64	(62.7)
	Mild	23	(45.1)	31	(60.8)	54	(52.9)
	Moderate	7	(13.7)	3	(5.9)	10	(9.8)
注射部位そう痒感	Total	2	(3.9)	0	(0.0)	2	(2.0)
	Mild	2	(3.9)	0	(0.0)	2	(2.0)
注射部位腫脹[a]	Total	2	(3.9)	0	(0.0)	2	(2.0)
	Mild	2	(3.9)	0	(0.0)	2	(2.0)
発熱	Total	1	(2.0)	3	(5.9)	4	(3.9)
	Mild	0	(0.0)	2	(3.9)	2	(2.0)
	Moderate	1	(2.0)	1	(2.0)	2	(2.0)
感染症および寄生虫症							
上咽頭炎	Total	1	(2.0)	1	(2.0)	2	(2.0)
	Mild	1	(2.0)	1	(2.0)	2	(2.0)
筋骨格系および結合組織障害							
関節痛[a]	Total	2	(3.9)	2	(3.9)	4	(3.9)
	Mild	2	(3.9)	1	(2.0)	3	(2.9)
	Moderate	0	(0.0)	1	(2.0)	1	(1.0)
関節可動域低下	Total	0	(0.0)	1	(2.0)	1	(1.0)
	Moderate	0	(0.0)	1	(2.0)	1	(1.0)
四肢不快感	Total	0	(0.0)	1	(2.0)	1	(1.0)
	Mild	0	(0.0)	1	(2.0)	1	(1.0)
筋肉痛[a]	Total	9	(17.6)	10	(19.6)	19	(18.6)
	Mild	9	(17.6)	8	(15.7)	17	(16.7)
	Moderate	0	(0.0)	2	(3.9)	2	(2.0)

Participants With Adverse Events by Maximum Intensity
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)

	Intensity Grading	pPCV		PPSV23		Total	
		n	(%)	n	(%)	n	(%)
四肢痛	Total	1	(2.0)	1	(2.0)	2	(2.0)
	Moderate	1	(2.0)	1	(2.0)	2	(2.0)
神経系障害							
Headache[a]	Total	6	(11.8)	5	(9.8)	11	(10.8)
	Mild	6	(11.8)	5	(9.8)	11	(10.8)
感覚鈍麻	Total	1	(2.0)	0	(0.0)	1	(1.0)
	Mild	1	(2.0)	0	(0.0)	1	(1.0)
感覚障害	Total	1	(2.0)	0	(0.0)	1	(1.0)
	Mild	1	(2.0)	0	(0.0)	1	(1.0)
味覚障害	Total	1	(2.0)	0	(0.0)	1	(1.0)
	Mild	1	(2.0)	0	(0.0)	1	(1.0)
血管障害							
内出血	Total	0	(0.0)	2	(3.9)	2	(2.0)

Participants With Adverse Events by Maximum Intensity
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)

	Intensity Grading	pPCV		PPSV23		Total	
		n	(%)	n	(%)	n	(%)
内出血	Mild	0	(0.0)	2	(3.9)	2	(2.0)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the highest non-missing intensity grading.

A participant with multiple adverse events within a system organ class is counted a single time for that system organ class.

[a] Solicited adverse events were collected from Day 1 to Day 5 following vaccination but may have been reported spontaneously after Day 5.

Non-solicited adverse events were collected from Day 1 to Day 30 following vaccination.

Injection site erythema and injection site swelling occurring from Day 1 to Day 5 postvaccination are not included in this table as these events were graded by size and are displayed in a separate summary.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the incidence specified in the report title.

MedDRA version 24.0 was used in the reporting of this study.

pPCV= polyvalent pneumococcal conjugate vaccine; PPSV23=PNEUMOVAX™23.

Source: [P002V116: adam-adsl; adae]

付録 2.7.4-7　サイズ別の事前に規定した注射部位紅斑及び注射部位腫脹（0%超）（APaT 集団）（002 試験）

Participants With Solicited Injection Site Erythema or Injection Site Swelling by Maximum Size
(Incidence >0 % in One or More Vaccination Groups)
(All Participants as Treated Population)
(Day 1 to Day 5 Postvaccination)

	Size Rating (centimeters)	pPCV		PPSV23		Total	
		n	(%)	n	(%)	n	(%)
Participants in population with follow-up		51		51		102	
注射部位紅斑	Total	5	(9.8)	5	(9.8)	10	(9.8)
	0 to ≤2.4	4	(7.8)	2	(3.9)	6	(5.9)
	>2.4 to ≤5.0	1	(2.0)	1	(2.0)	2	(2.0)
	>5.0 to ≤7.4	0	(0.0)	2	(3.9)	2	(2.0)
注射部位腫脹	Total	7	(13.7)	7	(13.7)	14	(13.7)
	0 to ≤2.4	4	(7.8)	6	(11.8)	10	(9.8)
	>2.4 to ≤5.0	1	(2.0)	0	(0.0)	1	(1.0)
	>5.0 to ≤7.4	2	(3.9)	0	(0.0)	2	(2.0)
	>7.4 to ≤10.0	0	(0.0)	1	(2.0)	1	(1.0)

Every participant is counted a single time for each applicable specific injection site adverse event, and is classified according to the highest non-missing size rating.
pPCV= polyvalent pneumococcal conjugate vaccine; PPSV23=PNEUMOVAX™23.

Source:　[P002V116: adam-adsl; adae; adex]

付録 2.7.4-8 持続期間別の事前に規定した有害事象（0%超）（APaT 集団）（002 試験）

Participants With Solicited Adverse Events by Maximum Duration
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Day 1 to Day 5 Postvaccination)

	Maximum Duration[a]	pPCV		PPSV23	
		n	(%)	n	(%)
Participants in population		51		51	
With one or more solicited adverse events	Total	30	(58.8)	35	(68.6)
	≤3 days	23	(45.1)	27	(52.9)
	>3 days and ≤5 days	4	(7.8)	6	(11.8)
	>5 days and ≤10 days	3	(5.9)	2	(3.9)
Solicited injection site adverse events					
注射部位紅斑[a]	Total	5	(9.8)	5	(9.8)
	≤3 days	3	(5.9)	3	(5.9)
	>3 days and ≤5 days	0	(0.0)	1	(2.0)
	>5 days and ≤10 days	2	(3.9)	1	(2.0)
注射部位疼痛[a]	Total	28	(54.9)	34	(66.7)
	≤3 days	22	(43.1)	29	(56.9)
	>3 days and ≤5 days	6	(11.8)	4	(7.8)
	>5 days and ≤10 days	0	(0.0)	1	(2.0)
注射部位腫脹[a]	Total	7	(13.7)	7	(13.7)
	≤3 days	5	(9.8)	5	(9.8)
	>3 days and ≤5 days	1	(2.0)	2	(3.9)
	>5 days and ≤10 days	1	(2.0)	0	(0.0)
Solicited systemic adverse events					
関節痛[a]	Total	2	(3.9)	2	(3.9)
	≤3 days	2	(3.9)	1	(2.0)
	>3 days and ≤5 days	0	(0.0)	1	(2.0)
疲労[a]	Total	7	(13.7)	5	(9.8)
	≤3 days	7	(13.7)	4	(7.8)
	>3 days and ≤5 days	0	(0.0)	1	(2.0)

Participants With Solicited Adverse Events by Maximum Duration
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Day 1 to Day 5 Postvaccination)

	Maximum Duration[a]	pPCV		PPSV23	
		n	(%)	n	(%)
頭痛[a]	Total	5	(9.8)	5	(9.8)
	≤3 days	4	(7.8)	5	(9.8)
	>5 days and ≤10 days	1	(2.0)	0	(0.0)
筋肉痛[a]	Total	9	(17.6)	10	(19.6)
	≤3 days	9	(17.6)	9	(17.6)
	>3 days and ≤5 days	0	(0.0)	1	(2.0)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the longest duration.

[a] These events were solicited from Day 1 to Day 5 following vaccination.

MedDRA version 24.0 was used in the reporting of this study.

pPCV= polyvalent pneumococcal conjugate vaccine; PPSV23=PNEUMOVAX™23.

Source: [P002V116: adam-adsl; adae]

2.7.4.7.3　海外第Ⅲ相試験（003試験）

付録 2.7.4-9　試験の内訳（APaT 集団）（003 試験　コホート 1 及びコホート 2）

Disposition of Participants
(All Randomized Participants)
(Cohort 1 and Cohort 2)

	V116		PCV20		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	1,382		1,281		2,663	
Vaccinated at Visit 1						
V116	1,379	(99.8)	0	(0.0)	1,379	(51.8)
PCV20	0	(0.0)	1,277	(99.7)	1,277	(48.0)
Trial Disposition						
Completed	1,355	(98.0)	1,248	(97.4)	2,603	(97.7)
Discontinued	27	(2.0)	33	(2.6)	60	(2.3)
Death	4	(0.3)	2	(0.2)	6	(0.2)
Lost To Follow-Up	15	(1.1)	18	(1.4)	33	(1.2)
Physician Decision	0	(0.0)	2	(0.2)	2	(0.1)
Randomized By Mistake Without Study Treatment	1	(0.1)	2	(0.2)	3	(0.1)
Withdrawal By Subject	5	(0.4)	9	(0.7)	14	(0.5)
Other	2	(0.1)	0	(0.0)	2	(0.1)

Each participant is counted once for Trial Disposition based on the latest corresponding disposition record.
PCV20=pneumococcal 20-valent conjugate vaccine.

Source:　[P003V116: adam-adsl; adex]

付録 2.7.4-10 人口統計学的特性（APaT 集団）（003 試験　コホート 1 及びコホート 2）

Participant Characteristics
(All Vaccinated Participants)
(Cohort 1 and Cohort 2)

	V116		PCV20		Total	
	n	(%)	n	(%)	n	(%)
Participants in population	1,379		1,277		2,656	
Sex						
Male	555	(40.2)	543	(42.5)	1,098	(41.3)
Female	824	(59.8)	734	(57.5)	1,558	(58.7)
Age (Years)						
18 to 49	200	(14.5)	100	(7.8)	300	(11.3)
50 to 64	589	(42.7)	587	(46.0)	1,176	(44.3)
65 to 74	464	(33.6)	464	(36.3)	928	(34.9)
75 to 84	112	(8.1)	113	(8.8)	225	(8.5)
≥85	14	(1.0)	13	(1.0)	27	(1.0)
Mean	59.7		61.6		60.7	
SD	13.2		11.5		12.4	
Median	62.0		63.0		63.0	
Range	18 to 91		18 to 97		18 to 97	
Race						
American Indian Or Alaska Native	4	(0.3)	5	(0.4)	9	(0.3)
Asian	186	(13.5)	183	(14.3)	369	(13.9)
Black Or African American	129	(9.4)	129	(10.1)	258	(9.7)
Multiple	35	(2.5)	36	(2.8)	71	(2.7)
Native Hawaiian Or Other Pacific Islander	18	(1.3)	18	(1.4)	36	(1.4)
White	1,006	(73.0)	906	(70.9)	1,912	(72.0)
Missing	1	(0.1)	0	(0.0)	1	(0.0)
Ethnicity						
Hispanic Or Latino	317	(23.0)	266	(20.8)	583	(22.0)
Not Hispanic Or Latino	1,050	(76.1)	998	(78.2)	2,048	(77.1)
Not Reported	8	(0.6)	10	(0.8)	18	(0.7)
Unknown	4	(0.3)	3	(0.2)	7	(0.3)
Country						
Australia	49	(3.6)	46	(3.6)	95	(3.6)
Belgium	84	(6.1)	71	(5.6)	155	(5.8)
Chile	76	(5.5)	59	(4.6)	135	(5.1)

Participant Characteristics
(All Vaccinated Participants)
(Cohort 1 and Cohort 2)

	V116		PCV20		Total	
	n	(%)	n	(%)	n	(%)
Germany	48	(3.5)	31	(2.4)	79	(3.0)
New Zealand	134	(9.7)	156	(12.2)	290	(10.9)
Puerto Rico	75	(5.4)	80	(6.3)	155	(5.8)
South Korea	101	(7.3)	99	(7.8)	200	(7.5)
Sweden	60	(4.4)	50	(3.9)	110	(4.1)
Taiwan	65	(4.7)	58	(4.5)	123	(4.6)
Turkey	26	(1.9)	28	(2.2)	54	(2.0)
United States	661	(47.9)	599	(46.9)	1,260	(47.4)

PCV20=pneumococcal 20-valent conjugate vaccine; SD=standard deviation.

Source:　[P003V116: adam-adsl]

付録 2.7.4-11 有害事象の要約（APaT 集団）（003 試験　コホート 2）

Adverse Event Summary
(All Participants as Treated Population)
(Cohort 2)

	V116		PCV20	
	n	(%)	n	(%)
Participants in population	200		100	
with one or more adverse events	164	(82.0)	79	(79.0)
injection-site	146	(73.0)	75	(75.0)
systemic	118	(59.0)	50	(50.0)
with no adverse event	36	(18.0)	21	(21.0)
with vaccine-related[a] adverse events	159	(79.5)	78	(78.0)
injection-site	146	(73.0)	75	(75.0)
systemic	102	(51.0)	42	(42.0)
with serious adverse events	1	(0.5)	3	(3.0)
with serious vaccine-related adverse events	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)

[a] Determined by the investigator to be related to the vaccine. All injection site adverse events and pyrexia (defined as maximum temperature ≥ 100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination) are considered to be vaccine-related.

Reported adverse events include nonserious adverse events within 30 days of vaccination and serious adverse events occurring Day 1 through the duration of participation in the study.

PCV20=pneumococcal 20-valent conjugate vaccine.

Source:　[P003V116: adam-adsl; adaece]

付録 2.7.4-12 事前に規定した有害事象（0%超）（003 試験　コホート 2）

Analysis of Participants With Solicited Adverse Events
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 2)

	V116		PCV20		Difference in % vs PCV20
	n	(%)	n	(%)	Estimate (95% CI)[a]
Participants in population	200		100		
with one or more solicited adverse events	161	(80.5)	78	(78.0)	
with no solicited adverse events	39	(19.5)	22	(22.0)	
Solicited injection site adverse event	**144**	**(72.0)**	**75**	**(75.0)**	
注射部位紅斑	31	(15.5)	13	(13.0)	2.5 (-6.6, 10.3)
注射部位疼痛	143	(71.5)	74	(74.0)	-2.5 (-12.7, 8.6)
注射部位腫脹	28	(14.0)	14	(14.0)	0.0 (-9.2, 7.9)
Solicited systemic adverse event	**107**	**(53.5)**	**44**	**(44.0)**	
疲労	81	(40.5)	34	(34.0)	6.5 (-5.3, 17.6)
頭痛	59	(29.5)	24	(24.0)	5.5 (-5.5, 15.5)
筋肉痛	33	(16.5)	14	(14.0)	2.5 (-6.8, 10.6)
発熱	7	(3.5)	1	(1.0)	2.5 (-2.2, 6.2)

[a] Estimated differences and CIs are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Every participant is counted a single time for each applicable row and column.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination. Pyrexia was defined as maximum temperature ≥ 100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination.

MedDRA version 26.0 was used in the reporting of this study.

CI=confidence interval; PCV20=pneumococcal 20-valent conjugate vaccine.

Source:　[P003V116: adam-adsl; adaece]

付録 2.7.4-13 重症度別の事前に規定した有害事象（0%超）（APaT 集団）（003 試験　コホート 1）

Participants With Solicited Adverse Events by Maximum Intensity Grade (Incidence > 0% in One or More Vaccination Groups) (All Participants as Treated Population) (Cohort 1)

	Intensity Grade	V116		PCV20	
		n	(%)	n	(%)
Participants in population		1,177		1,175	
with one or more solicited adverse events	Total	600	(51.0)	708	(60.3)
	Mild (Grade 1)	415	(35.3)	524	(44.6)
	Moderate (Grade 2)	178	(15.1)	172	(14.6)
	Severe (Grade 3)	6	(0.5)	12	(1.0)
	Potentially Life-threatening (Grade 4)	1	(0.1)	0	(0.0)
Solicited injection site adverse event					
注射部位紅斑	Total	64	(5.4)	74	(6.3)
	Mild (Grade 1)	51	(4.3)	59	(5.0)
	Moderate (Grade 2)	10	(0.8)	12	(1.0)
	Severe (Grade 3)	2	(0.2)	2	(0.2)
	Unknown	1	(0.1)	1	(0.1)
注射部位疼痛	Total	464	(39.4)	607	(51.7)
	Mild (Grade 1)	361	(30.7)	504	(42.9)
	Moderate (Grade 2)	102	(8.7)	102	(8.7)
	Severe (Grade 3)	1	(0.1)	1	(0.1)
注射部位腫脹	Total	71	(6.0)	98	(8.3)
	Mild (Grade 1)	53	(4.5)	79	(6.7)
	Moderate (Grade 2)	15	(1.3)	17	(1.4)
	Severe (Grade 3)	3	(0.3)	2	(0.2)
Solicited systemic adverse event					
疲労	Total	237	(20.1)	230	(19.6)
	Mild (Grade 1)	167	(14.2)	153	(13.0)
	Moderate (Grade 2)	70	(5.9)	72	(6.1)
	Severe (Grade 3)	0	(0.0)	5	(0.4)
頭痛	Total	135	(11.5)	152	(12.9)

Participants With Solicited Adverse Events by Maximum Intensity Grade
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 1)

	Intensity Grade	V116		PCV20	
		n	(%)	n	(%)
頭痛	Mild (Grade 1)	102	(8.7)	106	(9.0)
	Moderate (Grade 2)	33	(2.8)	45	(3.8)
	Severe (Grade 3)	0	(0.0)	1	(0.1)
筋肉痛	Total	70	(5.9)	79	(6.7)
	Mild (Grade 1)	40	(3.4)	42	(3.6)
	Moderate (Grade 2)	30	(2.5)	36	(3.1)
	Severe (Grade 3)	0	(0.0)	1	(0.1)
発熱	Total	15	(1.3)	15	(1.3)
	Mild (Grade 1)	7	(0.6)	7	(0.6)
	Moderate (Grade 2)	6	(0.5)	5	(0.4)
	Severe (Grade 3)	1	(0.1)	3	(0.3)
	Potentially Life-threatening (Grade 4)	1	(0.1)	0	(0.0)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the highest non-missing intensity grading.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 to Day 5 postvaccination. Pyrexia was defined as maximum temperature ≥ 100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination.

Injection site erythema and injection site swelling from Day 1 through Day 5 postvaccination are graded according to size and presented as intensity grade as follows: 0 to ≤5.0 cm=Mild; >5.0 to ≤10.0 cm=Moderate; >10.0 cm=Severe.

Pyrexia from Day 1 through Day 5 postvaccination is graded according to maximum temperature and presented as intensity grade as follows: 38.0°C (100.4°F) to <38.5°C (101.3°F)=Mild; 38.5°C (101.3°F) to <39.0°C (102.2°F)=Moderate; 39.0 °C (102.2°F) to <40.0°C (104.0°F)=Severe; ≥40.0°C (104.0°F)=Potentially Life-threatening.

Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.

MedDRA version 26.0 was used in the reporting of this study.

PCV20=pneumococcal 20-valent conjugate vaccine.

Source: [P003V116: adam-adsl; adaece]

付録 2.7.4-14 サイズ別の事前に規定した注射部位紅斑及び注射部位腫脹（0%超）（APaT 集団）（003 試験　コホート 1）

Participants With Solicited Injection Site Erythema or Injection Site Swelling by Maximum Size
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 1)

	Size (cm), Intensity Grade	V116		PCV20	
		n	(%)	n	(%)
Participants in population		1177		1175	
注射部位紅斑	Total	64	(5.4)	74	(6.3)
	0 to ≤2.4, Mild (Grade 1)	34	(2.9)	35	(3.0)
	>2.4 to ≤5.0, Mild (Grade 1)	12	(1.0)	16	(1.4)
	>5.0 to ≤7.4, Moderate (Grade 2)	3	(0.3)	8	(0.7)
	>7.4 to ≤10.0, Moderate (Grade 2)	7	(0.6)	4	(0.3)
	>10.0, Severe (Grade 3)	2	(0.2)	2	(0.2)
	Unknown	6	(0.5)	9	(0.8)
注射部位腫脹	Total	71	(6.0)	98	(8.3)
	0 to ≤2.4, Mild (Grade 1)	40	(3.4)	42	(3.6)
	>2.4 to ≤5.0, Mild (Grade 1)	10	(0.8)	29	(2.5)
	>5.0 to ≤7.4, Moderate (Grade 2)	9	(0.8)	12	(1.0)
	>7.4 to ≤10.0, Moderate (Grade 2)	6	(0.5)	5	(0.4)
	>10.0, Severe (Grade 3)	3	(0.3)	2	(0.2)

Participants With Solicited Injection Site Erythema or Injection Site Swelling by Maximum Size
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 1)

	Size (cm), Intensity Grade	V116		PCV20	
		n	(%)	n	(%)
	Unknown	3	(0.3)	8	(0.7)

Every participant is counted a single time for each applicable specific injection site adverse event, and is classified according to the highest non-missing size rating.
Injection site erythema and injection site swelling were solicited from Day 1 through Day 5 postvaccination.
Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.
MedDRA version 26.0 was used in the reporting of this study.
PCV20=pneumococcal 20-valent conjugate vaccine.

Source: [P003V116: adam-adsl; adaece]

付録 2.7.4-15 持続期間別の事前に規定した有害事象（0%超）（APaT 集団）（003 試験　コホート 1）

Participants With Solicited Adverse Events by Maximum Duration (Incidence > 0% in One or More Vaccination Groups) (All Participants as Treated Population) (Cohort 1)

	Maximum Duration	V116		PCV20	
		n	(%)	n	(%)
Participants in population		1,177		1,175	
with one or more solicited adverse events	Total	597	(50.7)	705	(60.0)
	≤3 days	492	(41.8)	584	(49.7)
	>3 days and ≤5 days	92	(7.8)	104	(8.9)
	>5 days and ≤10 days	9	(0.8)	15	(1.3)
	>10 days	4	(0.3)	2	(0.2)
Solicited injection site adverse event					
注射部位紅斑	Total	64	(5.4)	74	(6.3)
	≤3 days	53	(4.5)	55	(4.7)
	>3 days and ≤5 days	7	(0.6)	15	(1.3)
	>5 days and ≤10 days	2	(0.2)	4	(0.3)
	>10 days	2	(0.2)	0	(0.0)
注射部位疼痛	Total	464	(39.4)	607	(51.7)
	≤3 days	403	(34.2)	538	(45.8)
	>3 days and ≤5 days	58	(4.9)	62	(5.3)
	>5 days and ≤10 days	3	(0.3)	7	(0.6)
注射部位腫脹	Total	71	(6.0)	98	(8.3)
	≤3 days	57	(4.8)	79	(6.7)
	>3 days and ≤5 days	13	(1.1)	17	(1.4)
	>5 days and ≤10 days	1	(0.1)	2	(0.2)
Solicited systemic adverse event					
疲労	Total	237	(20.1)	230	(19.6)
	≤3 days	203	(17.2)	187	(15.9)
	>3 days and ≤5 days	28	(2.4)	37	(3.1)
	>5 days and ≤10 days	4	(0.3)	5	(0.4)
	>10 days	2	(0.2)	1	(0.1)

Participants With Solicited Adverse Events by Maximum Duration
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 1)

	Maximum Duration	V116		PCV20	
		n	(%)	n	(%)
頭痛	Total	135	(11.5)	152	(12.9)
	≤3 days	122	(10.4)	129	(11.0)
	>3 days and ≤5 days	13	(1.1)	17	(1.4)
	>5 days and ≤10 days	0	(0.0)	4	(0.3)
	>10 days	0	(0.0)	2	(0.2)
筋肉痛	Total	70	(5.9)	79	(6.7)
	≤3 days	62	(5.3)	70	(6.0)
	>3 days and ≤5 days	7	(0.6)	8	(0.7)
	>5 days and ≤10 days	1	(0.1)	1	(0.1)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the longest duration.

Ongoing adverse events are categorized as having duration >10 days.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 to Day 5 postvaccination.

MedDRA version 26.0 was used in the reporting of this study.

PCV20=pneumococcal 20-valent conjugate vaccine.

Source: [P003V116: adam-adsl; adaece]

2.7.4.7.4 海外第Ⅲ相試験（004試験）

付録 2.7.4-16 有害事象の要約（APaT 集団）（004 試験　ロット間の比較）

Within Group Analysis of Adverse Event Summary by V116 Lots
(All Participants as Treated Population)

	V116 Lot 1			V116 Lot 2			V116 Lot 3		
	n	(%)	(95% CI)[a]	n	(%)	(95% CI)[a]	n	(%)	(95% CI)[a]
Participants in population	539			536			541		
with one or more adverse events	438	(81.3)	(77.7, 84.5)	429	(80.0)	(76.4, 83.3)	433	(80.0)	(76.4, 83.3)
injection-site	400	(74.2)		393	(73.3)		407	(75.2)	
systemic	326	(60.5)		310	(57.8)		292	(54.0)	
with no adverse event	101	(18.7)		107	(20.0)		108	(20.0)	
with vaccine-related[b] adverse events	426	(79.0)	(75.4, 82.4)	416	(77.6)	(73.8, 81.1)	426	(78.7)	(75.1, 82.1)
injection-site	400	(74.2)		393	(73.3)		407	(75.2)	
systemic	279	(51.8)		259	(48.3)		254	(47.0)	
with serious adverse events	8	(1.5)	(0.6, 2.9)	5	(0.9)	(0.3, 2.2)	1	(0.2)	(0.0, 1.0)
with serious vaccine-related adverse events	0	(0.0)	(0.0, 0.7)	0	(0.0)	(0.0, 0.7)	0	(0.0)	(0.0, 0.7)
who died	0	(0.0)	(0.0, 0.7)	0	(0.0)	(0.0, 0.7)	0	(0.0)	(0.0, 0.7)

[a] Estimated CIs are calculated based on the exact binomial method proposed by Clopper and Pearson and are provided in accordance with the statistical analysis plan.

[b] Determined by the investigator to be related to the vaccine. All injection site adverse events and pyrexia (defined as maximum temperature ≥ 100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination) are considered to be vaccine-related.

Reported adverse events include nonserious adverse events within 30 days of vaccination and serious adverse events occurring Day 1 through the duration of participation in the study.

CI=confidence interval.

Source:　[P004V116: adam-adsl; adaece]

付録 2.7.4-17 有害事象の要約（APaT 集団）（004 試験　V116 群と PPSV23 群の比較）

Analysis of Adverse Event Summary
(All Participants as Treated Population)

	V116 (Combined Lots)		PPSV23		Difference in % vs PPSV23
	n	(%)	n	(%)	Estimate (95 % CI)[a]
Participants in population	1,616		541		
with one or more adverse events	1,300	(80.4)	405	(74.9)	5.6 (1.6, 9.8)
injection-site	1,200	(74.3)	335	(61.9)	
systemic	928	(57.4)	281	(51.9)	
with no adverse event	316	(19.6)	136	(25.1)	
with vaccine-related[b] adverse events	1,268	(78.5)	386	(71.3)	7.1 (2.9, 11.5)
injection-site	1,200	(74.3)	334	(61.7)	
systemic	792	(49.0)	237	(43.8)	
with serious adverse events	14	(0.9)	6	(1.1)	-0.2 (-1.6, 0.6)
with serious vaccine-related adverse events	0	(0.0)	0	(0.0)	0.0 (-0.7, 0.2)
who died	0	(0.0)	1	(0.2)	-0.2 (-1.0, 0.1)

[a] Estimated differences and CIs are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

[b] Determined by the investigator to be related to the vaccine. All injection site adverse events and pyrexia defined as maximum temperature ≥ 100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination are considered to be vaccine-related.

Reported adverse events include nonserious adverse events within 30 days of vaccination and serious adverse events occurring Day 1 through the duration of participation in the study.

CI=confidence interval; PPSV23=pneumococcal vaccine, polyvalent (23-valent).

Source:　[P004V116: adam-adsl; adaece]

付録 2.7.4-18 事前に規定した有害事象（0%超）（APaT 集団）（004 試験）

Analysis of Participants With Solicited Adverse Events
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)

	V116 (Combined Lots)		PPSV23		Difference in % vs PPSV23
	n	(%)	n	(%)	Estimate (95 % CI)[a]
Participants in population	1,616		541		
with one or more solicited adverse events	1,263	(78.2)	387	(71.5)	
with no solicited adverse events	353	(21.8)	154	(28.5)	
Solicited injection site adverse event	**1,199**	**(74.2)**	**334**	**(61.7)**	
注射部位紅斑	219	(13.6)	41	(7.6)	6.0 (3.0, 8.6)
注射部位疼痛	1,184	(73.3)	328	(60.6)	12.6 (8.0, 17.3)
注射部位腫脹	213	(13.2)	41	(7.6)	5.6 (2.6, 8.2)
Solicited systemic adverse event	**778**	**(48.1)**	**234**	**(43.3)**	
疲労	573	(35.5)	184	(34.0)	1.4 (-3.2, 6.0)
頭痛	440	(27.2)	116	(21.4)	5.8 (1.6, 9.7)
筋肉痛	264	(16.3)	47	(8.7)	7.6 (4.5, 10.5)
発熱	48	(3.0)	12	(2.2)	0.8 (-1.0, 2.1)

[a] Estimated differences and CIs are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Every participant is counted a single time for each applicable row and column.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination. Pyrexia was defined as maximum temperature ≥ 100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination.

MedDRA version 26.0 was used in the reporting of this study.

CI=confidence interval; PPSV23=pneumococcal vaccine, polyvalent (23-valent).

Source: [P004V116: adam-adsl; adaece]

2.7.4.7.5 海外第Ⅲ相試験（005試験）

付録 2.7.4-19 有害事象の要約（APaT 集団）（005 試験）

Analysis of Adverse Event Summary
(All Participants as Treated Population)
(Following Any Vaccination)

	Concomitant Group		Sequential Group		Difference in % vs Sequential Group
	n	(%)	n	(%)	Estimate (95% CI)[a]
Participants in population	534		535		
with one or more adverse events	395	(74.0)	375	(70.1)	3.9 (-1.5, 9.2)
injection-site	319	(59.7)	315	(58.9)	
systemic	279	(52.2)	298	(55.7)	
with no adverse event	139	(26.0)	160	(29.9)	
with vaccine-related[b] adverse events	362	(67.8)	343	(64.1)	3.7 (-2.0, 9.3)
injection-site	319	(59.7)	314	(58.7)	
systemic	206	(38.6)	217	(40.6)	
with serious adverse events	10	(1.9)	17	(3.2)	-1.3 (-3.4, 0.6)
with serious vaccine-related adverse events	0	(0.0)	1	(0.2)	-0.2 (-1.1, 0.5)
who died	1	(0.2)	2	(0.4)	-0.2 (-1.2, 0.7)
discontinued vaccine due to an adverse event	2	(0.4)	1	(0.2)	0.2 (-0.7, 1.2)
discontinued vaccine due to a vaccine-related adverse event	1	(0.2)	0	(0.0)	
discontinued vaccine due to a serious adverse event	1	(0.2)	0	(0.0)	
discontinued vaccine due to a serious vaccine-related adverse event	0	(0.0)	0	(0.0)	

[a] Estimated differences and CIs are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

[b] Determined by the investigator to be related to the vaccine. All injection site adverse events and pyrexia (defined as maximum temperature ≥ 100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination) are considered to be vaccine-related.

Reported adverse events include nonserious adverse events within 30 days of vaccination and serious adverse events occurring Day 1 through the duration of participation in the study.

CI=confidence interval

Source: [P005V116: adam-adsl; adaece]

付録 2.7.4-20 事前に規定した有害事象（0%超）（APaT 集団）（005 試験）

Analysis of Participants With Solicited Adverse Events
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Following Any Vaccination)

	Concomitant Group		Sequential Group		Difference in % vs Sequential Group
	n	(%)	n	(%)	Estimate (95% CI)[a]
Participants in population	534		535		
with one or more solicited adverse events	361	(67.6)	348	(65.0)	
with no solicited adverse events	173	(32.4)	187	(35.0)	
Solicited injection site adverse event	**317**	**(59.4)**	**314**	**(58.7)**	
注射部位紅斑	61	(11.4)	59	(11.0)	0.4 (-3.4, 4.2)
注射部位疼痛	309	(57.9)	303	(56.6)	1.2 (-4.7, 7.1)
注射部位腫脹	67	(12.5)	63	(11.8)	0.8 (-3.2, 4.7)
Solicited systemic adverse event	**219**	**(41.0)**	**224**	**(41.9)**	
疲労	160	(30.0)	175	(32.7)	-2.7 (-8.3, 2.8)
頭痛	107	(20.0)	118	(22.1)	-2.0 (-6.9, 2.9)
筋肉痛	74	(13.9)	80	(15.0)	-1.1 (-5.3, 3.1)
発熱	10	(1.9)	13	(2.4)	-0.6 (-2.5, 1.3)

[a] Estimated differences and CIs are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Every participant is counted a single time for each applicable row and column.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination. Pyrexia was defined as maximum temperature ≥ 100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination.

MedDRA version 26.0 was used in the reporting of this study.

CI=confidence interval.

Source: [P005V116: adam-adsl; adaece]

2.7.4.7.6　国際共同第Ⅲ相試験（006試験）

2.7.4.7.6.1　全集団

付録 2.7.4-21 試験の内訳（006 試験）（全集団）

Disposition of Participants by Cohort
(All Randomized Participants)

	Cohort 1				Cohort 2				Cohort 3		Total	
	V116		PCV15		V116		PPSV23		V116			
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	231		119		176		85		106		717	
Vaccinated at Visit 1												
V116	229	(99.1)	1	(0.8)	174	(98.9)	0	(0.0)	105	(99.1)	509	(71.0)
PCV15	0	(0.0)	117	(98.3)	0	(0.0)	0	(0.0)	0	(0.0)	117	(16.3)
PPSV23	0	(0.0)	1	(0.8)	0	(0.0)	85	(100.0)	0	(0.0)	86	(12.0)
Trial Disposition												
Completed	229	(99.1)	118	(99.2)	173	(98.3)	85	(100.0)	105	(99.1)	710	(99.0)
Discontinued	2	(0.9)	1	(0.8)	3	(1.7)	0	(0.0)	1	(0.9)	7	(1.0)
Lost To Follow-Up	0	(0.0)	0	(0.0)	1	(0.6)	0	(0.0)	0	(0.0)	1	(0.1)
Randomized By Mistake Without Study Treatment	0	(0.0)	0	(0.0)	1	(0.6)	0	(0.0)	1	(0.9)	2	(0.3)
Withdrawal By Subject	2	(0.9)	1	(0.8)	1	(0.6)	0	(0.0)	0	(0.0)	4	(0.6)

Each participant is counted once for Trial Disposition based on the latest corresponding disposition record.

PCV15=pneumococcal 15-valent conjugate vaccine; PPSV23=pneumococcal vaccine, polyvalent (23-valent).

Source:　[P006V116: adam-adsl; adex]

付録 2.7.4-22 人口統計学的特性（APaT 集団）（006 試験）（全集団）

Participant Characteristics by Cohort
(All Vaccinated Participants)

	Cohort 1				Cohort 2				Cohort 3		Total	
	V116		PCV15		V116		PPSV23		V116			
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	229		119		174		85		105		712	
Sex												
Male	112	(48.9)	59	(49.6)	74	(42.5)	36	(42.4)	50	(47.6)	331	(46.5)
Female	117	(51.1)	60	(50.4)	100	(57.5)	49	(57.6)	55	(52.4)	381	(53.5)
Age (Years)												
50 to 64	48	(21.0)	25	(21.0)	80	(46.0)	39	(45.9)	17	(16.2)	209	(29.4)
≥65	181	(79.0)	94	(79.0)	94	(54.0)	46	(54.1)	88	(83.8)	503	(70.6)
Mean	68.7		69.0		65.5		65.4		71.0		67.9	
SD	7.5		7.1		7.8		6.6		7.6		7.7	
Median	69.0		69.0		66.0		65.0		71.0		68.0	
Range	50 to 86		51 to 88		50 to 83		51 to 81		53 to 91		50 to 91	
Race												
Asian	96	(41.9)	47	(39.5)	55	(31.6)	25	(29.4)	13	(12.4)	236	(33.1)
Black Or African American	6	(2.6)	3	(2.5)	3	(1.7)	1	(1.2)	6	(5.7)	19	(2.7)
Multiple	2	(0.9)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)	3	(0.4)
White	125	(54.6)	69	(58.0)	116	(66.7)	59	(69.4)	85	(81.0)	454	(63.8)

Participant Characteristics by Cohort
(All Vaccinated Participants)

	Cohort 1				Cohort 2				Cohort 3		Total	
	V116		PCV15		V116		PPSV23		V116			
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Ethnicity												
Hispanic Or Latino	21	(9.2)	17	(14.3)	34	(19.5)	16	(18.8)	14	(13.3)	102	(14.3)
Not Hispanic Or Latino	206	(90.0)	102	(85.7)	140	(80.5)	69	(81.2)	91	(86.7)	608	(85.4)
Not Reported	1	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.1)
Unknown	1	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.1)
Country												
Canada	23	(10.0)	10	(8.4)	21	(12.1)	14	(16.5)	7	(6.7)	75	(10.5)
France	1	(0.4)	1	(0.8)	0	(0.0)	2	(2.4)	0	(0.0)	4	(0.6)
Israel	46	(20.1)	25	(21.0)	3	(1.7)	3	(3.5)	22	(21.0)	99	(13.9)
Italy	0	(0.0)	0	(0.0)	24	(13.8)	7	(8.2)	0	(0.0)	31	(4.4)
Japan	31	(13.5)	19	(16.0)	11	(6.3)	2	(2.4)	0	(0.0)	63	(8.8)
South Korea	51	(22.3)	22	(18.5)	17	(9.8)	10	(11.8)	0	(0.0)	100	(14.0)
Spain	17	(7.4)	12	(10.1)	15	(8.6)	6	(7.1)	0	(0.0)	50	(7.0)
Taiwan	13	(5.7)	5	(4.2)	25	(14.4)	13	(15.3)	11	(10.5)	67	(9.4)
United States	47	(20.5)	25	(21.0)	58	(33.3)	28	(32.9)	65	(61.9)	223	(31.3)
Time since Last Pneumococcal Vaccination												
1 to 4 years	108	(47.2)	54	(45.4)	135	(77.6)	66	(77.6)	78	(74.3)	441	(61.9)
5 to 9 years	85	(37.1)	45	(37.8)	33	(19.0)	18	(21.2)	27	(25.7)	208	(29.2)

Participant Characteristics by Cohort
(All Vaccinated Participants)

	Cohort 1				Cohort 2				Cohort 3		Total	
	V116		PCV15		V116		PPSV23		V116			
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
≥ 10 years	36	(15.7)	20	(16.8)	6	(3.4)	1	(1.2)	0	(0.0)	63	(8.8)

PCV15=pneumococcal 15-valent conjugate vaccine; PPSV23=pneumococcal vaccine, polyvalent (23-valent); SD=standard deviation.

Source: [P006V116: adam-adsl]

付録 2.7.4-23 重症度別の事前に規定した有害事象（0%超）（APaT 集団）（006 試験　コホート 1）（全集団）

Participants With Solicited Adverse Events by Maximum Intensity Grade (Incidence > 0% in One or More Vaccination Groups) (All Participants as Treated Population) (Cohort 1)

	Intensity Grade	V116		PCV15	
		n	(%)	n	(%)
Participants in population		230		117	
with one or more solicited adverse events	Total	107	(46.5)	65	(55.6)
	Mild (Grade 1)	73	(31.7)	45	(38.5)
	Moderate (Grade 2)	30	(13.0)	18	(15.4)
	Severe (Grade 3)	4	(1.7)	2	(1.7)
Solicited injection site adverse event					
注射部位紅斑	Total	17	(7.4)	9	(7.7)
	Mild (Grade 1)	10	(4.3)	6	(5.1)
	Moderate (Grade 2)	5	(2.2)	2	(1.7)
	Severe (Grade 3)	2	(0.9)	1	(0.9)
注射部位疼痛	Total	82	(35.7)	51	(43.6)
	Mild (Grade 1)	65	(28.3)	43	(36.8)
	Moderate (Grade 2)	16	(7.0)	8	(6.8)
	Severe (Grade 3)	1	(0.4)	0	(0.0)
注射部位腫脹	Total	19	(8.3)	10	(8.5)
	Mild (Grade 1)	15	(6.5)	9	(7.7)
	Moderate (Grade 2)	4	(1.7)	1	(0.9)
Solicited systemic adverse event					
疲労	Total	33	(14.3)	20	(17.1)
	Mild (Grade 1)	25	(10.9)	11	(9.4)
	Moderate (Grade 2)	8	(3.5)	9	(7.7)
頭痛	Total	16	(7.0)	11	(9.4)
	Mild (Grade 1)	10	(4.3)	9	(7.7)
	Moderate (Grade 2)	5	(2.2)	2	(1.7)
	Severe (Grade 3)	1	(0.4)	0	(0.0)

Participants With Solicited Adverse Events by Maximum Intensity Grade
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 1)

	Intensity Grade	V116		PCV15	
		n	(%)	n	(%)
筋肉痛	Total	17	(7.4)	3	(2.6)
	Mild (Grade 1)	9	(3.9)	2	(1.7)
	Moderate (Grade 2)	8	(3.5)	1	(0.9)
発熱	Total	4	(1.7)	3	(2.6)
	Mild (Grade 1)	2	(0.9)	0	(0.0)
	Moderate (Grade 2)	2	(0.9)	2	(1.7)
	Severe (Grade 3)	0	(0.0)	1	(0.9)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the highest non-missing intensity grading.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination. Pyrexia was defined as maximum temperature ≥100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination.

Injection site erythema and injection site swelling from Day 1 through Day 5 postvaccination are graded according to size and presented as intensity grade as follows: 0 to ≤5.0 cm=Mild; >5.0 to ≤10.0 cm=Moderate; >10.0 cm=Severe.

Pyrexia from Day 1 through Day 5 postvaccination is graded according to maximum temperature and presented as intensity grade as follows: 38.0°C (100.4°F) to <38.5°C (101.3°F)=Mild; 38.5°C (101.3°F) to <39.0°C (102.2°F)=Moderate; 39.0°C (102.2°F) to <40.0°C (104.0°F)=Severe; ≥40.0°C (104.0°F)=Potentially Life-threatening.

Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.

MedDRA version 26.0 was used in the reporting of this study.

PCV15=pneumococcal 15-valent conjugate vaccine.

Source: [P006V116: adam-adsl; adaece]

付録 2.7.4-24 重症度別の事前に規定した有害事象（0%超）（APaT 集団）（006 試験　コホート 2）（全集団）

Participants With Solicited Adverse Events by Maximum Intensity Grade (Incidence > 0% in One or More Vaccination Groups) (All Participants as Treated Population) (Cohort 2)

	Intensity Grade	V116		PPSV23	
		n	(%)	n	(%)
Participants in population		174		85	
with one or more solicited adverse events	Total	86	(49.4)	52	(61.2)
	Mild (Grade 1)	52	(29.9)	33	(38.8)
	Moderate (Grade 2)	29	(16.7)	19	(22.4)
	Severe (Grade 3)	5	(2.9)	0	(0.0)
Solicited injection site adverse event					
注射部位紅斑	Total	13	(7.5)	8	(9.4)
	Mild (Grade 1)	5	(2.9)	2	(2.4)
	Moderate (Grade 2)	6	(3.4)	6	(7.1)
	Severe (Grade 3)	2	(1.1)	0	(0.0)
注射部位疼痛	Total	72	(41.4)	40	(47.1)
	Mild (Grade 1)	52	(29.9)	30	(35.3)
	Moderate (Grade 2)	20	(11.5)	10	(11.8)
注射部位腫脹	Total	8	(4.6)	14	(16.5)
	Mild (Grade 1)	6	(3.4)	7	(8.2)
	Moderate (Grade 2)	2	(1.1)	7	(8.2)
Solicited systemic adverse event					
疲労	Total	33	(19.0)	11	(12.9)
	Mild (Grade 1)	24	(13.8)	6	(7.1)
	Moderate (Grade 2)	8	(4.6)	5	(5.9)
	Severe (Grade 3)	1	(0.6)	0	(0.0)
頭痛	Total	18	(10.3)	10	(11.8)
	Mild (Grade 1)	10	(5.7)	7	(8.2)
	Moderate (Grade 2)	8	(4.6)	3	(3.5)
筋肉痛	Total	17	(9.8)	8	(9.4)

Participants With Solicited Adverse Events by Maximum Intensity Grade
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 2)

	Intensity Grade	V116		PPSV23	
		n	(%)	n	(%)
筋肉痛	Mild (Grade 1)	7	(4.0)	4	(4.7)
	Moderate (Grade 2)	9	(5.2)	4	(4.7)
	Severe (Grade 3)	1	(0.6)	0	(0.0)
	Total	5	(2.9)	1	(1.2)
発熱	Mild (Grade 1)	1	(0.6)	0	(0.0)
	Moderate (Grade 2)	2	(1.1)	1	(1.2)
	Severe (Grade 3)	2	(1.1)	0	(0.0)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the highest non-missing intensity grading.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination. Pyrexia was defined as maximum temperature ≥100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination.

Injection site erythema and injection site swelling from Day 1 through Day 5 postvaccination are graded according to size and presented as intensity grade as follows: 0 to ≤5.0 cm=Mild; >5.0 to ≤10.0 cm=Moderate; >10.0 cm=Severe.

Pyrexia from Day 1 through Day 5 postvaccination is graded according to maximum temperature and presented as intensity grade as follows: 38.0°C (100.4°F) to <38.5°C (101.3°F)=Mild; 38.5°C (101.3°F) to <39.0°C (102.2°F)=Moderate; 39.0°C (102.2°F) to <40.0°C (104.0°F)=Severe; ≥40.0°C (104.0°F)=Potentially Life-threatening.

Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.

MedDRA version 26.0 was used in the reporting of this study.

PPSV23=pneumococcal vaccine, polyvalent (23-valent).

Source: [P006V116: adam-adsl; adaece]

付録 2.7.4-25 重症度別の事前に規定した有害事象（0%超）（APaT 集団）（006 試験　コホート 3）（全集団）

Participants With Solicited Adverse Events by Maximum Intensity Grade (Incidence > 0%) (All Participants as Treated Population) (Cohort 3)

	Intensity Grade	V116	
		n	(%)
Participants in population		105	
with one or more solicited adverse events	Total	51	(48.6)
	Mild (Grade 1)	38	(36.2)
	Moderate (Grade 2)	11	(10.5)
	Severe (Grade 3)	2	(1.9)
Solicited injection site adverse event			
注射部位紅斑	Total	8	(7.6)
	Mild (Grade 1)	4	(3.8)
	Moderate (Grade 2)	3	(2.9)
	Severe (Grade 3)	1	(1.0)
注射部位疼痛	Total	46	(43.8)
	Mild (Grade 1)	37	(35.2)
	Moderate (Grade 2)	9	(8.6)
注射部位腫脹	Total	11	(10.5)
	Mild (Grade 1)	6	(5.7)
	Moderate (Grade 2)	4	(3.8)
	Severe (Grade 3)	1	(1.0)
Solicited systemic adverse event			
疲労	Total	23	(21.9)
	Mild (Grade 1)	19	(18.1)
	Moderate (Grade 2)	4	(3.8)
頭痛	Total	9	(8.6)
	Mild (Grade 1)	9	(8.6)
筋肉痛	Total	9	(8.6)
	Mild (Grade 1)	7	(6.7)

Participants With Solicited Adverse Events by Maximum Intensity Grade
(Incidence > 0%)
(All Participants as Treated Population)
(Cohort 3)

	Intensity Grade	V116	
		n	(%)
筋肉痛	Moderate (Grade 2)	2	(1.9)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the highest non-missing intensity grading.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination. Pyrexia was defined as maximum temperature ≥100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination.

Injection site erythema and injection site swelling from Day 1 through Day 5 postvaccination are graded according to size and presented as intensity grade as follows: 0 to ≤5.0 cm=Mild; >5.0 to ≤10.0 cm=Moderate; >10.0 cm=Severe.

Pyrexia from Day 1 through Day 5 postvaccination is graded according to maximum temperature and presented as intensity grade as follows: 38.0°C (100.4°F) to <38.5°C (101.3°F)=Mild; 38.5°C (101.3°F) to <39.0°C (102.2°F)=Moderate; 39.0°C (102.2°F) to <40.0°C (104.0°F)=Severe; ≥40.0°C (104.0°F)=Potentially Life-threatening.

Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.

MedDRA version 26.0 was used in the reporting of this study.

Source: [P006V116: adam-adsl; adaece]

付録 2.7.4-26 サイズ別の事前に規定した注射部位紅斑及び注射部位腫脹（0%超）（APaT 集団）（006 試験　コホート 1）（全集団）

Participants With Solicited Injection Site Erythema or Injection Site Swelling by Maximum Size
(Incidence >0 % in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 1)

	Size (cm), Intensity Grade	V116		PCV15	
		n	(%)	n	(%)
Participants in population		230		117	
注射部位紅斑	Total	17	(7.4)	9	(7.7)
	0 to ≤2.4, Mild (Grade 1)	7	(3.0)	4	(3.4)
	>2.4 to ≤5.0, Mild (Grade 1)	2	(0.9)	2	(1.7)
	>5.0 to ≤7.4, Moderate (Grade 2)	2	(0.9)	2	(1.7)
	>7.4 to ≤10.0, Moderate (Grade 2)	3	(1.3)	0	(0.0)
	>10.0, Severe (Grade 3)	2	(0.9)	1	(0.9)
	Unknown	1	(0.4)	0	(0.0)
注射部位腫脹	Total	19	(8.3)	10	(8.5)
	0 to ≤2.4, Mild (Grade 1)	10	(4.3)	6	(5.1)
	>2.4 to ≤5.0, Mild (Grade 1)	5	(2.2)	3	(2.6)
	>7.4 to ≤10.0, Moderate (Grade 2)	4	(1.7)	1	(0.9)

Every participant is counted a single time for each applicable specific injection site adverse event, and is classified according to the highest non-missing size rating.
Injection site erythema and injection site swelling were solicited from Day 1 through Day 5 postvaccination.
Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.
MedDRA version 26.0 was used in the reporting of this study.
PCV15=pneumococcal 15-valent conjugate vaccine.

Source:　[P006V116: adam-adsl; adaece; adex]

付録 2.7.4-27 サイズ別の事前に規定した注射部位紅斑及び注射部位腫脹（0%超）（APaT 集団）（006 試験　コホート 2）（全集団）

Participants With Solicited Injection Site Erythema or Injection Site Swelling by Maximum Size
(Incidence >0 % in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 2)

	Size (cm), Intensity Grade	V116		PPSV23	
		n	(%)	n	(%)
Participants in population		174		85	
注射部位紅斑	Total	13	(7.5)	8	(9.4)
	0 to ≤2.4, Mild (Grade 1)	5	(2.9)	2	(2.4)
	>5.0 to ≤7.4, Moderate (Grade 2)	2	(1.1)	0	(0.0)
	>7.4 to ≤10.0, Moderate (Grade 2)	4	(2.3)	5	(5.9)
	>10.0, Severe (Grade 3)	2	(1.1)	0	(0.0)
	Unknown	0	(0.0)	1	(1.2)
注射部位腫脹	Total	8	(4.6)	14	(16.5)
	0 to ≤2.4, Mild (Grade 1)	3	(1.7)	4	(4.7)
	>2.4 to ≤5.0, Mild (Grade 1)	3	(1.7)	2	(2.4)
	>5.0 to ≤7.4, Moderate (Grade 2)	1	(0.6)	1	(1.2)
	>7.4 to ≤10.0, Moderate (Grade 2)	1	(0.6)	6	(7.1)
	Unknown	0	(0.0)	1	(1.2)

Every participant is counted a single time for each applicable specific injection site adverse event, and is classified according to the highest non-missing size rating.
Injection site erythema and injection site swelling were solicited from Day 1 through Day 5 postvaccination.
Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.
MedDRA version 26.0 was used in the reporting of this study.
PPSV23=pneumococcal vaccine, polyvalent (23-valent).

Source:　[P006V116: adam-adsl; adaece; adex]

付録 2.7.4-28 サイズ別の事前に規定した注射部位紅斑及び注射部位腫脹（0%超）（APaT 集団）（006 試験　コホート 3）（全集団）

Participants With Solicited Injection Site Erythema or Injection Site Swelling by Maximum Size
(Incidence >0 %)
(All Participants as Treated Population)
(Cohort 3)

	Size (cm), Intensity Grade	V116	
		n	(%)
Participants in population		105	
注射部位紅斑	Total	8	(7.6)
	>2.4 to ≤5.0, Mild (Grade 1)	2	(1.9)
	>7.4 to ≤10.0, Moderate (Grade 2)	3	(2.9)
	>10.0, Severe (Grade 3)	1	(1.0)
	Unknown	2	(1.9)
注射部位腫脹	Total	11	(10.5)
	0 to ≤2.4, Mild (Grade 1)	3	(2.9)
	>2.4 to ≤5.0, Mild (Grade 1)	2	(1.9)
	>5.0 to ≤7.4, Moderate (Grade 2)	2	(1.9)
	>7.4 to ≤10.0, Moderate (Grade 2)	2	(1.9)
	>10.0, Severe (Grade 3)	1	(1.0)
	Unknown	1	(1.0)

Every participant is counted a single time for each applicable specific injection site adverse event, and is classified according to the highest non-missing size rating.
Injection site erythema and injection site swelling were solicited from Day 1 through Day 5 postvaccination.
Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.
MedDRA version 26.0 was used in the reporting of this study.

Source:　[P006V116: adam-adsl; adaece; adex]

付録 2.7.4-29 持続期間別の事前に規定した有害事象（0%超）（APaT 集団）（006 試験　コホート 1）（全集団）

Participants With Solicited Adverse Events by Maximum Duration (Incidence > 0% in One or More Vaccination Groups) (All Participants as Treated Population) (Cohort 1)

	Maximum Duration	V116		PCV15	
		n	(%)	n	(%)
Participants in population		230		117	
with one or more solicited adverse events	Total	105	(45.7)	64	(54.7)
	≤3 days	96	(41.7)	54	(46.2)
	>3 days and ≤5 days	8	(3.5)	8	(6.8)
	>5 days and ≤10 days	1	(0.4)	1	(0.9)
	>10 days	0	(0.0)	1	(0.9)
Solicited injection site adverse event					
注射部位紅斑	Total	17	(7.4)	9	(7.7)
	≤3 days	15	(6.5)	7	(6.0)
	>3 days and ≤5 days	2	(0.9)	1	(0.9)
	>5 days and ≤10 days	0	(0.0)	1	(0.9)
注射部位疼痛	Total	82	(35.7)	51	(43.6)
	≤3 days	77	(33.5)	45	(38.5)
	>3 days and ≤5 days	4	(1.7)	5	(4.3)
	>5 days and ≤10 days	1	(0.4)	0	(0.0)
	>10 days	0	(0.0)	1	(0.9)
注射部位腫脹	Total	19	(8.3)	10	(8.5)
	≤3 days	16	(7.0)	10	(8.5)
	>3 days and ≤5 days	3	(1.3)	0	(0.0)
Solicited systemic adverse event					
疲労	Total	33	(14.3)	20	(17.1)
	≤3 days	30	(13.0)	17	(14.5)
	>3 days and ≤5 days	3	(1.3)	3	(2.6)
頭痛	Total	16	(7.0)	11	(9.4)
	≤3 days	14	(6.1)	10	(8.5)
	>3 days and ≤5 days	2	(0.9)	1	(0.9)

Participants With Solicited Adverse Events by Maximum Duration
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 1)

	Maximum Duration	V116		PCV15	
		n	(%)	n	(%)
筋肉痛	Total	17	(7.4)	3	(2.6)
	≤3 days	16	(7.0)	3	(2.6)
	>3 days and ≤5 days	1	(0.4)	0	(0.0)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the longest duration.

Ongoing adverse events are categorized as having duration >10 days.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination.

MedDRA version 26.0 was used in the reporting of this study.

PCV15=pneumococcal 15-valent conjugate vaccine.

Source: [P006V116: adam-adsl; adaece]

付録 2.7.4-30 持続期間別の事前に規定した有害事象（0%超）（APaT 集団）（006 試験　コホート 2）（全集団）

Participants With Solicited Adverse Events by Maximum Duration (Incidence > 0% in One or More Vaccination Groups) (All Participants as Treated Population) (Cohort 2)

	Maximum Duration	V116		PPSV23	
		n	(%)	n	(%)
Participants in population		174		85	
with one or more solicited adverse events	Total	85	(48.9)	52	(61.2)
	≤3 days	72	(41.4)	46	(54.1)
	>3 days and ≤5 days	12	(6.9)	6	(7.1)
	>5 days and ≤10 days	1	(0.6)	0	(0.0)
Solicited injection site adverse event					
注射部位紅斑	Total	13	(7.5)	8	(9.4)
	≤3 days	12	(6.9)	8	(9.4)
	>5 days and ≤10 days	1	(0.6)	0	(0.0)
注射部位疼痛	Total	72	(41.4)	40	(47.1)
	≤3 days	64	(36.8)	34	(40.0)
	>3 days and ≤5 days	8	(4.6)	6	(7.1)
注射部位腫脹	Total	8	(4.6)	14	(16.5)
	≤3 days	7	(4.0)	13	(15.3)
	>3 days and ≤5 days	1	(0.6)	1	(1.2)
Solicited systemic adverse event					
疲労	Total	33	(19.0)	11	(12.9)
	≤3 days	28	(16.1)	10	(11.8)
	>3 days and ≤5 days	5	(2.9)	1	(1.2)
頭痛	Total	18	(10.3)	10	(11.8)
	≤3 days	14	(8.0)	10	(11.8)
	>3 days and ≤5 days	4	(2.3)	0	(0.0)
筋肉痛	Total	17	(9.8)	8	(9.4)
	≤3 days	15	(8.6)	8	(9.4)

Participants With Solicited Adverse Events by Maximum Duration
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 2)

	Maximum Duration	V116		PPSV23	
		n	(%)	n	(%)
筋肉痛	>3 days and ≤5 days	2	(1.1)	0	(0.0)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the longest duration.

Ongoing adverse events are categorized as having duration >10 days.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination.

MedDRA version 26.0 was used in the reporting of this study.

PPSV23=pneumococcal vaccine, polyvalent (23-valent).

Source: [P006V116: adam-adsl; adaece]

付録 2.7.4-31 持続期間別の事前に規定した有害事象（0%超）（APaT 集団）（006 試験　コホート 3）（全集団）

Participants With Solicited Adverse Events by Maximum Duration (Incidence > 0%) (All Participants as Treated Population) (Cohort 3)

	Maximum Duration	V116	
		n	(%)
Participants in population		105	
with one or more solicited adverse events	Total	51	(48.6)
	≤3 days	42	(40.0)
	>3 days and ≤5 days	9	(8.6)
Solicited injection site adverse event			
注射部位紅斑	Total	8	(7.6)
	≤3 days	5	(4.8)
	>3 days and ≤5 days	3	(2.9)
注射部位疼痛	Total	46	(43.8)
	≤3 days	39	(37.1)
	>3 days and ≤5 days	7	(6.7)
注射部位腫脹	Total	11	(10.5)
	≤3 days	7	(6.7)
	>3 days and ≤5 days	4	(3.8)
Solicited systemic adverse event			
疲労	Total	23	(21.9)
	≤3 days	19	(18.1)
	>3 days and ≤5 days	4	(3.8)
頭痛	Total	9	(8.6)
	≤3 days	8	(7.6)
	>3 days and ≤5 days	1	(1.0)
筋肉痛	Total	9	(8.6)
	≤3 days	6	(5.7)

Participants With Solicited Adverse Events by Maximum Duration
(Incidence > 0%)
(All Participants as Treated Population)
(Cohort 3)

	Maximum Duration	V116	
		n	(%)
筋肉痛	>3 days and ≤5 days	3	(2.9)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the longest duration.

Ongoing adverse events are categorized as having duration >10 days.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination.

MedDRA version 26.0 was used in the reporting of this study.

Source: [P006V116: adam-adsl; adaece]

2.7.4.7.6.2 日本人集団

付録 2.7.4-32 試験の内訳（006 試験）（日本人集団）

Disposition of Participants by Cohort
(All Randomized Participants) (Japan Subgroup)

	Cohort 1				Cohort 2			
	V116		PCV15		V116		PPSV23	
	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	31		19		11		2	
Vaccinated at Visit 1								
V116	31	(100.0)	0	(0.0)	11	(100.0)	0	(0.0)
PCV15	0	(0.0)	19	(100.0)	0	(0.0)	0	(0.0)
PPSV23	0	(0.0)	0	(0.0)	0	(0.0)	2	(100.0)
Trial Disposition								
Completed	31	(100.0)	19	(100.0)	11	(100.0)	2	(100.0)
Each participant is counted once for Trial Disposition based on the latest corresponding disposition record.								
PCV15=pneumococcal 15-valent conjugate vaccine; PPSV23=pneumococcal vaccine, polyvalent (23-valent).								

Source:　[P006V116: adam-adsl; adex]

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付録 2.7.4-33 人口統計学的特性（APaT 集団）（006 試験）（日本人集団）

Participant Characteristics by Cohort
(All Vaccinated Participants)
(Japan Subgroup)

	Cohort 1				Cohort 2				Total	
	V116		PCV15		V116		PPSV23			
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Participants in population	31		19		11		2		63	
Sex										
Male	16	(51.6)	10	(52.6)	4	(36.4)	1	(50.0)	31	(49.2)
Female	15	(48.4)	9	(47.4)	7	(63.6)	1	(50.0)	32	(50.8)
Age (Years)										
50 to 64	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
≥65	31	(100.0)	19	(100.0)	11	(100.0)	2	(100.0)	63	(100.0)
Mean	70.3		69.4		73.8		72.5		70.7	
SD	3.8		3.0		3.1		2.1		3.7	
Median	70.0		69.0		74.0		72.5		70.0	
Range	66 to 80		66 to 75		69 to 79		71 to 74		66 to 80	
Race										
Asian	31	(100.0)	19	(100.0)	11	(100.0)	2	(100.0)	63	(100.0)
Ethnicity										
Not Hispanic Or Latino	31	(100.0)	19	(100.0)	11	(100.0)	2	(100.0)	63	(100.0)

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Participant Characteristics by Cohort
(All Vaccinated Participants)
(Japan Subgroup)

	Cohort 1				Cohort 2				Total	
	V116		PCV15		V116		PPSV23			
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Country										
Japan	31	(100.0)	19	(100.0)	11	(100.0)	2	(100.0)	63	(100.0)
Time since Last Pneumococcal Vaccination										
1 to 4 years	21	(67.7)	13	(68.4)	8	(72.7)	1	(50.0)	43	(68.3)
5 to 9 years	10	(32.3)	6	(31.6)	3	(27.3)	1	(50.0)	20	(31.7)

PCV15=pneumococcal 15-valent conjugate vaccine; PPSV23=pneumococcal vaccine, polyvalent (23-valent); SD=standard deviation.

Source:　[P006V116: adam-adsl]

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付録 2.7.4-34 重症度別の事前に規定した有害事象（0%超）（APaT 集団）（006 試験　コホート 1）（日本人集団）

Participants With Solicited Adverse Events by Maximum Intensity Grade (Incidence > 0% in One or More Vaccination Groups) (All Participants as Treated Population) (Cohort 1) (Japan Subgroup)

	Intensity Grade	V116		PCV15	
		n	(%)	n	(%)
Participants in population		31		19	
with one or more solicited adverse events	Total	11	(35.5)	8	(42.1)
	Mild (Grade 1)	11	(35.5)	8	(42.1)
Solicited injection site adverse event					
注射部位疼痛	Total	8	(25.8)	7	(36.8)
	Mild (Grade 1)	8	(25.8)	7	(36.8)
注射部位腫脹	Total	0	(0.0)	2	(10.5)
	Mild (Grade 1)	0	(0.0)	2	(10.5)
Solicited systemic adverse event					
疲労	Total	3	(9.7)	1	(5.3)
	Mild (Grade 1)	3	(9.7)	1	(5.3)
頭痛	Total	0	(0.0)	1	(5.3)

Participants With Solicited Adverse Events by Maximum Intensity Grade
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 1) (Japan Subgroup)

	Intensity Grade	V116		PCV15	
		n	(%)	n	(%)
頭痛	Mild (Grade 1)	0	(0.0)	1	(5.3)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the highest non-missing intensity grading.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination. Pyrexia was defined as maximum temperature ≥100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination.

Injection site erythema and injection site swelling from Day 1 through Day 5 postvaccination are graded according to size and presented as intensity grade as follows: 0 to ≤5.0 cm=Mild; >5.0 to ≤10.0 cm=Moderate; >10.0 cm=Severe.

Pyrexia from Day 1 through Day 5 postvaccination is graded according to maximum temperature and presented as intensity grade as follows: 38.0°C (100.4°F) to <38.5°C (101.3°F)=Mild; 38.5°C (101.3°F) to <39.0°C (102.2 °F)=Moderate; 39.0°C (102.2°F) to <40.0°C (104.0°F)=Severe; ≥40.0°C (104.0°F)=Potentially Life Threatening.

Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.

MedDRA version 26.0 was used in the reporting of this study.

PCV15=pneumococcal 15-valent conjugate vaccine.

Source: [P006V116: adam-adsl; adaece]

付録 2.7.4-35 重症度別の事前に規定した有害事象（0%超）（APaT 集団）（006 試験　コホート 2）（日本人集団）

Participants With Solicited Adverse Events by Maximum Intensity Grade (Incidence > 0% in One or More Vaccination Groups) (All Participants as Treated Population) (Cohort 2) (Japan Subgroup)

	Intensity Grade	V116		PPSV23	
		n	(%)	n	(%)
Participants in population		11		2	
with one or more solicited adverse events	Total	2	(18.2)	2	(100.0)
	Mild (Grade 1)	2	(18.2)	1	(50.0)
	Moderate (Grade 2)	0	(0.0)	1	(50.0)
Solicited injection site adverse event					
注射部位紅斑	Total	0	(0.0)	1	(50.0)
	Moderate (Grade 2)	0	(0.0)	1	(50.0)
注射部位疼痛	Total	1	(9.1)	1	(50.0)
	Mild (Grade 1)	1	(9.1)	0	(0.0)
	Moderate (Grade 2)	0	(0.0)	1	(50.0)
注射部位腫脹	Total	0	(0.0)	2	(100.0)
	Mild (Grade 1)	0	(0.0)	1	(50.0)
	Moderate (Grade 2)	0	(0.0)	1	(50.0)
Solicited systemic adverse event					
疲労	Total	1	(9.1)	0	(0.0)

Participants With Solicited Adverse Events by Maximum Intensity Grade
(Incidence > 0% in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 2) (Japan Subgroup)

	Intensity Grade	V116		PPSV23	
		n	(%)	n	(%)
疲労	Mild (Grade 1)	1	(9.1)	0	(0.0)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the highest non-missing intensity grading.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination. Pyrexia was defined as maximum temperature ≥100.4 °F (38.0 °C) solicited from Day 1 through Day 5 postvaccination.

Injection site erythema and injection site swelling from Day 1 through Day 5 postvaccination are graded according to size and presented as intensity grade as follows: 0 to ≤5.0 cm=Mild; >5.0 to ≤10.0 cm=Moderate; >10.0 cm=Severe.

Pyrexia from Day 1 through Day 5 postvaccination is graded according to maximum temperature and presented as intensity grade as follows: 38.0°C (100.4°F) to <38.5°C (101.3°F)=Mild; 38.5°C (101.3°F) to <39.0°C (102.2 °F)=Moderate; 39.0°C (102.2°F) to <40.0°C (104.0°F)=Severe; ≥40.0°C (104.0°F)=Potentially Life Threatening.

Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.

MedDRA version 26.0 was used in the reporting of this study.

PPSV23=pneumococcal vaccine, polyvalent (23-valent).

Source: [P006V116: adam-adsl; adaece]

付録 2.7.4-36 サイズ別の事前に規定した注射部位紅斑及び注射部位腫脹（0%超）（APaT 集団）（006 試験　コホート 1）（日本人集団）

Participants With Solicited Injection Site Erythema or Injection Site Swelling by Maximum Size
(Incidence >0 % in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 1) (Japan Subgroup)

	Size (cm), Intensity Grade	V116		PCV15	
		n	(%)	n	(%)
Participants in population		31		19	
注射部位腫脹	Total	0	(0.0)	2	(10.5)
	0 to ≤2.4, Mild (Grade 1)	0	(0.0)	2	(10.5)

Every participant is counted a single time for each applicable specific injection site adverse event, and is classified according to the highest non-missing size rating.
Injection site erythema and injection site swelling were solicited from Day 1 through Day 5 postvaccination.
Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.
MedDRA version 26.0 was used in the reporting of this study.
PCV15=pneumococcal 15-valent conjugate vaccine.

Source:　[P006V116: adam-adsl; adaece; adex]

付録 2.7.4-37 サイズ別の事前に規定した注射部位紅斑及び注射部位腫脹（0%超）（APaT 集団）（006 試験　コホート 2）（日本人集団）

Participants With Solicited Injection Site Erythema or Injection Site Swelling by Maximum Size
(Incidence >0 % in One or More Vaccination Groups)
(All Participants as Treated Population)
(Cohort 2) (Japan Subgroup)

	Size (cm), Intensity Grade	V116		PPSV23	
		n	(%)	n	(%)
Participants in population		11		2	
注射部位紅斑	Total	0	(0.0)	1	(50.0)
	Unknown	0	(0.0)	1	(50.0)
注射部位腫脹	Total	0	(0.0)	2	(100.0)
	>2.4 to ≤5.0, Mild (Grade 1)	0	(0.0)	1	(50.0)
	>5.0 to ≤7.4, Moderate (Grade 2)	0	(0.0)	1	(50.0)

Every participant is counted a single time for each applicable specific injection site adverse event, and is classified according to the highest non-missing size rating.
Injection site erythema and injection site swelling were solicited from Day 1 through Day 5 postvaccination.
Intensity grades are adapted from and aligned with the FDA Guidance for Industry, September 2007.
MedDRA version 26.0 was used in the reporting of this study.
PPSV23=pneumococcal vaccine, polyvalent (23-valent).

Source:　[P006V116: adam-adsl; adaece; adex]

付録 2.7.4-38 持続期間別の事前に規定した有害事象（0%超）（APaT 集団）（006 試験　コホート 1）（日本人集団）

Participants With Solicited Adverse Events by Maximum Duration (Incidence > 0% in One or More Vaccination Groups) (All Participants as Treated Population) (Cohort 1) (Japan Subgroup)

	Maximum Duration	V116		PCV15	
		n	(%)	n	(%)
Participants in population		31		19	
with one or more solicited adverse events	Total	11	(35.5)	8	(42.1)
	≤3 days	11	(35.5)	8	(42.1)
Solicited injection site adverse event					
注射部位疼痛	Total	8	(25.8)	7	(36.8)
	≤3 days	8	(25.8)	7	(36.8)
注射部位腫脹	Total	0	(0.0)	2	(10.5)
	≤3 days	0	(0.0)	2	(10.5)
Solicited systemic adverse event					
疲労	Total	3	(9.7)	1	(5.3)
	≤3 days	3	(9.7)	1	(5.3)
頭痛	Total	0	(0.0)	1	(5.3)
	≤3 days	0	(0.0)	1	(5.3)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the longest duration.

Ongoing adverse events are categorized as having duration >10 days.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination.

MedDRA version 26.0 was used in the reporting of this study.

PCV15=pneumococcal 15-valent conjugate vaccine.

Source:　[P006V116: adam-adsl; adaece]

付録 2.7.4-39 持続期間別の事前に規定した有害事象（0%超）（APaT 集団）（006 試験　コホート 2）（日本人集団）

Participants With Solicited Adverse Events by Maximum Duration (Incidence > 0% in One or More Vaccination Groups) (All Participants as Treated Population) (Cohort 2) (Japan Subgroup)

	Maximum Duration	V116		PPSV23	
		n	(%)	n	(%)
Participants in population		11		2	
with one or more solicited adverse events	Total	2	(18.2)	2	(100.0)
	≤3 days	2	(18.2)	2	(100.0)
Solicited injection site adverse event					
注射部位紅斑	Total	0	(0.0)	1	(50.0)
	≤3 days	0	(0.0)	1	(50.0)
注射部位疼痛	Total	1	(9.1)	1	(50.0)
	≤3 days	1	(9.1)	1	(50.0)
注射部位腫脹	Total	0	(0.0)	2	(100.0)
	≤3 days	0	(0.0)	2	(100.0)
Solicited systemic adverse event					
疲労	Total	1	(9.1)	0	(0.0)
	≤3 days	1	(9.1)	0	(0.0)

Every participant is counted a single time for each applicable specific adverse event, and is classified according to the longest duration.

Ongoing adverse events are categorized as having duration >10 days.

Injection site erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination.

MedDRA version 26.0 was used in the reporting of this study.

PPSV23=pneumococcal vaccine, polyvalent (23-valent).

Source:　[P006V116: adam-adsl; adaece]

2.7.4　臨床的安全性

本申請における安全性の評価資料は2試験（国際共同第Ⅲ相008試験、海外第Ⅲ相007試験）であり、併合解析は実施しないため、各試験の概要は[at risk_2.7.6.2.2.1 項]及び[at risk_2.7.6.2.1.1 項]に、安全性の評価方法、安全性の結果、市販後の安全性及び結論は、それぞれ[at risk_2.5.5.1 項]、[at risk_2.5.5.2 項]～[at risk_2.5.5.6 項]、[2.7.4.6 項]及び[at risk_2.5.5.8 項]に記載した。

2.7.5　参考文献

参考文献は、[1.12　項]及び[at risk_1.12　項]の「5.4参考文献」に示した。