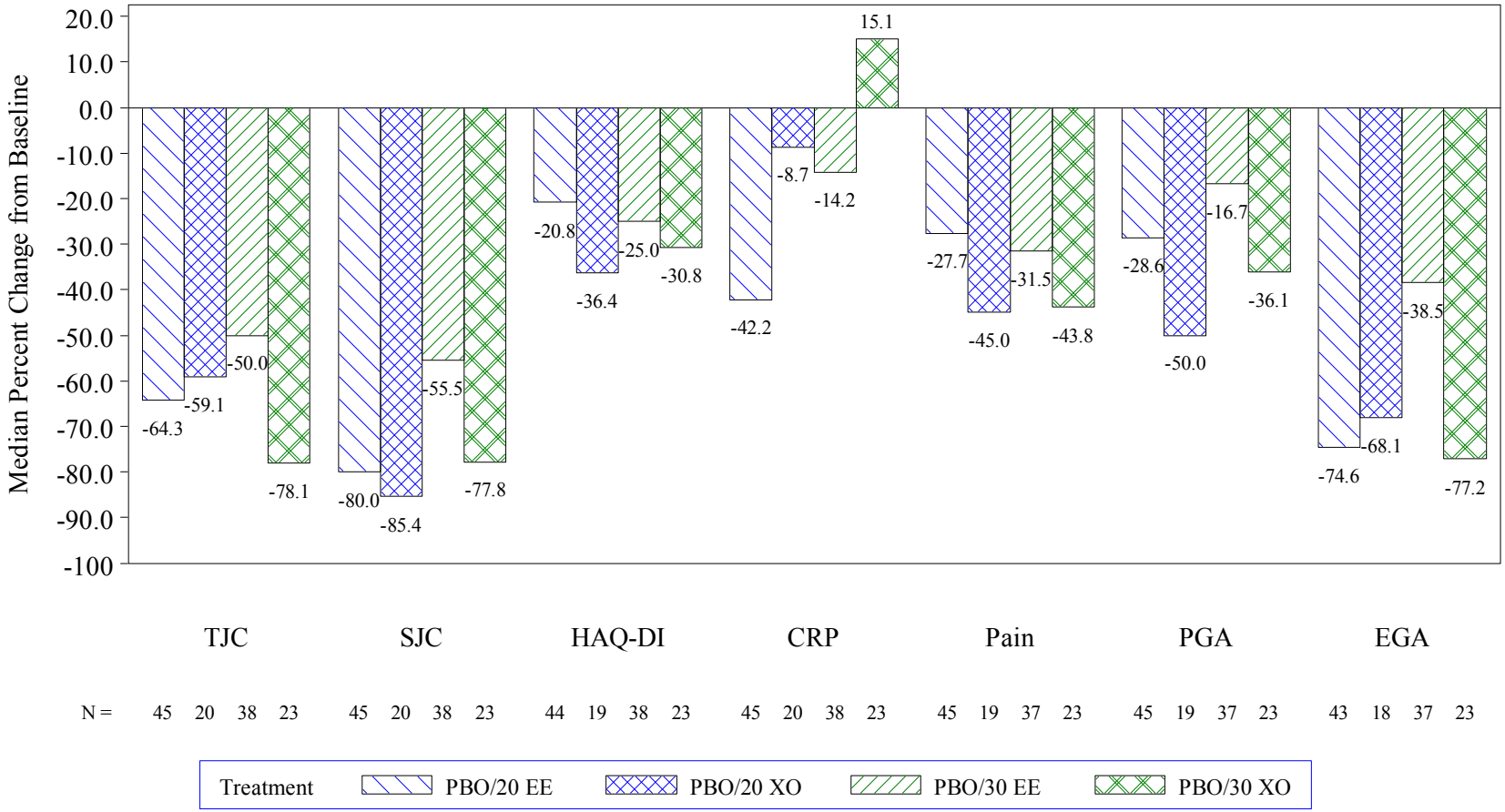
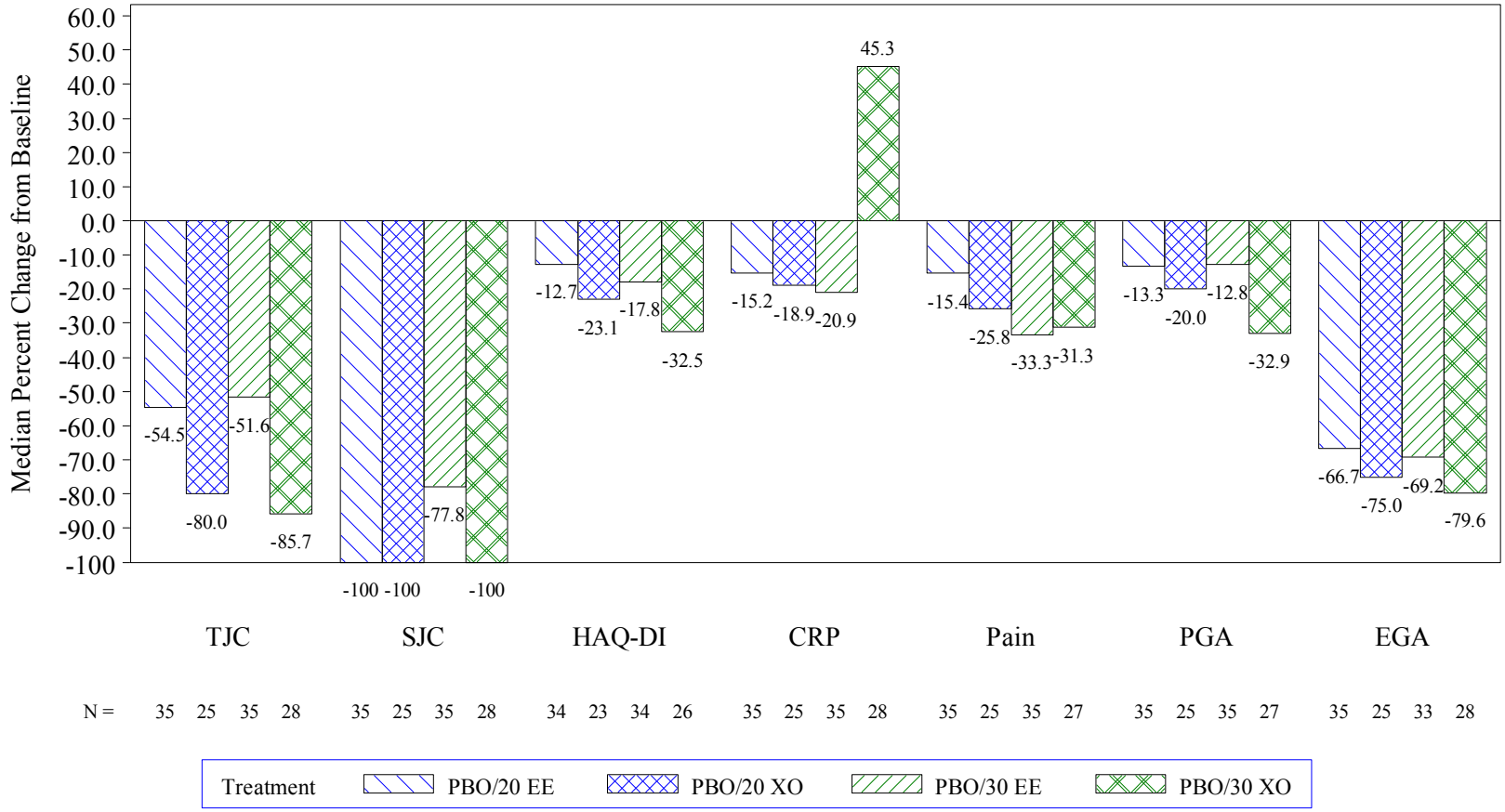
6.7. ACR コンポーネント

Figure 26: Median Percent Change From Baseline in ACR Component Scores at Week 52 in Subjects Initially Randomized to Placebo (Study PSA-002; AAR Population; Data as Observed)



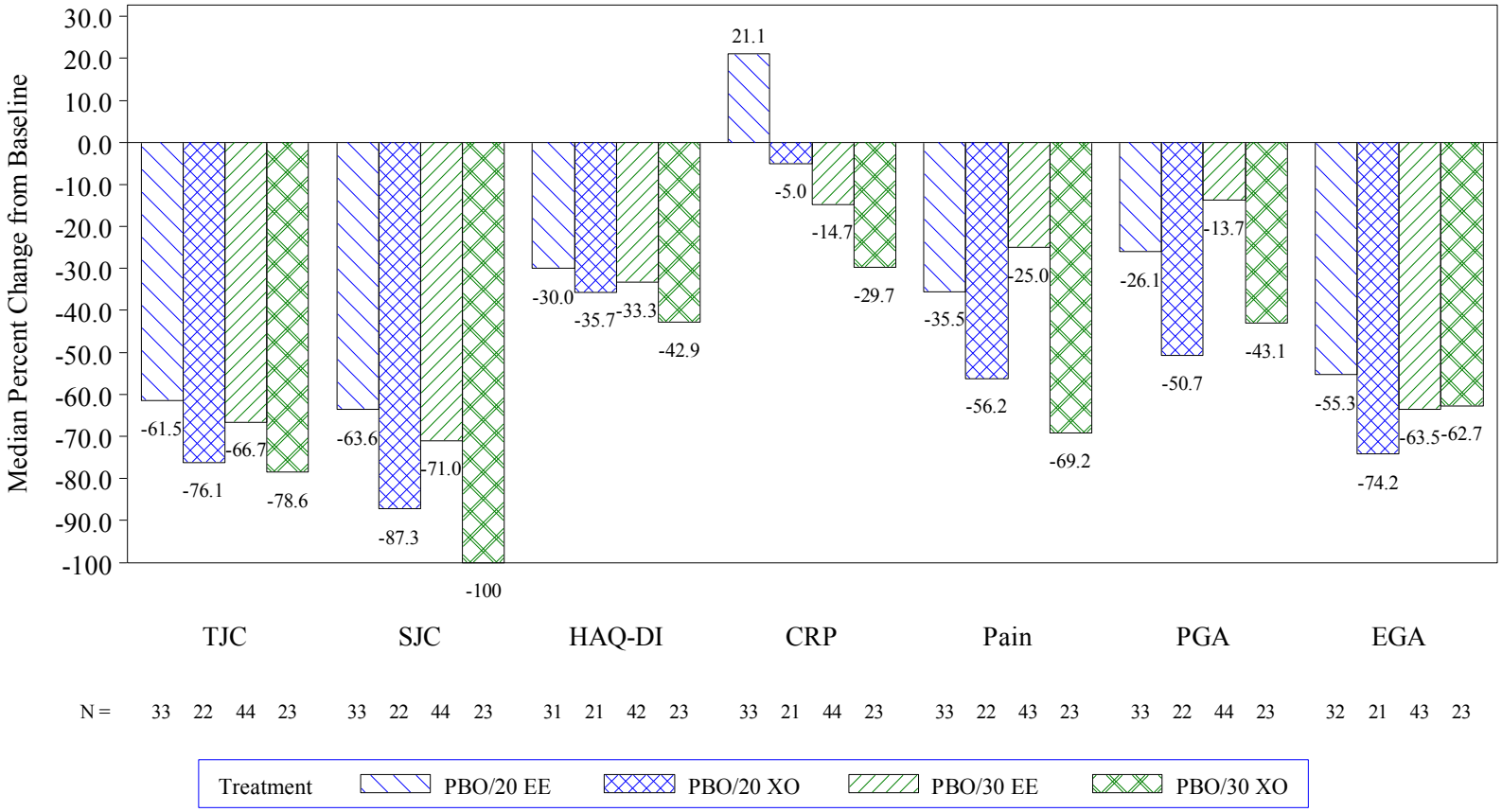
AAR = apremilast subjects as initially randomized/re-randomized; ACR = American College of Rheumatology; BID = twice daily; CRP = C-reactive protein; EE = early escape (re-randomized to apremilast at Week 16); EGA = evaluator's (physician's) global assessment of disease activity; HAQ-DI = Health Assessment Questionnaire – Disability Index; PBO = placebo; PGA = patient's (subject's) global assessment of disease activity; SJC = swollen joint count; TJC = tender joint count; XO = cross-over (re-randomized to apremilast at Week 24).
Source: PSA-002 治験総括報告書 Table 14.2.46, Table 14.2.47, Table 14.2.48.1, Table 14.2.49, Table 14.2.50, Table 14.2.51.1, Table 14.2.52.1.

Figure 27: Median Percent Change From Baseline in ACR Component Scores at Week 52 in Subjects Initially Randomized to Placebo (Study PSA-003; AAR Population; Data as Observed)



AAR = apremilast subjects as initially randomized/re-randomized; ACR = American College of Rheumatology; BID = twice daily; CRP = C-reactive protein; EE = early escape (re-randomized to apremilast at Week 16); EGA = evaluator's (physician's) global assessment of disease activity; HAQ-DI = Health Assessment Questionnaire – Disability Index; PBO = placebo; PGA = patient's (subject's) global assessment of disease activity; SJC = swollen joint count; TJC = tender joint count; XO = cross-over (re-randomized to apremilast at Week 24).
Source: PSA-003 治験総括報告書 Table 14.2.46, Table 14.2.47, Table 14.2.48.1, Table 14.2.49, Table 14.2.50, Table 14.2.51.1, Table 14.2.52.1.

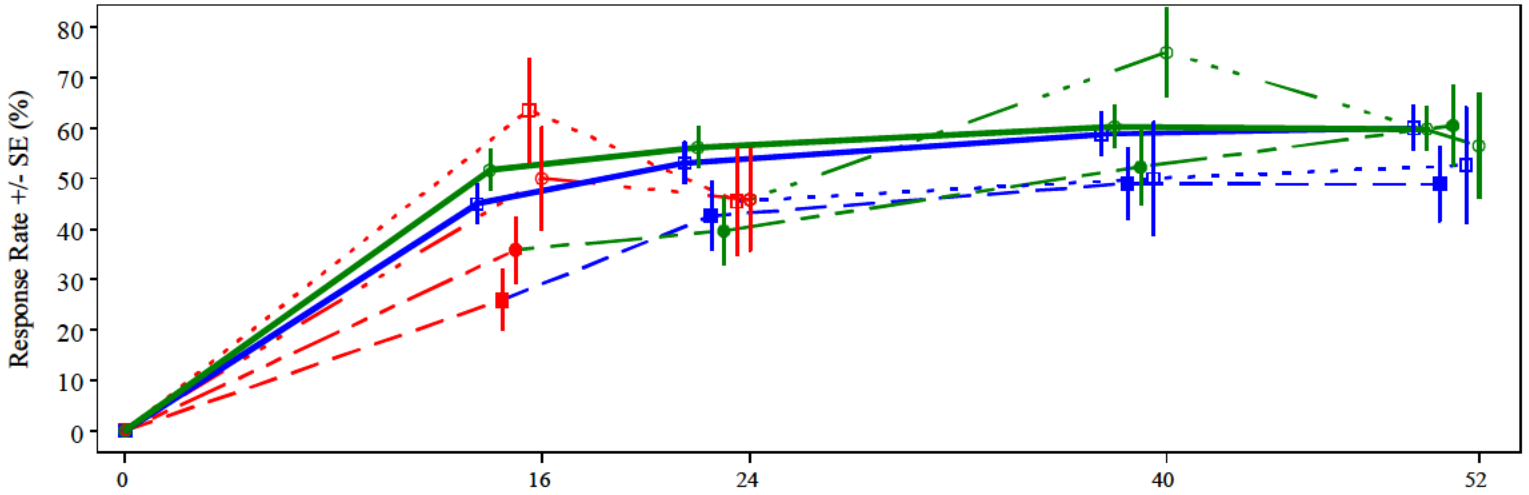
Figure 28: Median Percent Change From Baseline in ACR Component Scores at Week 52 in Subjects Initially Randomized to Placebo (Study PSA-004; AAR Population; Data as Observed)



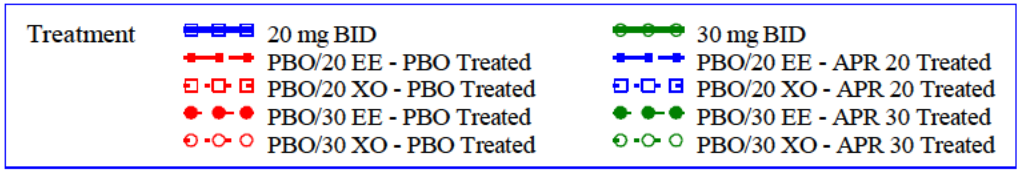
AAR = apremilast subjects as initially randomized/re-randomized; ACR = American College of Rheumatology; BID = twice daily; CRP = C-reactive protein; EE = early escape (re-randomized to apremilast at Week 16); EGA = evaluator's (physician's) global assessment of disease activity; HAQ-DI = Health Assessment Questionnaire – Disability Index; PBO = placebo; PGA = patient's (subject's) global assessment of disease activity; SJC = swollen joint count; TJC = tender joint count; XO = cross-over (re-randomized to apremilast at Week 24).
Source: PSA-004 治験総括報告書 Table 14.2.46, Table 14.2.47, Table 14.2.48.1, Table 14.2.49, Table 14.2.50, Table 14.2.51.1, Table 14.2.52.1.

6.8. その他の有効性評価項目

Figure 29: Proportion of All Subjects Exposed to Apremilast Achieving HAQ-DI Improvements of at Least 0.13 During the Apremilast-exposure Period up to Week 52 in Study PSA-002 (AAR Population; Data as Observed)



Treatment	n/m (%)	n/m (%)	n/m (%)	n/m (%)
20 mg BID	72/160 (45.0)	78/147 (53.1)	77/131 (58.8)	72/120 (60.0)
30 mg BID	78/151 (51.7)	82/146 (56.2)	85/141 (60.3)	79/132 (59.8)
PBO/20 EE	14/ 54 (25.9)	23/ 54 (42.6)	24/ 49 (49.0)	22/ 45 (48.9)
PBO/20 XO	14/ 22 (63.6)	10/ 22 (45.5)	10/ 20 (50.0)	10/ 19 (52.6)
PBO/30 EE	19/ 53 (35.8)	21/ 53 (39.6)	23/ 44 (52.3)	23/ 38 (60.5)
PBO/30 XO	12/ 24 (50.0)	11/ 24 (45.8)	18/ 24 (75.0)	13/ 23 (56.5)

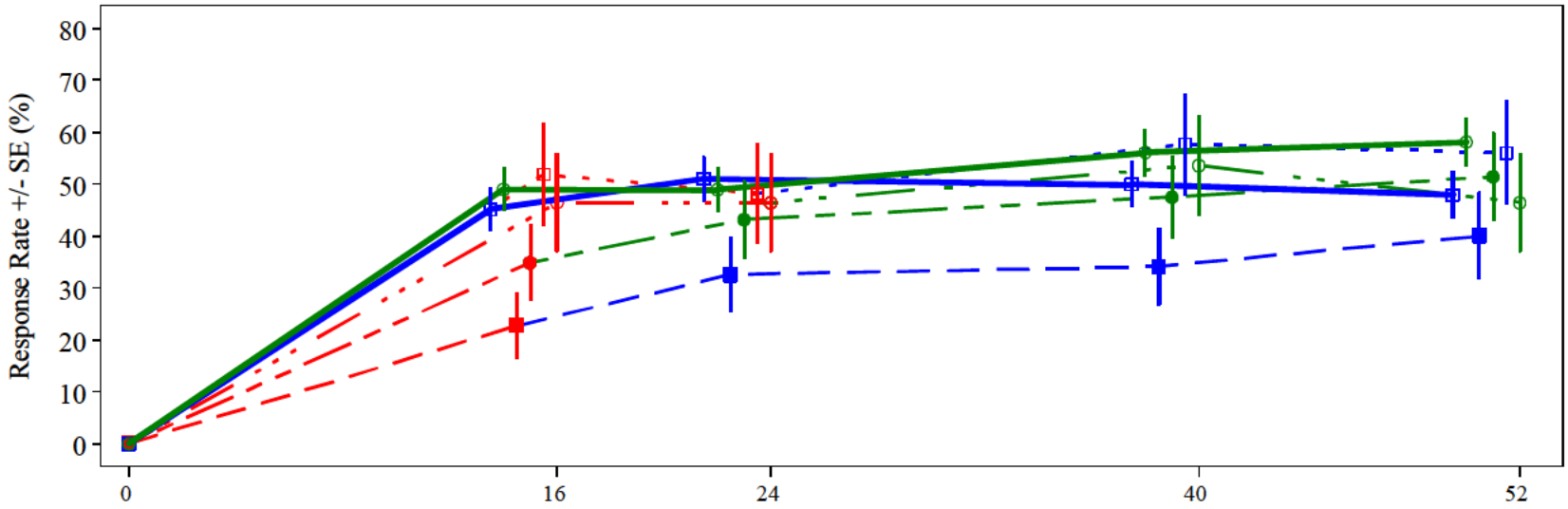


AAR = apremilast subjects as initially randomized/re-randomized; APR = apremilast; BID = twice daily; EE = early escape (re-randomized to apremilast at Week 16); HAQ-DI = Health Assessment Questionnaire – Disability Index; n/m = number of responders/number of subjects with sufficient data for definitive determination of response status at each time point (including subjects who discontinued early between the preceding visit and the visit in question); PBO = placebo; XO = cross-over (re-randomized to apremilast at Week 24).

Note: To enhance visual clarity, the data points collected at Weeks 16, 24, 40, and 52 are displayed in a staggered fashion above the hash mark for the corresponding time point.

Source: PSA-002 治験総括報告書 Table 14.2.51.2.

Figure 30:Proportion of All Subjects Exposed to Apremilast Achieving HAQ-DI Improvements of at Least 0.13 During the Apremilast-exposure Period up to Week 52 in Study PSA-003 (AAR Population; Data as Observed)



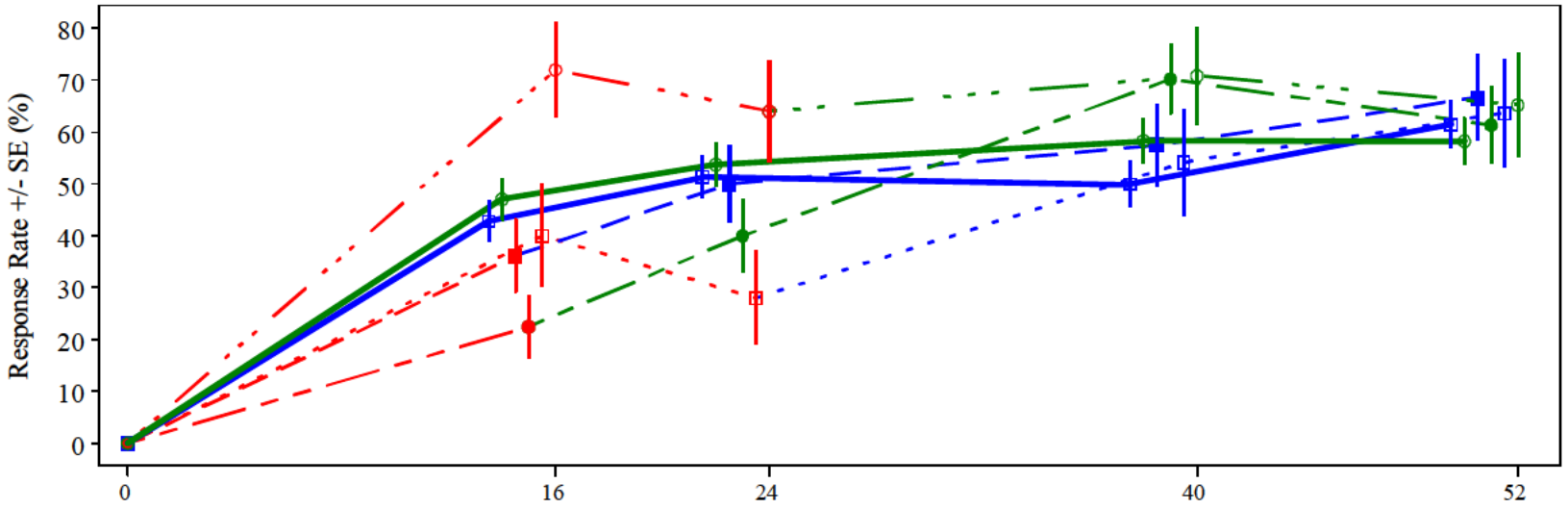
Treatment	n/m (%)	n/m (%)	n/m (%)	n/m (%)
20 mg BID	69/153 (45.1)	74/145 (51.0)	65/130 (50.0)	60/125 (48.0)
30 mg BID	72/147 (49.0)	69/141 (48.9)	69/123 (56.1)	68/117 (58.1)
PBO/20 EE	10/ 44 (22.7)	14/ 43 (32.6)	14/ 41 (34.1)	14/ 35 (40.0)
PBO/20 XO	14/ 27 (51.9)	13/ 27 (48.1)	15/ 26 (57.7)	14/ 25 (56.0)
PBO/30 EE	15/ 43 (34.9)	19/ 44 (43.2)	19/ 40 (47.5)	18/ 35 (51.4)
PBO/30 XO	13/ 28 (46.4)	13/ 28 (46.4)	15/ 28 (53.6)	13/ 28 (46.4)

AAR = apremilast subjects as initially randomized/re-randomized; APR = apremilast; BID = twice daily; EE = early escape (re-randomized to apremilast at Week 16); HAQ-DI = Health Assessment Questionnaire – Disability Index; n/m = number of responders/number of subjects with sufficient data for definitive determination of response status at each time point (including subjects who discontinued early between the preceding visit and the visit in question); PBO = placebo; XO = cross-over (re-randomized to apremilast at Week 24).

Note: To enhance visual clarity, the data points collected at Weeks 16, 24, 40, and 52 are displayed in a staggered fashion above the hash mark for the corresponding time point.

Source: PSA-003 治験総括報告書 Table 14.2.51.2.

Figure 31: Proportion of All Subjects Exposed to Apremilast Achieving HAQ-DI Improvements of at Least 0.13 During the Apremilast-exposure Period up to Week 52 in Study PSA-004 (AAR Population; Data as Observed)



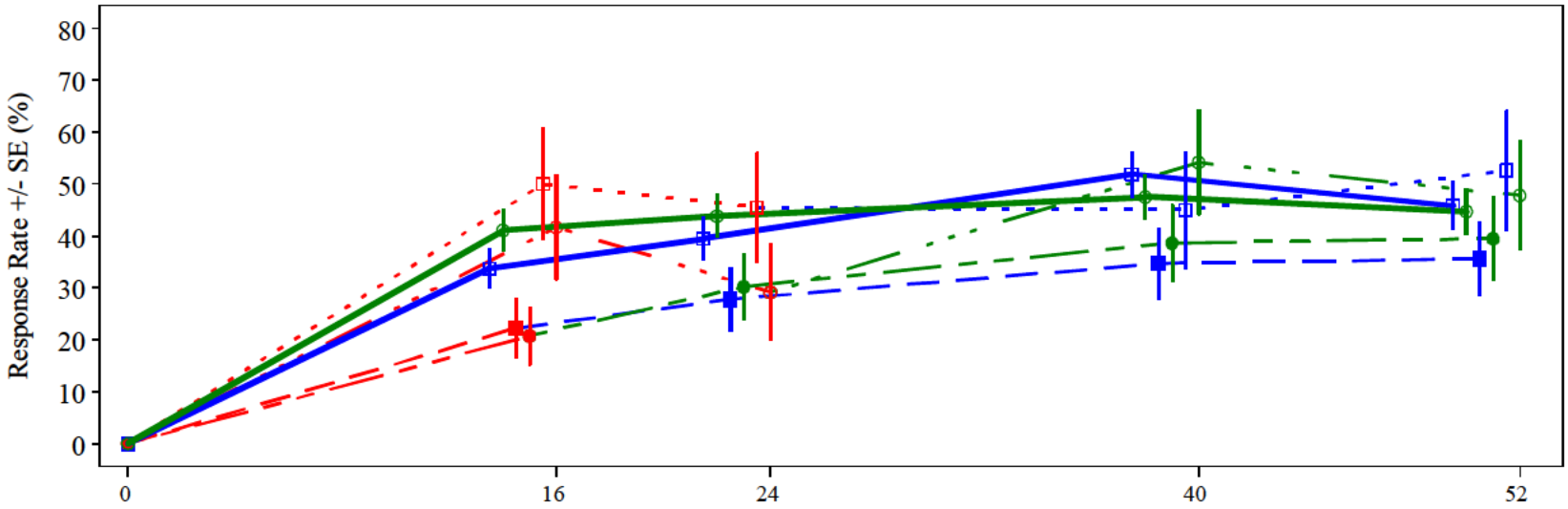
Treatment	n/m (%)	n/m (%)	n/m (%)	n/m (%)
20 mg BID	69/161 (42.9)	75/146 (51.4)	63/126 (50.0)	75/122 (61.5)
30 mg BID	72/153 (47.1)	79/147 (53.7)	77/132 (58.3)	74/127 (58.3)
PBO/20 EE	17/ 47 (36.2)	23/ 46 (50.0)	23/ 40 (57.5)	22/ 33 (66.7)
PBO/20 XO	10/ 25 (40.0)	7/ 25 (28.0)	13/ 24 (54.2)	14/ 22 (63.6)
PBO/30 EE	11/ 49 (22.4)	20/ 50 (40.0)	33/ 47 (70.2)	27/ 44 (61.4)
PBO/30 XO	18/ 25 (72.0)	16/ 25 (64.0)	17/ 24 (70.8)	15/ 23 (65.2)

AAR = apremilast subjects as initially randomized/re-randomized; APR = apremilast; BID = twice daily; EE = early escape (re-randomized to apremilast at Week 16); HAQ-DI = Health Assessment Questionnaire – Disability Index; n/m = number of responders/number of subjects with sufficient data for definitive determination of response status at each time point (including subjects who discontinued early between the preceding visit and the visit in question); PBO = placebo; XO = cross-over (re-randomized to apremilast at Week 24).

Note: To enhance visual clarity, the data points collected at Weeks 16, 24, 40, and 52 are displayed in a staggered fashion above the hash mark for the corresponding time point.

Source: PSA-004 治験総括報告書 Table 14.2.51.2.

Figure 32:Proportion of All Subjects Exposed to Apremilast Achieving HAQ-DI Improvements of at Least 0.30 During the Apremilast-exposure Period up to Week 52 in Study PSA-002 (AAR Population; Data as Observed)



Treatment	n/m (%)	n/m (%)	n/m (%)	n/m (%)
20 mg BID	54/160 (33.8)	58/147 (39.5)	68/131 (51.9)	55/120 (45.8)
30 mg BID	62/151 (41.1)	64/146 (43.8)	67/141 (47.5)	59/132 (44.7)
PBO/20 EE	12/ 54 (22.2)	15/ 54 (27.8)	17/ 49 (34.7)	16/ 45 (35.6)
PBO/20 XO	11/ 22 (50.0)	10/ 22 (45.5)	9/ 20 (45.0)	10/ 19 (52.6)
PBO/30 EE	11/ 53 (20.8)	16/ 53 (30.2)	17/ 44 (38.6)	15/ 38 (39.5)
PBO/30 XO	10/ 24 (41.7)	7/ 24 (29.2)	13/ 24 (54.2)	11/ 23 (47.8)

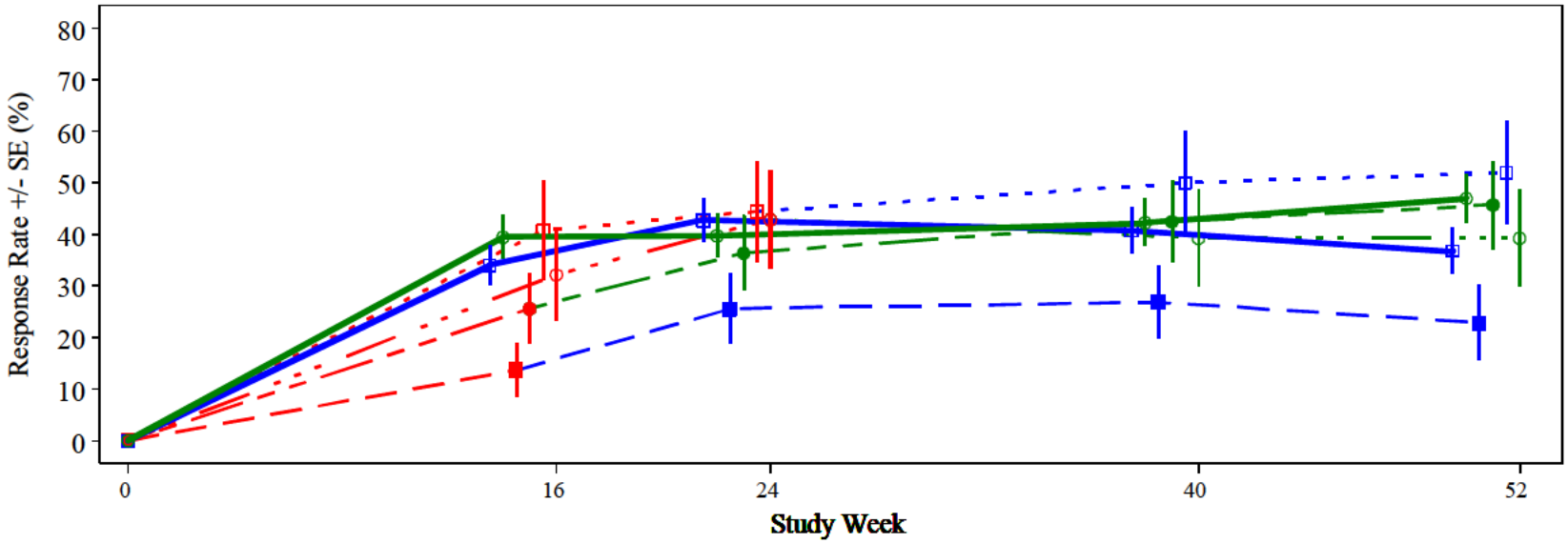


AAR = apremilast subjects as initially randomized/re-randomized; APR = apremilast; BID = twice daily; EE = early escape (re-randomized to apremilast at Week 16); HAQ-DI = Health Assessment Questionnaire – Disability Index; n/m = number of responders/number of subjects with sufficient data for definitive determination of response status at each time point (including subjects who discontinued early between the preceding visit and the visit in question); PBO = placebo; XO = cross-over (re-randomized to apremilast at Week 24).

Note: To enhance visual clarity, the data points collected at Weeks 16, 24, 40, and 52 are displayed in a staggered fashion above the hash mark for the corresponding time point.

Source: PSA-002 治験総括報告書 Table 14.2.51.2.

Figure 33:Proportion of All Subjects Exposed to Apremilast Achieving HAQ-DI Improvements of at Least 0.30 During the Apremilast-exposure Period up to Week 52 in Study PSA-003 (AAR Population; Data as Observed)



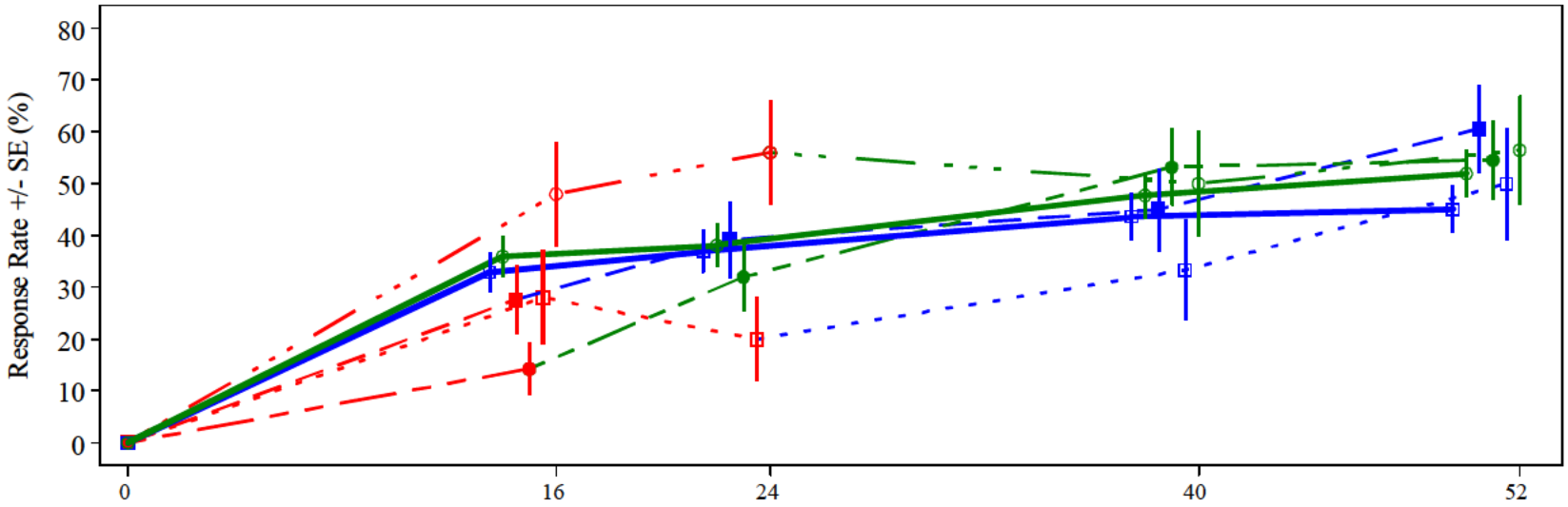
Treatment	n/m (%)	n/m (%)	n/m (%)	n/m (%)
20 mg BID	52/153 (34.0)	62/145 (42.8)	53/130 (40.8)	46/125 (36.8)
30 mg BID	58/147 (39.5)	56/141 (39.7)	52/123 (42.3)	55/117 (47.0)
PBO/20 EE	6/ 44 (13.6)	11/ 43 (25.6)	11/ 41 (26.8)	8/ 35 (22.9)
PBO/20 XO	11/ 27 (40.7)	12/ 27 (44.4)	13/ 26 (50.0)	13/ 25 (52.0)
PBO/30 EE	11/ 43 (25.6)	16/ 44 (36.4)	17/ 40 (42.5)	16/ 35 (45.7)
PBO/30 XO	9/ 28 (32.1)	12/ 28 (42.9)	11/ 28 (39.3)	11/ 28 (39.3)

AAR = apremilast subjects as initially randomized/re-randomized; APR = apremilast; BID = twice daily; EE = early escape (re-randomized to apremilast at Week 16); HAQ-DI = Health Assessment Questionnaire – Disability Index; n/m = number of responders/number of subjects with sufficient data for definitive determination of response status at each time point (including subjects who discontinued early between the preceding visit and the visit in question); PBO = placebo; XO = cross-over (re-randomized to apremilast at Week 24).

Note: To enhance visual clarity, the data points collected at Weeks 16, 24, 40, and 52 are displayed in a staggered fashion above the hash mark for the corresponding time point.

Source: PSA-003 治験総括報告書 Table 14.2.51.2.

Figure 34:Proportion of All Subjects Exposed to Apremilast Achieving HAQ-DI Improvements of at Least 0.30 During the Apremilast-exposure Period up to Week 52 in Study PSA-004 (AAR Population; Data as Observed)



Treatment	n/m (%)	n/m (%)	n/m (%)	n/m (%)
20 mg BID	53/161 (32.9)	54/146 (37.0)	55/126 (43.7)	55/122 (45.1)
30 mg BID	55/153 (35.9)	56/147 (38.1)	63/132 (47.7)	66/127 (52.0)
PBO/20 EE	13/ 47 (27.7)	18/ 46 (39.1)	18/ 40 (45.0)	20/ 33 (60.6)
PBO/20 XO	7/ 25 (28.0)	5/ 25 (20.0)	8/ 24 (33.3)	11/ 22 (50.0)
PBO/30 EE	7/ 49 (14.3)	16/ 50 (32.0)	25/ 47 (53.2)	24/ 44 (54.5)
PBO/30 XO	12/ 25 (48.0)	14/ 25 (56.0)	12/ 24 (50.0)	13/ 23 (56.5)

AAR = apremilast subjects as initially randomized/re-randomized; APR = apremilast; BID = twice daily; EE = early escape (re-randomized to apremilast at Week 16); HAQ-DI = Health Assessment Questionnaire – Disability Index; n/m = number of responders/number of subjects with sufficient data for definitive determination of response status at each time point (including subjects who discontinued early between the preceding visit and the visit in question); PBO = placebo; XO = cross-over (re-randomized to apremilast at Week 24).

Note: To enhance visual clarity, the data points collected at Weeks 16, 24, 40, and 52 are displayed in a staggered fashion above the hash mark for the corresponding time point.

Source: PSA-004 治験総括報告書 Table 14.2.51.2.

Table 9: CDAI Score Categories at Baseline, Week 16, and Week 24 in Studies PSA-002, PSA-003, and PSA-004 (FAS)

Visit CDAI Score Category	Number (%) of Subjects								
	PSA-002			PSA-003			PSA-004		
	Placebo N = 168	APR 20 BID N = 168	APR 30 BID N = 168	Placebo N = 159	APR 20 BID N = 163	APR 30 BID N = 162	Placebo N = 169	APR 20 BID N = 169	APR 30 BID N = 167
Baseline									
≤ 2.8	0	1 (0.6)	0	0	0	0	0	0	0
> 2.8 to ≤ 10	6 (3.6)	5 (3.0)	6 (3.6)	4 (2.5)	7 (4.3)	4 (2.5)	8 (4.7)	5 (3.0)	2 (1.2)
> 10 to ≤ 22	41 (24.4)	57 (33.9)	41 (24.4)	68 (42.8)	61 (37.4)	60 (37.0)	72 (42.6)	64 (37.9)	66 (39.5)
> 22	115 (68.5)	103 (61.3)	119 (70.8)	81 (50.9)	92 (56.4)	89 (54.9)	83 (49.1)	93 (55.0)	94 (56.3)
Missing	6 (3.6)	2 (1.2)	2 (1.2)	6 (3.8)	3 (1.8)	9 (5.6)	6 (3.6)	7 (4.1)	5 (3.0)
Week 16									
≤ 2.8	2 (1.2)	11 (6.5)	7 (4.2)	1 (0.6)	6 (3.7)	2 (1.2)	3 (1.8)	10 (5.9)	7 (4.2)
> 2.8 to ≤ 10	14 (8.3)	31 (18.5)	36 (21.4)	28 (17.6)	40 (24.5)	40 (24.7)	26 (15.4)	30 (17.8)	41 (24.6)
> 10 to ≤ 22	59 (35.1)	59 (35.1)	56 (33.3)	65 (40.9)	64 (39.3)	61 (37.7)	60 (35.5)	57 (33.7)	60 (35.9)
> 22	88 (52.4)	61 (36.3)	60 (35.7)	58 (36.5)	46 (28.2)	48 (29.6)	74 (43.8)	64 (37.9)	52 (31.1)
Missing	5 (3.0)	6 (3.6)	9 (5.4)	7 (4.4)	7 (4.3)	11 (6.8)	6 (3.6)	8 (4.7)	7 (4.2)
Week 24									
≤ 2.8	2 (1.2)	11 (6.5)	14 (8.3)	4 (2.5)	6 (3.7)	5 (3.1)	6 (3.6)	8 (4.7)	9 (5.4)
> 2.8 to ≤ 10	19 (11.3)	27 (16.1)	41 (24.4)	24 (15.1)	47 (28.8)	33 (20.4)	24 (14.2)	44 (26.0)	44 (26.3)
> 10 to ≤ 22	45 (26.8)	57 (33.9)	46 (27.4)	65 (40.9)	57 (35.0)	64 (39.5)	59 (34.9)	49 (29.0)	56 (33.5)
> 22	97 (57.7)	68 (40.5)	61 (36.3)	60 (37.7)	47 (28.8)	51 (31.5)	74 (43.8)	62 (36.7)	53 (31.7)
Missing	5 (3.0)	5 (3.0)	6 (3.6)	6 (3.8)	6 (3.7)	9 (5.6)	6 (3.6)	6 (3.6)	5 (3.0)

APR = apremilast; BID = twice daily; CDAI = clinical disease activity index; FAS = full analysis set; PsA = psoriatic arthritis.
Source: PSA-002 治験総括報告書 Table 48, PSA-003 治験総括報告書 Table 48, and PSA-004 治験総括報告書 Table 48.

Table 10: Summary of DAS28(CRP) Categories in All Subjects Exposed to Apremilast During the Apremilast-exposure Period (Weeks 0-52) (Study PSA-002; AAR Population; Data as Observed)

Visit DAS28(CRP) Category	Number (%) of Subjects[a]									
	PBO/APR 20 BID[b]		PBO/APR 30 BID[b]		APR 20 BID[c]			APR 30 BID[c]		
	PBO/20 EE N = 54	PBO/20 XO N = 23	PBO/30 EE N = 53	PBO/30 XO N = 24	APR 20 BID EE N = 78	APR 20 BID NEE N = 74	Total Randomized N = 168	APR 30 BID EE N = 58	APR 30 BID NEE N = 91	Total Randomized N = 168
Baseline										
n	54	22	53	24	78	73	167	58	91	168
< 2.6	1 (1.9)	1 (4.5)	1 (1.9)	0 (0.0)	2 (2.6)	4 (5.5)	6 (3.6)	0 (0.0)	0 (0.0)	2 (1.2)
≥ 2.6 to < 3.2	1 (1.9)	1 (4.5)	0 (0.0)	2 (8.3)	3 (3.8)	3 (4.1)	7 (4.2)	1 (1.7)	7 (7.7)	8 (4.8)
≥ 3.2 to ≤ 5.1	30 (55.6)	10 (45.5)	29 (54.7)	13 (54.2)	46 (59.0)	37 (50.7)	91 (54.5)	32 (55.2)	44 (48.4)	84 (50.0)
> 5.1	22 (40.7)	10 (45.5)	23 (43.4)	9 (37.5)	27 (34.6)	29 (39.7)	63 (37.7)	25 (43.1)	40 (44.0)	74 (44.0)
Week 16										
n	53	21	51	24	76	74	159	56	85	146
< 2.6	0 (0.0)	1 (4.8)	2 (3.9)	3 (12.5)	2 (2.6)	20 (27.0)	22 (13.8)	1 (1.8)	21 (24.7)	22 (15.1)
≥ 2.6 to < 3.2	4 (7.5)	4 (19.0)	1 (2.0)	5 (20.8)	6 (7.9)	15 (20.3)	22 (13.8)	3 (5.4)	15 (17.6)	18 (12.3)
≥ 3.2 to ≤ 5.1	28 (52.8)	13 (61.9)	21 (41.2)	14 (58.3)	42 (55.3)	34 (45.9)	81 (50.9)	26 (46.4)	47 (55.3)	76 (52.1)
> 5.1	21 (39.6)	3 (14.3)	27 (52.9)	2 (8.3)	26 (34.2)	5 (6.8)	34 (21.4)	26 (46.4)	2 (2.4)	30 (20.5)
Week 24										
n	53	23	53	23	74	71	145	56	88	144
< 2.6	6 (11.3)	5 (21.7)	5 (9.4)	0 (0.0)	6 (8.1)	19 (26.8)	25 (17.2)	4 (7.1)	30 (34.1)	34 (23.6)
≥ 2.6 to < 3.2	10 (18.9)	3 (13.0)	10 (18.9)	3 (13.0)	11 (14.9)	10 (14.1)	21 (14.5)	5 (8.9)	16 (18.2)	21 (14.6)
≥ 3.2 to ≤ 5.1	28 (52.8)	10 (43.5)	23 (43.4)	15 (65.2)	37 (50.0)	37 (52.1)	74 (51.0)	31 (55.4)	41 (46.6)	72 (50.0)
> 5.1	9 (17.0)	5 (21.7)	15 (28.3)	5 (21.7)	20 (27.0)	5 (7.0)	25 (17.2)	16 (28.6)	1 (1.1)	17 (11.8)

Table 10: Summary of DAS28(CRP) Categories in All Subjects Exposed to Apremilast During the Apremilast-exposure Period (Weeks 0-52) (Study PSA-002; AAR Population; Data as Observed)（つづき）

Visit DAS28(CRP) Category	Number (%) of Subjects[a]									
	PBO/APR 20 BID[b]		PBO/APR 30 BID[b]		APR 20 BID[c]			APR 30 BID[c]		
	PBO/20 EE N = 54	PBO/20 XO N = 23	PBO/30 EE N = 53	PBO/30 XO N = 24	APR 20 BID EE N = 78	APR 20 BID NEE N = 74	Total Randomized N = 168	APR 30 BID EE N = 58	APR 30 BID NEE N = 91	Total Randomized N = 168
Week 40										
n	48	21	44	24	63	69	132	56	85	141
< 2.6	12 (25.0)	0 (0.0)	7 (15.9)	5 (20.8)	12 (19.0)	28 (40.6)	40 (30.3)	2 (3.6)	28 (32.9)	30 (21.3)
≥ 2.6 to < 3.2	6 (12.5)	8 (38.1)	1 (2.3)	5 (20.8)	11 (17.5)	14 (20.3)	25 (18.9)	8 (14.3)	16 (18.8)	24 (17.0)
≥ 3.2 to ≤ 5.1	26 (54.2)	11 (52.4)	29 (65.9)	13 (54.2)	34 (54.0)	25 (36.2)	59 (44.7)	31 (55.4)	34 (40.0)	65 (46.1)
> 5.1	4 (8.3)	2 (9.5)	7 (15.9)	1 (4.2)	6 (9.5)	2 (2.9)	8 (6.1)	15 (26.8)	7 (8.2)	22 (15.6)
Week 52										
n	45	20	37	23	56	64	120	51	78	129
< 2.6	13 (28.9)	4 (20.0)	7 (18.9)	4 (17.4)	15 (26.8)	24 (37.5)	39 (32.5)	6 (11.8)	24 (30.8)	30 (23.3)
≥ 2.6 to < 3.2	7 (15.6)	3 (15.0)	3 (8.1)	3 (13.0)	10 (17.9)	7 (10.9)	17 (14.2)	7 (13.7)	12 (15.4)	19 (14.7)
≥ 3.2 to ≤ 5.1	24 (53.3)	11 (55.0)	20 (54.1)	15 (65.2)	26 (46.4)	28 (43.8)	54 (45.0)	23 (45.1)	40 (51.3)	63 (48.8)
> 5.1	1 (2.2)	2 (10.0)	7 (18.9)	1 (4.3)	5 (8.9)	5 (7.8)	10 (8.3)	15 (29.4)	2 (2.6)	17 (13.2)

AAR = apremilast subjects as initially randomized/re-randomized; APR = apremilast; BID = twice daily; DAS28(CRP) = 28-joint Disease Activity Score using C-reactive protein as the acute-phase reactant; EE = early escape (for placebo subjects, re-randomized to apremilast at Week 16; for apremilast subjects, continue treatment as randomized); NEE = no early escape; PBO = placebo; XO = cross-over (re-randomized to apremilast at Week 24).

[a] Percentage calculated based on the number of subjects with a post-baseline value at each time point.

[b] Subjects in the PBO/20 EE and PBO/30 EE treatment groups were re-randomized to receive apremilast at Week 16. Subjects in the PBO/20 XO and PBO/30 XO treatment groups were re-randomized to receive apremilast at Week 24.

[c] All subjects initially randomized to apremilast continued on the same treatment regimen irrespective of early escape.

Source: PSA-002 治験総括報告書 Table 14.2.58.2.

Table 11: Summary of DAS28(CRP) Categories in All Subjects Exposed to Apremilast During the Apremilast-exposure Period (Weeks 0-52) (Study PSA-003; AAR Population; Data as Observed)

Visit DAS28(CRP) Category	Number (%) of Subjects[a]									
	PBO/APR 20 BID[b]		PBO/APR 30 BID[b]		APR 20 BID[c]			APR 30 BID[c]		
	PBO/20 EE N = 44	PBO/20 XO N = 27	PBO/30 EE N = 44	PBO/30 XO N = 28	APR 20 BID EE N = 59	APR 20 BID NEE N = 87	Total Randomized N = 163	APR 30 BID EE N = 64	APR 30 BID NEE N = 79	Total Randomized N = 162
Baseline										
n	44	27	44	27	59	87	162	62	79	159
< 2.6	2 (4.5)	1 (3.7)	3 (6.8)	1 (3.7)	3 (5.1)	3 (3.4)	6 (3.7)	0 (0.0)	3 (3.8)	3 (1.9)
≥ 2.6 to < 3.2	1 (2.3)	2 (7.4)	1 (2.3)	1 (3.7)	2 (3.4)	9 (10.3)	11 (6.8)	1 (1.6)	3 (3.8)	6 (3.8)
≥ 3.2 to ≤ 5.1	29 (65.9)	19 (70.4)	29 (65.9)	19 (70.4)	43 (72.9)	49 (56.3)	100 (61.7)	37 (59.7)	45 (57.0)	93 (58.5)
> 5.1	12 (27.3)	5 (18.5)	11 (25.0)	6 (22.2)	11 (18.6)	26 (29.9)	45 (27.8)	24 (38.7)	28 (35.4)	57 (35.8)
Week 16										
n	44	27	42	27	57	86	150	63	78	146
< 2.6	1 (2.3)	4 (14.8)	4 (9.5)	4 (14.8)	3 (5.3)	26 (30.2)	29 (19.3)	1 (1.6)	17 (21.8)	19 (13.0)
≥ 2.6 to < 3.2	1 (2.3)	9 (33.3)	2 (4.8)	7 (25.9)	3 (5.3)	15 (17.4)	19 (12.7)	6 (9.5)	17 (21.8)	23 (15.8)
≥ 3.2 to ≤ 5.1	27 (61.4)	14 (51.9)	24 (57.1)	14 (51.9)	36 (63.2)	40 (46.5)	80 (53.3)	33 (52.4)	38 (48.7)	74 (50.7)
> 5.1	15 (34.1)	0 (0.0)	12 (28.6)	2 (7.4)	15 (26.3)	5 (5.8)	22 (14.7)	23 (36.5)	6 (7.7)	30 (20.5)
Week 24										
n	43	27	44	28	57	87	144	64	77	141
< 2.6	9 (20.9)	6 (22.2)	6 (13.6)	6 (21.4)	6 (10.5)	24 (27.6)	30 (20.8)	7 (10.9)	20 (26.0)	27 (19.1)
≥ 2.6 to < 3.2	7 (16.3)	5 (18.5)	9 (20.5)	5 (17.9)	9 (15.8)	20 (23.0)	29 (20.1)	11 (17.2)	14 (18.2)	25 (17.7)
≥ 3.2 to ≤ 5.1	23 (53.5)	16 (59.3)	22 (50.0)	13 (46.4)	30 (52.6)	39 (44.8)	69 (47.9)	34 (53.1)	37 (48.1)	71 (50.4)
> 5.1	4 (9.3)	0 (0.0)	7 (15.9)	4 (14.3)	12 (21.1)	4 (4.6)	16 (11.1)	12 (18.8)	6 (7.8)	18 (12.8)

Table 11: Summary of DAS28(CRP) Categories in All Subjects Exposed to Apremilast During the Apremilast-exposure Period (Weeks 0-52) (Study PSA-003; AAR Population; Data as Observed)（つづき）

Visit DAS28(CRP) Category	Number (%) of Subjects[a]									
	PBO/APR 20 BID[b]		PBO/APR 30 BID[b]		APR 20 BID[c]			APR 30 BID[c]		
	PBO/20 EE N = 44	PBO/20 XO N = 27	PBO/30 EE N = 44	PBO/30 XO N = 28	APR 20 BID EE N = 59	APR 20 BID NEE N = 87	Total Randomized N = 163	APR 30 BID EE N = 64	APR 30 BID NEE N = 79	Total Randomized N = 162
Week 40										
n	39	26	39	27	46	81	127	51	70	121
< 2.6	7 (17.9)	10 (38.5)	8 (20.5)	10 (37.0)	3 (6.5)	35 (43.2)	38 (29.9)	6 (11.8)	25 (35.7)	31 (25.6)
≥ 2.6 to < 3.2	4 (10.3)	9 (34.6)	10 (25.6)	6 (22.2)	14 (30.4)	14 (17.3)	28 (22.0)	8 (15.7)	11 (15.7)	19 (15.7)
≥ 3.2 to ≤ 5.1	23 (59.0)	7 (26.9)	17 (43.6)	9 (33.3)	25 (54.3)	28 (34.6)	53 (41.7)	28 (54.9)	32 (45.7)	60 (49.6)
> 5.1	5 (12.8)	0 (0.0)	4 (10.3)	2 (7.4)	4 (8.7)	4 (4.9)	8 (6.3)	9 (17.6)	2 (2.9)	11 (9.1)
Week 52										
n	35	25	35	27	44	81	125	51	67	118
< 2.6	7 (20.0)	8 (32.0)	8 (22.9)	13 (48.1)	7 (15.9)	28 (34.6)	35 (28.0)	6 (11.8)	15 (22.4)	21 (17.8)
≥ 2.6 to < 3.2	8 (22.9)	5 (20.0)	6 (17.1)	6 (22.2)	9 (20.5)	16 (19.8)	25 (20.0)	10 (19.6)	16 (23.9)	26 (22.0)
≥ 3.2 to ≤ 5.1	18 (51.4)	11 (44.0)	17 (48.6)	5 (18.5)	24 (54.5)	31 (38.3)	55 (44.0)	28 (54.9)	33 (49.3)	61 (51.7)
> 5.1	2 (5.7)	1 (4.0)	4 (11.4)	3 (11.1)	4 (9.1)	6 (7.4)	10 (8.0)	7 (13.7)	3 (4.5)	10 (8.5)

AAR = apremilast subjects as initially randomized/re-randomized; APR = apremilast; BID = twice daily; DAS28(CRP) = 28-joint Disease Activity Score using C-reactive protein as the acute-phase reactant; EE = early escape (for placebo subjects, re-randomized to apremilast at Week 16; for apremilast subjects, continue treatment as randomized); NEE = no early escape; PBO = placebo; XO = cross-over (re-randomized to apremilast at Week 24).

[a] Percentage calculated based on the number of subjects with a post-baseline value at each time point.

[b] Subjects in the PBO/20 EE and PBO/30 EE treatment groups were re-randomized to receive apremilast at Week 16. Subjects in the PBO/20 XO and PBO/30 XO treatment groups were re-randomized to receive apremilast at Week 24.

[c] All subjects initially randomized to apremilast continued on the same treatment regimen irrespective of early escape.

Source: PSA-003 治験総括報告書 Table 14.2.58.2.

Table 12: Summary of DAS28(CRP) Categories in All Subjects Exposed to Apremilast During the Apremilast-exposure Period (Weeks 0-52) (Study PSA-004; AAR Population; Data as Observed)

Visit DAS28(CRP) Category	Number (%) of Subjects[a]									
	PBO/APR 20 BID[b]		PBO/APR 30 BID[b]		APR 20 BID[c]			APR 30 BID[c]		
	PBO/20 EE N = 47	PBO/20 XO N = 25	PBO/30 EE N = 50	PBO/30 XO N = 25	APR 20 BID EE N = 76	APR 20 BID NEE N = 73	Total Randomized N = 169	APR 30 BID EE N = 53	APR 30 BID NEE N = 95	Total Randomized N = 167
Baseline										
n	47	25	50	25	76	73	169	53	95	167
< 2.6	1 (2.1)	1 (4.0)	2 (4.0)	0 (0.0)	2 (2.6)	2 (2.7)	4 (2.4)	0 (0.0)	0 (0.0)	1 (0.6)
≥ 2.6 to < 3.2	3 (6.4)	0 (0.0)	2 (4.0)	2 (8.0)	7 (9.2)	5 (6.8)	14 (8.3)	1 (1.9)	7 (7.4)	9 (5.4)
≥ 3.2 to ≤ 5.1	27 (57.4)	20 (80.0)	33 (66.0)	19 (76.0)	40 (52.6)	48 (65.8)	102 (60.4)	37 (69.8)	60 (63.2)	107 (64.1)
> 5.1	16 (34.0)	4 (16.0)	13 (26.0)	4 (16.0)	27 (35.5)	18 (24.7)	49 (29.0)	15 (28.3)	28 (29.5)	50 (29.9)
Week 16										
n	47	25	50	25	74	72	158	53	94	154
< 2.6	2 (4.3)	5 (20.0)	2 (4.0)	4 (16.0)	2 (2.7)	25 (34.7)	30 (19.0)	0 (0.0)	29 (30.9)	31 (20.1)
≥ 2.6 to < 3.2	2 (4.3)	5 (20.0)	1 (2.0)	9 (36.0)	4 (5.4)	16 (22.2)	21 (13.3)	3 (5.7)	13 (13.8)	17 (11.0)
≥ 3.2 to ≤ 5.1	27 (57.4)	14 (56.0)	27 (54.0)	11 (44.0)	37 (50.0)	28 (38.9)	68 (43.0)	32 (60.4)	50 (53.2)	86 (55.8)
> 5.1	16 (34.0)	1 (4.0)	20 (40.0)	1 (4.0)	31 (41.9)	3 (4.2)	39 (24.7)	18 (34.0)	2 (2.1)	20 (13.0)
Week 24										
n	46	23	50	25	70	73	143	52	93	145
< 2.6	3 (6.5)	5 (21.7)	6 (12.0)	9 (36.0)	9 (12.9)	31 (42.5)	40 (28.0)	3 (5.8)	30 (32.3)	33 (22.8)
≥ 2.6 to < 3.2	5 (10.9)	4 (17.4)	6 (12.0)	6 (24.0)	11 (15.7)	8 (11.0)	19 (13.3)	3 (5.8)	16 (17.2)	19 (13.1)
≥ 3.2 to ≤ 5.1	32 (69.6)	13 (56.5)	29 (58.0)	7 (28.0)	31 (44.3)	31 (42.5)	62 (43.4)	33 (63.5)	40 (43.0)	73 (50.3)
> 5.1	6 (13.0)	1 (4.3)	9 (18.0)	3 (12.0)	19 (27.1)	3 (4.1)	22 (15.4)	13 (25.0)	7 (7.5)	20 (13.8)

Table 12: Summary of DAS28(CRP) Categories in All Subjects Exposed to Apremilast During the Apremilast-exposure Period (Weeks 0-52) (Study PSA-004; AAR Population; Data as Observed)（つづき）

Visit DAS28(CRP) Category	Number (%) of Subjects[a]									
	PBO/APR 20 BID[b]		PBO/APR 30 BID[b]		APR 20 BID[c]			APR 30 BID[c]		
	PBO/20 EE N = 54	PBO/20 XO N = 23	PBO/30 EE N = 53	PBO/30 XO N = 24	APR 20 BID EE N = 78	APR 20 BID NEE N = 74	Total Randomized N = 168	APR 30 BID EE N = 58	APR 30 BID NEE N = 91	Total Randomized N = 168
Week 40										
n	39	23	46	24	59	67	126	44	87	131
< 2.6	9 (23.1)	7 (30.4)	15 (32.6)	15 (62.5)	8 (13.6)	32 (47.8)	40 (31.7)	6 (13.6)	33 (37.9)	39 (29.8)
≥ 2.6 to < 3.2	4 (10.3)	5 (21.7)	9 (19.6)	2 (8.3)	7 (11.9)	11 (16.4)	18 (14.3)	10 (22.7)	19 (21.8)	29 (22.1)
≥ 3.2 to ≤ 5.1	23 (59.0)	11 (47.8)	18 (39.1)	7 (29.2)	33 (55.9)	21 (31.3)	54 (42.9)	20 (45.5)	34 (39.1)	54 (41.2)
> 5.1	3 (7.7)	0 (0.0)	4 (8.7)	0 (0.0)	11 (18.6)	3 (4.5)	14 (11.1)	8 (18.2)	1 (1.1)	9 (6.9)
Week 52										
n	33	21	44	23	56	65	121	42	85	127
< 2.6	13 (39.4)	5 (23.8)	16 (36.4)	10 (43.5)	10 (17.9)	24 (36.9)	34 (28.1)	4 (9.5)	34 (40.0)	38 (29.9)
≥ 2.6 to < 3.2	2 (6.1)	7 (33.3)	7 (15.9)	9 (39.1)	5 (8.9)	12 (18.5)	17 (14.0)	9 (21.4)	21 (24.7)	30 (23.6)
≥ 3.2 to ≤ 5.1	16 (48.5)	9 (42.9)	15 (34.1)	3 (13.0)	32 (57.1)	28 (43.1)	60 (49.6)	21 (50.0)	29 (34.1)	50 (39.4)
> 5.1	2 (6.1)	0 (0.0)	6 (13.6)	1 (4.3)	9 (16.1)	1 (1.5)	10 (8.3)	8 (19.0)	1 (1.2)	9 (7.1)

AAR = apremilast subjects as initially randomized/re-randomized; APR = apremilast; BID = twice daily; DAS28(CRP) = 28-joint Disease Activity Score using C-reactive protein as the acute-phase reactant; EE = early escape (for placebo subjects, re-randomized to apremilast at Week 16; for apremilast subjects, continue treatment as randomized); NEE = no early escape; PBO = placebo; XO = cross-over (re-randomized to apremilast at Week 24).

[a] Percentage calculated based on the number of subjects with a postbaseline value at each time point.

[b] Subjects in the PBO/20 EE and PBO/30 EE treatment groups were re-randomized to receive apremilast at Week 16. Subjects in the PBO/20 XO and PBO/30 XO treatment groups were re-randomized to receive apremilast at Week 24.

[c] All subjects initially randomized to apremilast continued on the same treatment regimen irrespective of early escape.

Source: PSA-004 治験総括報告書 Table 14.2.58.2.

6.9. 併合解析

Table 13: Summary of Reduction of Signs and Symptoms of Active PsA Endpoints from the Pooled Analysis at Weeks 16 and 24 (FAS)

Endpoint Visit	Placebo N = 496	APR 20 BID N = 500			APR 30 BID N = 497		
	Response (n [%]) or Change from Baseline[a]	Response (n [%]) or Change from Baseline[a]	Trt. Effect[b]	P-value[c]	Response (n [%]) or Change from Baseline[a]	Trt. Effect[b]	P-value[c]
ACR 20 response							
Week 16	93 (18.8)	160 (32.0)	13.2	*<0.0001*	184 (37.0)	18.3	*<0.0001*
Week 24	73 (14.7)	139 (27.8)	13.0	*<0.0001*	151 (30.4)	15.8	*<0.0001*
ACR 50 response							
Week 16	32 (6.5)	71 (14.2)	7.7	*0.0001*	69 (13.9)	7.5	*0.0001*
Week 24	34 (6.9)	70 (14.0)	7.1	*0.0002*	78 (15.7)	8.9	*<0.0001*
ACR 70 response							
Week 16	7 (1.4)	24 (4.8)	3.4	*0.0020*	15 (3.0)	1.7	*0.0753*
Week 24	12 (2.4)	25 (5.0)	2.6	*0.0323*	30 (6.0)	3.6	*0.0044*
TJC % change from BL							
Week 16	-8.33	-30.00	-22.40	*<0.0001*	-38.76	-26.29	*<0.0001*
Week 24	-2.50	-28.57	-23.81	*<0.0001*	-37.07	-27.14	*<0.0001*
SJC % change from BL							
Week 16	-25.00	-42.86	-16.67	*<0.0001*	-50.00	-23.21	*<0.0001*
Week 24	-20.00	-40.37	-14.29	*0.0003*	-51.76	-22.35	*<0.0001*
Subject's assessment of pain % change from BL							
Week 16	-6.75	-16.28	-9.02	*0.0028*	-24.62	-13.95	*<0.0001*
Week 24	-6.94	-15.89	-8.76	*0.0028*	-20.66	-12.62	*0.0001*
PGA % change from BL							
Week 16	-5.41	-14.29	-9.03	*0.0007*	-17.01	-11.62	*0.0003*
Week 24	-4.00	-11.69	-7.90	*0.0021*	-17.11	-12.94	*0.0001*
EGA % change from BL							
Week 16	-13.92	-30.61	-14.77	*<0.0001*	-38.75	-20.70	*<0.0001*
Week 24	-12.22	-28.75	-14.18	*<0.0001*	-36.07	-20.11	*<0.0001*
HAQ-DI % change from BL							
Week 16	-7.14	-14.29	-7.58	*0.0044*	-20.00	-12.50	*<0.0001*
Week 24	-6.67	-14.29	-8.33	*0.0013*	-20.00	-14.29	*<0.0001*

Table 13: Summary of Reduction of Signs and Symptoms of Active PsA Endpoints from the Pooled Analysis at Weeks 16 and 24 (FAS)（つづき）

Endpoint Visit	Placebo N = 496	APR 20 BID N = 500			APR 30 BID N = 497		
	Response (n [%]) or Change from Baseline[a]	Response (n [%]) or Change from Baseline[a]	Trt. Effect[b]	P-value[c]	Response (n [%]) or Change from Baseline[a]	Trt. Effect[b]	P-value[c]
CRP % change from BL							
Week 16	-0.89	-13.10	-14.58	*<0.0001*	-8.45	-13.29	*0.0001*
Week 24	2.52	-11.24	-13.95	*0.0001*	-5.86	-12.90	*0.0003*
HAQ-DI change from BL							
Week 16	-0.068 (0.0202)	-0.162 (0.0202)	-0.094	*0.0009*	-0.211 (0.0203)	-0.143	*<0.0001*
Week 24	-0.071 (0.0210)	-0.171 (0.0210)	-0.100	*0.0006*	-0.219 (0.0211)	-0.148	*<0.0001*
HAQ-DI improvement ≥ 0.13							
Week 16	181 (36.5)	213 (42.6)	6.1	*0.0500*	231 (46.5)	10.0	*0.0014*
Week 24	171 (34.5)	217 (43.4)	8.9	*0.0040*	240 (48.3)	13.8	*<0.0001*
HAQ-DI improvement ≥ 0.3							
Week 16	129 (26.0)	161 (32.2)	6.2	*0.0326*	181 (36.4)	10.5	*0.0004*
Week 24	129 (26.0)	164 (32.8)	6.8	*0.0194*	180 (36.2)	10.3	*0.0005*

ACR 20/50/70 = American College of Rheumatology 20%/50%/70% response; ACR-N = American College of Rheumatology – N index; ANCOVA = analysis of covariance; APR = apremilast; BID = twice daily; BL = baseline; CMH = Cochran-Mantel-Haenszel; CRP = C-reactive protein; DMARD = disease-modifying antirheumatic drug; EGA = evaluator's (physician's) global assessment of disease activity; FAS = Full Analysis Set; HAQ-DI = Health Assessment Questionnaire Disability Index; LS = least squares; PGA = patient's (subject's) global assessment of disease activity; SE = standard error; SJC = swollen joint count; TJC = tender joint count; Trt. = treatment.

[a] Change from Baseline is median percent change from baseline for TJC, SJC, subject's assessment of pain, PGA, EGA, HAQ-DI (signs/symptoms), CRP, and LS mean change (SE) for HAQ-DI (physical function).

[b] Treatment effect for categorical endpoints (ACR 20/50/70) is based on adjusted difference in proportions for apremilast versus placebo (weighted average of the treatment differences across the strata of baseline disease-modifying antirheumatic drug (DMARD) use and study with the CMH weights). Treatment effect for ACR components (TJC, SJC, PGA, EGA, HAQ-DI [signs and symptoms], CRP, and ACR-N) is based on Hodges-Lehmann estimate of location shift. Treatment effect for other continuous endpoints (HAQ-DI [disease activity]) is the difference in LS means based on an analysis of covariance (ANCOVA) model for the change from baseline at the respective visit, with treatment group, baseline DMARD use, and study as factors, and baseline value as a covariate.

[c] For categorical endpoints, 2-sided P-value is based on Cochran-Mantel-Haenszel (CMH) test adjusting for baseline DMARD use and study. For ACR components (TJC, SJC, PGA, EGA, HAQ-DI [signs and symptoms], CRP, and ACR-N), P-value is based on an ANCOVA model for the van der Waerden normal scores of the percent change from baseline, with treatment group, baseline DMARD use, and study as factors, and the van der Waerden normal scores of the baseline value as a covariate. For other continuous endpoints, P-value is based on an ANCOVA model for the change from baseline at the respective visit, with treatment group, baseline DMARD use, and study as factors, and baseline value as a covariate. P-values in italics for the pooled analysis are ≤ 0.050 and considered nominally significant as there was no adjustment for multiplicity.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 2.1.1, Table 2.1.2, Table 2.2.1, Table 2.2.2., Table 2.3.1, Table 2.3.2, Table 2.5.1, Table 2.5.2, Table 2.5.6, Table 2.5.7, Table 2.5.8, Table 2.5.9, Table 2.15.1, Table 2.15.2.

Table 14: Summary of Improvement of Quality of Life Endpoints from the Pooled Analysis at Weeks 16 and 24 (FAS)

Endpoint Visit	Placebo N = 496	APR 20 BID N = 500			APR 30 BID N = 497		
	Response (n [%]) or Change from Baseline[a]	Response (n [%]) or Change from Baseline[a]	Trt. Effect[b]	P-value[c]	Response (n [%]) or Change from Baseline[a]	Trt. Effect[b]	P-value[c]
SF-36v2 PF domain score change from BL							
Week 16	1.27 (0.362)	2.66 (0.360)	1.39	*0.0057*	3.56 (0.363)	2.29	*<0.0001*
Week 24	1.30 (0.372)	3.04 (0.371)	1.73	*0.0008*	3.91 (0.372)	2.61	*<0.0001*
SF-36v2 PF domain score improvement ≥ 2.5							
Week 16	188 (37.9)	216 (43.2)	5.2	0.0944	234 (47.1)	9.2	*0.0034*
Week 24	191 (38.5)	227 (45.4)	6.8	*0.0299*	243 (48.9)	10.4	*0.0010*
SF-36v2 PCS change from BL							
Week 16	1.85 (0.335)	3.31 (0.334)	1.46	*0.0016*	3.89 (0.336)	2.04	*<0.0001*
Week 24	1.97 (0.345)	3.50 (0.344)	1.53	*0.0014*	4.29 (0.345)	2.32	*<0.0001*
SF-36v2 PCS score improvement ≥ 2.5							
Week 16	221 (44.6)	265 (53.0)	8.3	*0.0082*	281 (56.5)	12.0	*0.0002*
Week 24	224 (45.2)	265 (53.0)	7.7	*0.0146*	290 (58.4)	13.2	*<0.0001*
FACIT-Fatigue change from BL							
Week 16	1.14 (0.394)	1.47 (0.393)	0.33	0.5405	3.45 (0.394)	2.32	*<0.0001*
Week 24	0.82 (0.395)	1.41 (0.394)	0.58	0.2864	3.07 (0.394)	2.25	*<0.0001*
FACIT-Fatigue score improvement ≥ 3.56							
Week 16	178 (35.9)	173 (34.6)	-1.3	0.6653	227 (45.7)	10.0	*0.0013*
Week 24	165 (33.3)	169 (33.8)	0.5	0.8694	221 (44.5)	11.4	*0.0002*

ANCOVA = analysis of covariance; APR = apremilast; BID = twice daily; BL = baseline; CMH = Cochran-Mantel-Haenszel; DMARD = disease-modifying antirheumatic drug; FACIT = Functional Assessment of Chronic Illness Therapy; FAS = Full Analysis Set; LOCF = last observation carried forward; LS = least squares; NRI = nonresponder imputation; PCS = physical component summary score; PF = physical functioning domain score; SE = standard error; SF-36v2 = 36-item Short Form Health Survey, version 2; Trt. = treatment.

[a] Change from Baseline is LS mean change (SE).

[b] Treatment effect for categorical endpoints is based on adjusted difference in proportions for apremilast versus placebo (weighted average of the treatment differences across the strata of baseline disease-modifying antirheumatic drug (DMARD) use and study with the CMH weights). Treatment effect for continuous endpoints is the difference in LS means based on an analysis of covariance (ANCOVA) model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and study as factors, and baseline value as a covariate.

[c] For categorical endpoints, 2-sided P-value is based on Cochran-Mantel-Haenszel (CMH) test adjusting for baseline DMARD use and study. For continuous endpoints, P-value is based on an ANCOVA model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and study as factors, and baseline value as a covariate. P-values in italics for the pooled analysis are ≤ 0.050 and considered nominally significant as there was no adjustment for multiplicity.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 2.6.1, Table 2.6.2, Table 2.6.5, Table 2.6.6, Table 2.6.7, Table 2.6.8, Table 2.6.9, Table 2.6.10, Table 2.12.1, Table 2.12.2, Table 2.12.4, Table 2.12.5.

Table 15: Summary of Other Indices of Disease Activity of Active PsA Endpoints from the Pooled Analysis (FAS)

Endpoint Visit	Placebo N = 496	APR 20 BID N = 500			APR 30 BID N = 497		
	Response (n [%]) or Change from Baseline[a]	Response (n [%]) or Change from Baseline[a]	Trt. Effect[b]	P-value[c]	Response (n [%]) or Change from Baseline[a]	Trt. Effect[b]	P-value[c]
PASI-75[d]							
Week 16	12 (5.2)	50 (20.2)	15.0	*<0.0001*	55 (22.1)	17.1	*<0.0001*
Week 24	16 (6.9)	53 (21.4)	14.6	*<0.0001*	61 (24.5)	18.0	*<0.0001*
PsARC response							
Week 16	149 (30.0)	207 (41.4)	11.3	*0.0002*	244 (49.1)	19.1	*<0.0001*
Week 24	109 (22.0)	171 (34.2)	12.1	*<0.0001*	198 (39.8)	18.0	*<0.0001*
CDAI change from BL							
Week 16	-3.34 (0.516)	-6.81 (0.515)	-3.48	*<0.0001*	-7.76 (0.518)	-4.42	*<0.0001*
Week 24	-3.00 (0.530)	-6.74 (0.527)	-3.75	*<0.0001*	-7.92 (0.528)	-4.92	*<0.0001*
DAS28(CRP) change from BL							
Week 16	-0.27 (0.048)	-0.67 (0.048)	-0.40	*<0.0001*	-0.74 (0.048)	-0.47	*<0.0001*
Week 24	-0.25 (0.050)	-0.65 (0.049)	-0.40	*<0.0001*	-0.77 (0.050)	-0.52	*<0.0001*
EULAR Good/Moderate Response							
Week 16	149 (30.0)	233 (46.6)	16.5	*<0.0001*	247 (49.7)	19.7	*<0.0001*
Week 24	95 (19.2)	173 (34.6)	15.4	*<0.0001*	196 (39.4)	20.4	*<0.0001*
MASES change from BL[e]							
Week 16	-0.9 (0.16)	-1.0 (0.16)	-0.1	0.6232	-1.2 (0.16)	-0.3	0.1798
Week 24	-0.8 (0.17)	-1.2 (0.17)	-0.3	0.1538	-1.4 (0.17)	-0.5	*0.0194*
MASES ≥ 20% improvement							
Week 16	161/311 (51.8)	163/307 (53.1)	1.4	0.7233	178/327 (54.4)	2.7	0.4974
Week 24	155/311 (49.8)	171/307 (55.7)	6.0	0.1363	188/327 (57.5)	7.6	0.0549
MASES zero score							
Week 16	66/311 (21.2)	78/307 (25.4)	4.0	0.2373	70/327 (21.4)	0.3	0.9207
Week 24	70/311 (22.5)	84/307 (27.4)	4.8	0.1686	90/327 (27.5)	5.1	0.1370
Dactylitis severity score change from BL[f]							
Week 16	-1.3 (0.18)	-1.4 (0.17)	-0.2	0.4520	-1.7 (0.17)	-0.5	*0.0485*
Week 24	-1.2 (0.17)	-1.5 (0.17)	-0.3	0.2520	-1.8 (0.16)	-0.6	*0.0097*

Table 15: Summary of Other Indices of Disease Activity of Active PsA Endpoints from the Pooled Analysis (FAS)（つづき）

Endpoint Visit	Placebo N = 496	APR 20 BID N = 500			APR 30 BID N = 497		
	Response (n [%]) or Change from Baseline[a]	Response (n [%]) or Change from Baseline[a]	Trt. Effect[b]	P-value[c]	Response (n [%]) or Change from Baseline[a]	Trt. Effect[b]	P-value[c]
Dactylitis severity score ≥ 1-point improvement							
Week 16	120/205 (58.5)	134/207 (64.7)	6.0	0.2132	143/221 (64.7)	6.1	0.1979
Week 24	125/205 (61.0)	142/207 (68.6)	7.2	0.1246	156/221 (70.6)	9.7	*0.0351*
Dactylitis severity score zero score							
Week 16	79/205 (38.5)	87/207 (42.0)	3.3	0.4953	89/221 (40.3)	1.8	0.7062
Week 24	80/205 (39.0)	95/207 (45.9)	6.8	0.1683	102/221 (46.2)	7.3	0.1303

ANCOVA = analysis of covariance; APR = apremilast; BID = twice daily; BL = baseline; CDAI = Clinical Disease Activity Index; CMH = Cochran-Mantel-Haenszel; CRP = C-reactive protein; DAS28(CRP) = 28-joint Disease Activity Score; DMARD = disease-modifying antirheumatic drug; EULAR = European League Against Rheumatism; FAS = Full Analysis Set; LS = least squares; MASES = Maastricht Ankylosing Spondylitis Enthesitis Score; NRI = nonresponder imputation; PASI = Psoriasis Area and Severity Index; PsARC = Psoriatic Arthritis Response Criteria; SE = standard error; Trt. = treatment.

[a] Change from Baseline is LS mean change (SE).

[b] Treatment effect for categorical endpoints is based on adjusted difference in proportions for apremilast versus placebo (weighted average of the treatment differences across the strata of baseline disease-modifying antirheumatic drug (DMARD) use and study with the CMH weights). Treatment effect for continuous endpoints is the difference in LS means based on an analysis of covariance (ANCOVA) model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and study as factors, and baseline value as a covariate.

[c] For categorical endpoints, 2-sided P-value is based on Cochran-Mantel-Haenszel (CMH) test adjusting for baseline DMARD use and study. For continuous endpoints, P-value is based on an ANCOVA model for the change from baseline at Week 16, with treatment group, baseline DMARD use, and study as factors, and baseline value as a covariate. P-values in italics for the pooled analysis are ≤ 0.050 and considered nominally significant as there was no adjustment for multiplicity.

[d] PASI-75 responses were evaluated in subjects with Baseline psoriatic skin involvement ≥ 3% body surface area (N = 231 placebo, 248 APR 20 BID, and 249 APR 30 BID).

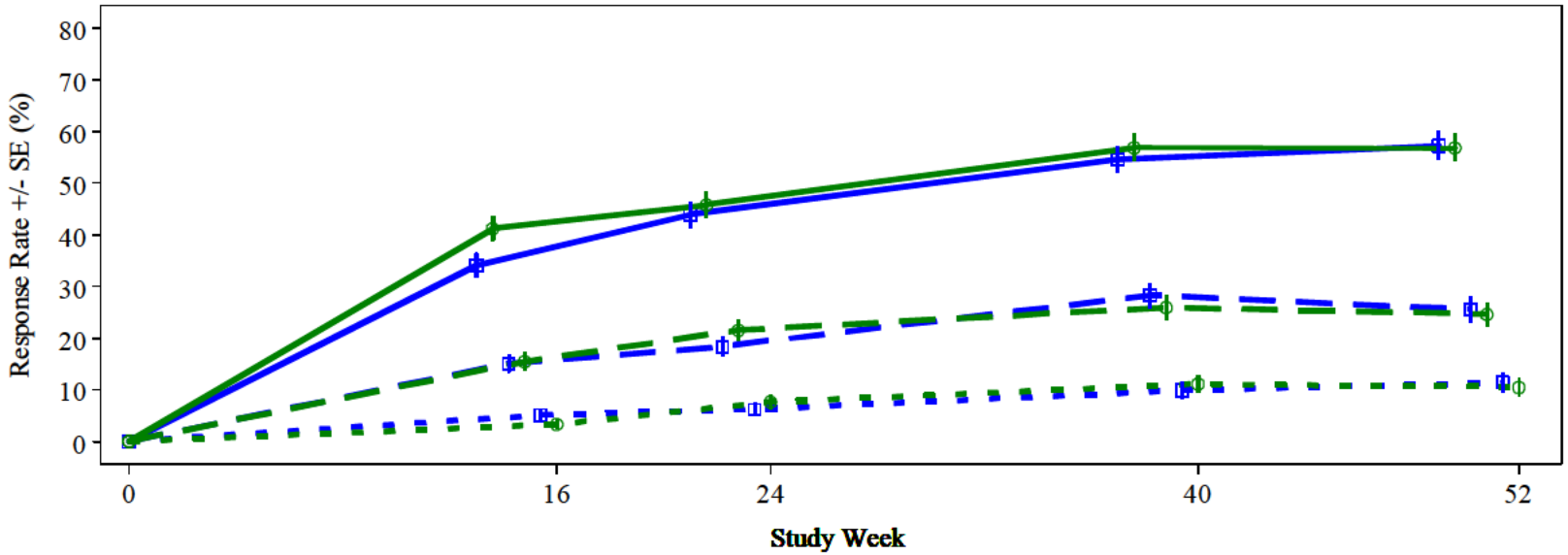
[e] Change from Baseline in MASES score evaluated in subjects with pre-existing enthesopathy (MASES > 0) at Baseline and at least 1 post-baseline value.

[f] Change from Baseline in dactylitis severity score evaluated in subjects with pre-existing dactylitis (dactylitis severity score > 0) at Baseline and at least 1 post-baseline value.

Note: For categorical analyses, subjects who did not have sufficient data (observed or imputed) for a definitive determination of response status at Week 16/24 are counted as non-responders.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 2.4.1, Table 2.4.2, Table 2.7.1, Table 2.7.2, Table 2.7.3, Table 2.7.4, Table 2.7.5, Table 2.7.6, Table 2.8.1, Table 2.8.2, Table 2.8.3, Table 2.8.4, Table 2.8.5, Table 2.8.6, Table 2.9.1, Table 2.9.2, Table 2.10.1, Table 2.10.2, Table 2.11.1, Table 2.11.2, Table 2.13.3, Table 2.13.4, Table 2.14.1, Table 2.14.2.

Figure 35:Modified ACR 20/50/70 Responses During Weeks 0-52 in Subjects Initially Randomized to Apremilast (Pooled Analysis of Studies PSA-002, PSA-003, and PSA-004; Data as Observed)



Treatment	n/m (%)	n/m (%)	n/m (%)	n/m (%)
ACR 20 - 20 mg BID	160/469 (34.1)	191/435 (43.9)	208/381 (54.6)	204/356 (57.3)
ACR 20 - 30 mg BID	185/449 (41.2)	196/428 (45.8)	223/392 (56.9)	212/373 (56.8)
ACR 50 - 20 mg BID	71/470 (15.1)	80/435 (18.4)	108/382 (28.3)	91/356 (25.6)
ACR 50 - 30 mg BID	70/453 (15.5)	93/432 (21.5)	102/393 (26.0)	92/374 (24.6)
ACR 70 - 20 mg BID	24/473 (5.1)	27/435 (6.2)	38/385 (9.9)	41/360 (11.4)
ACR 70 - 30 mg BID	15/457 (3.3)	33/432 (7.6)	44/396 (11.1)	39/373 (10.5)

ACR 20/50/70 = American College of Rheumatology 20%/50%/70% response criteria; APR = apremilast; BID = twice daily; n/m = number of responders/number of subjects initially randomized to apremilast.

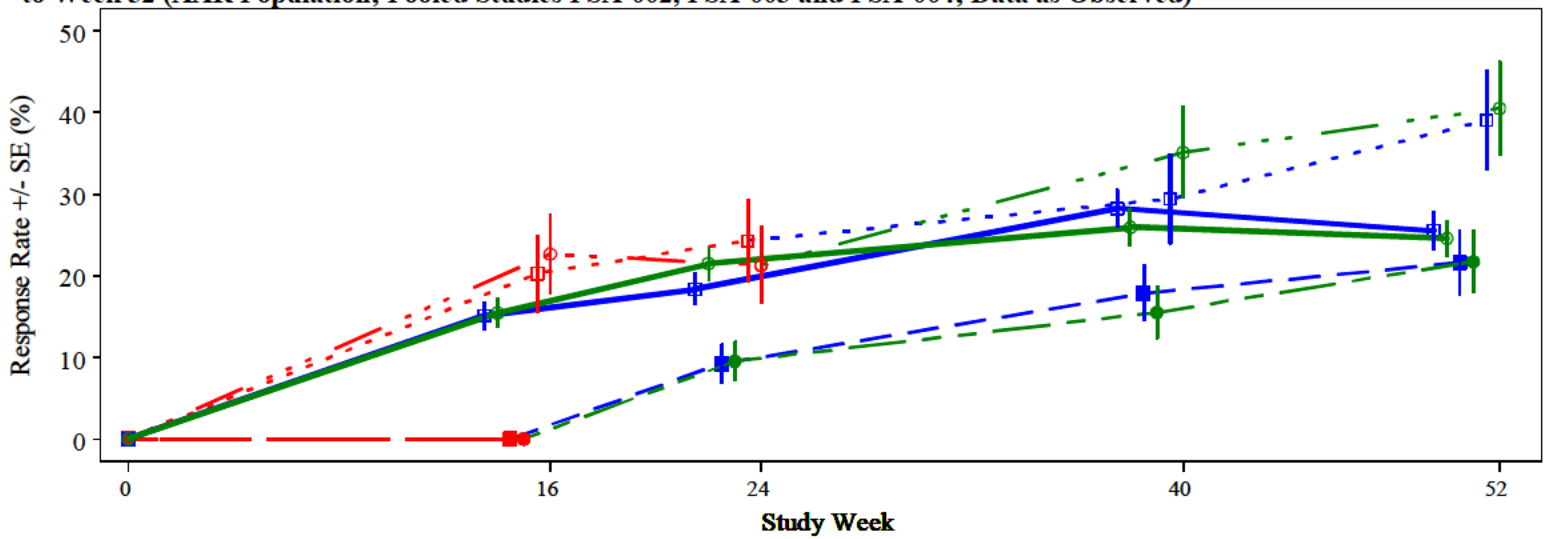
Note: Subjects who discontinued early prior to the time point and subjects who did not have sufficient data for a definitive determination of response status at the time point are counted as non-responders.

Note: This analysis includes only subjects who were randomized to apremilast at baseline; therefore, study visits correspond also to exposure to apremilast.

Note: To enhance visual clarity, the data points collected at Weeks 16, 24, 40, and 52 are displayed in a staggered fashion above the hash mark for the corresponding time point.

Source: 5.3.5.3.2 項 有効性併合解析（PsA） Table 2.18.1, Table 2.19.1, Table 2.20.1.

Figure 36:Proportion of All Subjects Exposed to Apremilast Achieving Modified ACR 50 Responses During the Apremilast-exposure Period up to Week 52 (AAR Population; Pooled Studies PSA-002, PSA-003 and PSA-004; Data as Observed)



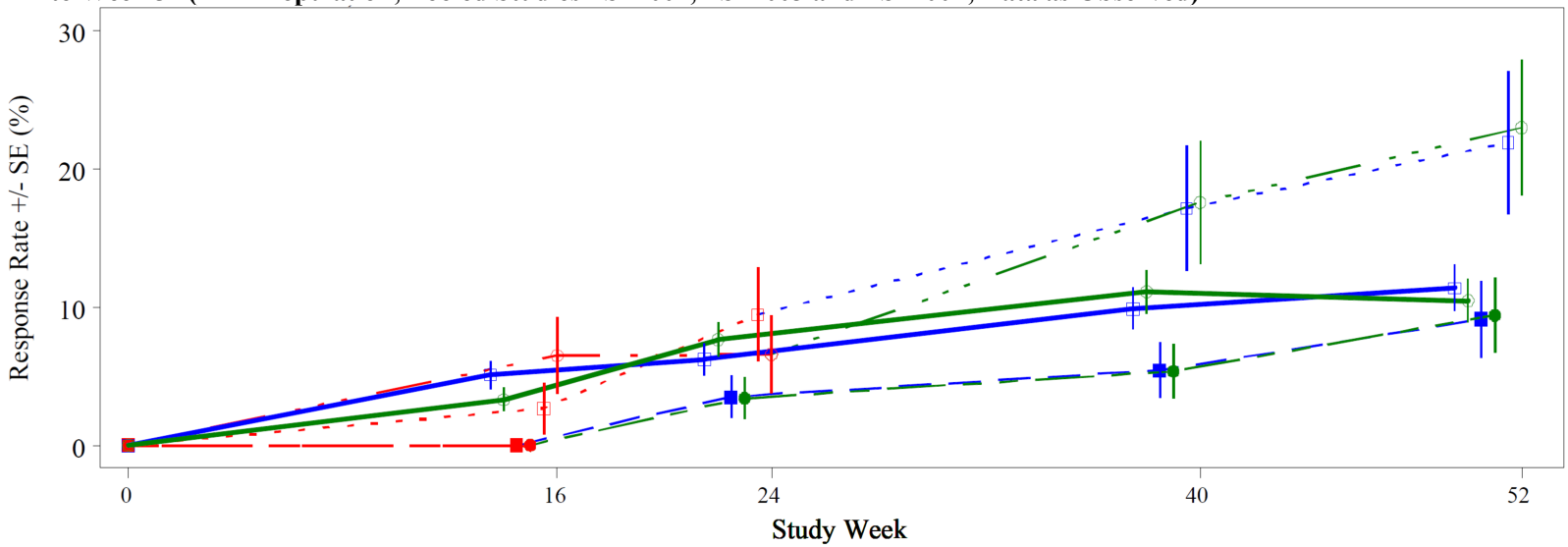
Treatment	n/m (%)	n/m (%)	n/m (%)	n/m (%)
20 mg BID	71/470 (15.1)	80/435 (18.4)	108/382 (28.3)	91/356 (25.6)
30 mg BID	70/453 (15.5)	93/432 (21.5)	102/393 (26.0)	92/374 (24.6)
PBO/20 EE	0/145 (0.0)	13/141 (9.2)	23/129 (17.8)	24/111 (21.6)
PBO/20 XO	15/ 74 (20.3)	18/ 74 (24.3)	20/ 68 (29.4)	25/ 64 (39.1)
PBO/30 EE	0/147 (0.0)	14/147 (9.5)	20/129 (15.5)	25/115 (21.7)
PBO/30 XO	17/ 75 (22.7)	16/ 75 (21.3)	26/ 74 (35.1)	30/ 74 (40.5)

AAR = apremilast subjects as initially randomized/re-randomized; ACR 70 = American College of Rheumatology 70% response criteria; APR = apremilast; BID = twice daily; EE = early escape (re-randomized to apremilast at Week 16); n/m = number of responders/number of subjects with sufficient data for definitive determination of response status at each time point (including subjects who discontinued early between the preceding visit and the visit in question); PBO = placebo; XO = cross-over (re-randomized to apremilast at Week 24).

Note: To enhance visual clarity, the data points collected at Weeks 16, 24, 40, and 52 are displayed in a staggered fashion above the hash mark for the corresponding time point.

Source: 5.3.5.3.2 項 有効性併合解析（PsA） Table 2.19.1.

Figure 37: Proportion of All Subjects Exposed to Apremilast Achieving Modified ACR 70 Responses During the Apremilast-exposure Period up to Week 52 (AAR Population; Pooled Studies PSA-002, PSA-003 and PSA-004; Data as Observed)



Treatment	n/m (%)	n/m (%)	n/m (%)	n/m (%)
20 mg BID	24/473 (5.1)	27/435 (6.2)	38/385 (9.9)	41/360 (11.4)
30 mg BID	15/457 (3.3)	33/432 (7.6)	44/396 (11.1)	39/373 (10.5)
PBO/20 EE	0/145 (0.0)	5/143 (3.5)	7/129 (5.4)	10/110 (9.1)
PBO/20 XO	2/ 75 (2.7)	7/ 74 (9.5)	12/ 70 (17.1)	14/ 64 (21.9)
PBO/30 EE	0/147 (0.0)	5/147 (3.4)	7/131 (5.3)	11/117 (9.4)
PBO/30 XO	5/ 77 (6.5)	5/ 76 (6.6)	13/ 74 (17.6)	17/ 74 (23.0)

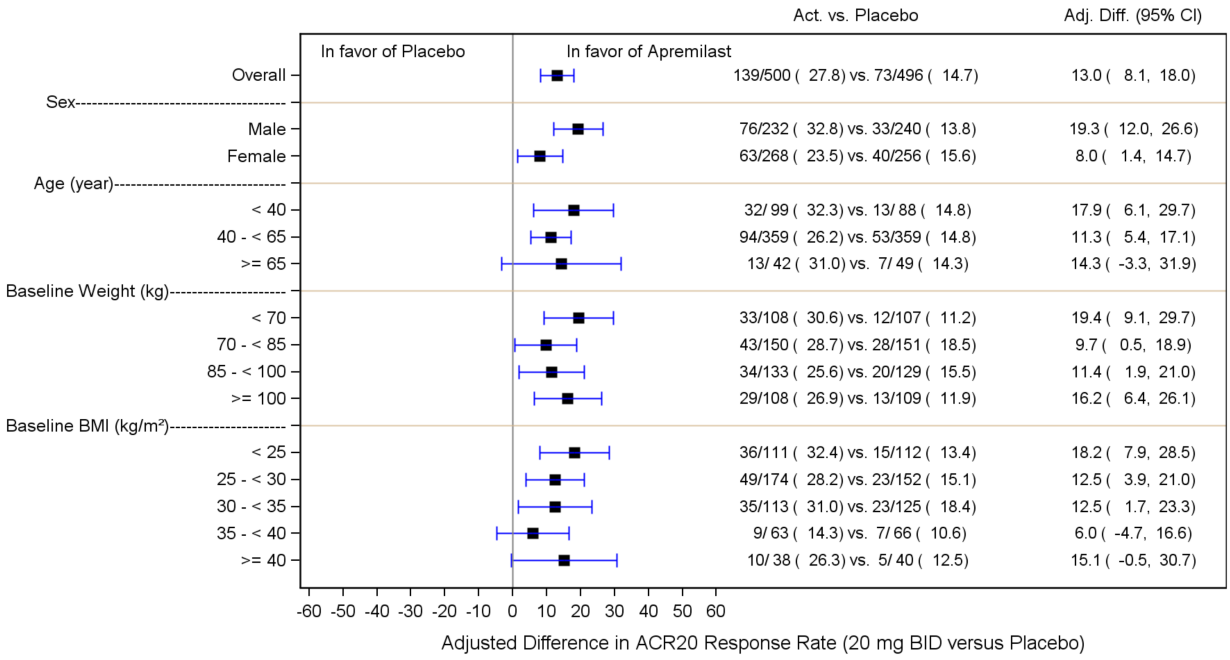
AAR = apremilast subjects as initially randomized/re-randomized; ACR 50 = American College of Rheumatology 50% response criteria; APR = apremilast; BID = twice daily; EE = early escape (re-randomized to apremilast at Week 16); n/m = number of responders/number of subjects with sufficient data for definitive determination of response status at each time point (including subjects who discontinued early between the preceding visit and the visit in question); PBO = placebo; XO = cross-over (re-randomized to apremilast at Week 24).

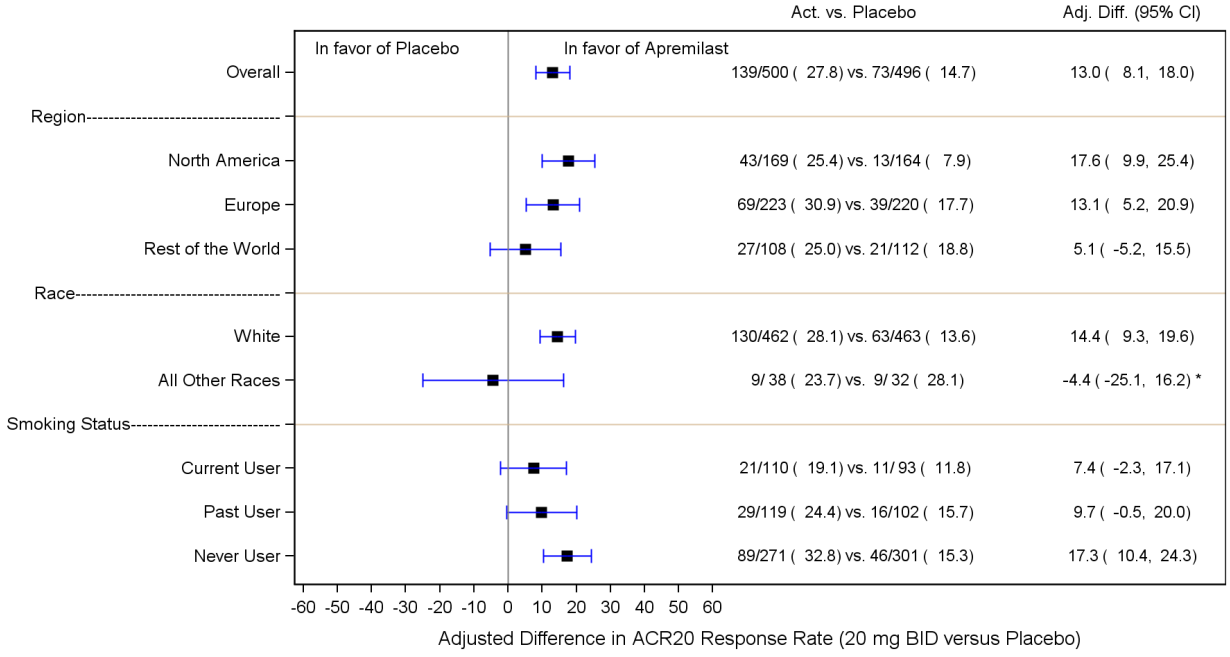
Note: To enhance visual clarity, the data points collected at Weeks 16, 24, 40, and 52 are displayed in a staggered fashion above the hash mark for the corresponding time point.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 2.20.1.

6.10. 部分集団解析

Figure 38: Modified ACR 20 Response in the APR 20 BID Treatment Group at Week 24 by Demographic Subpopulation (Pooled Analysis; FAS; NRI)





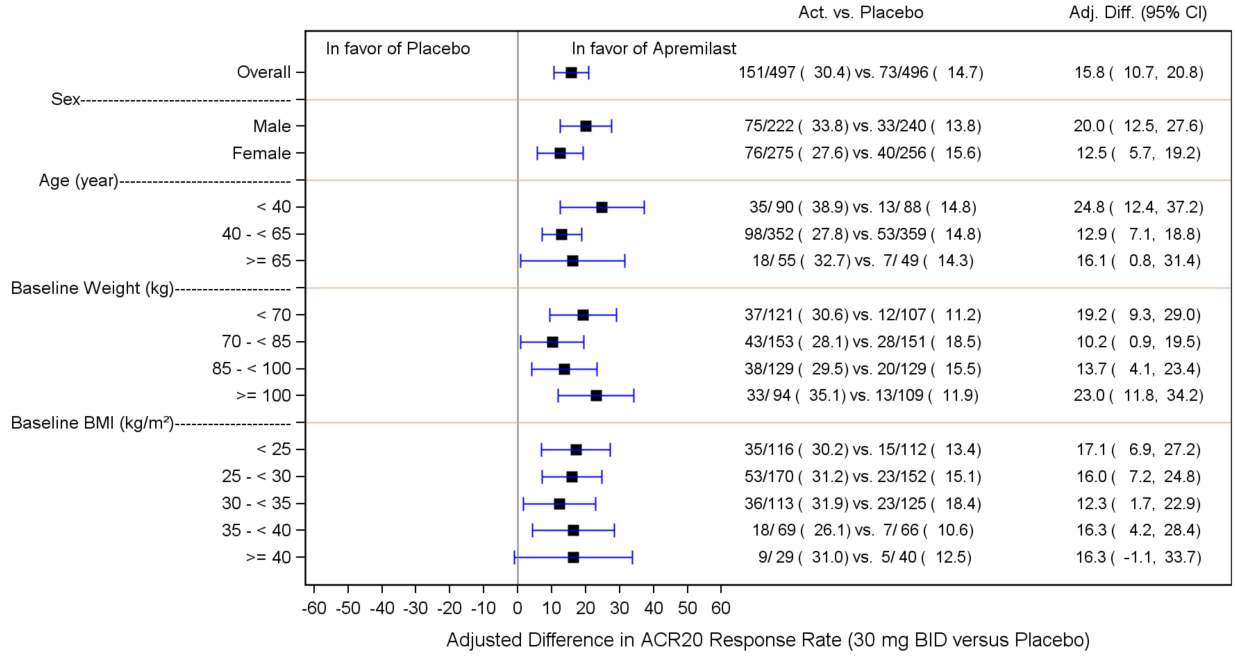
ACR 20 = 20% improvement in American College of Rheumatology response criteria; Act = active treatment; Adj = adjusted; APR = apremilast; BID = twice daily; BMI = body mass index; CI = confidence interval; Diff = difference; FAS = full analysis set; NRI = non-responder imputation; vs. = versus.

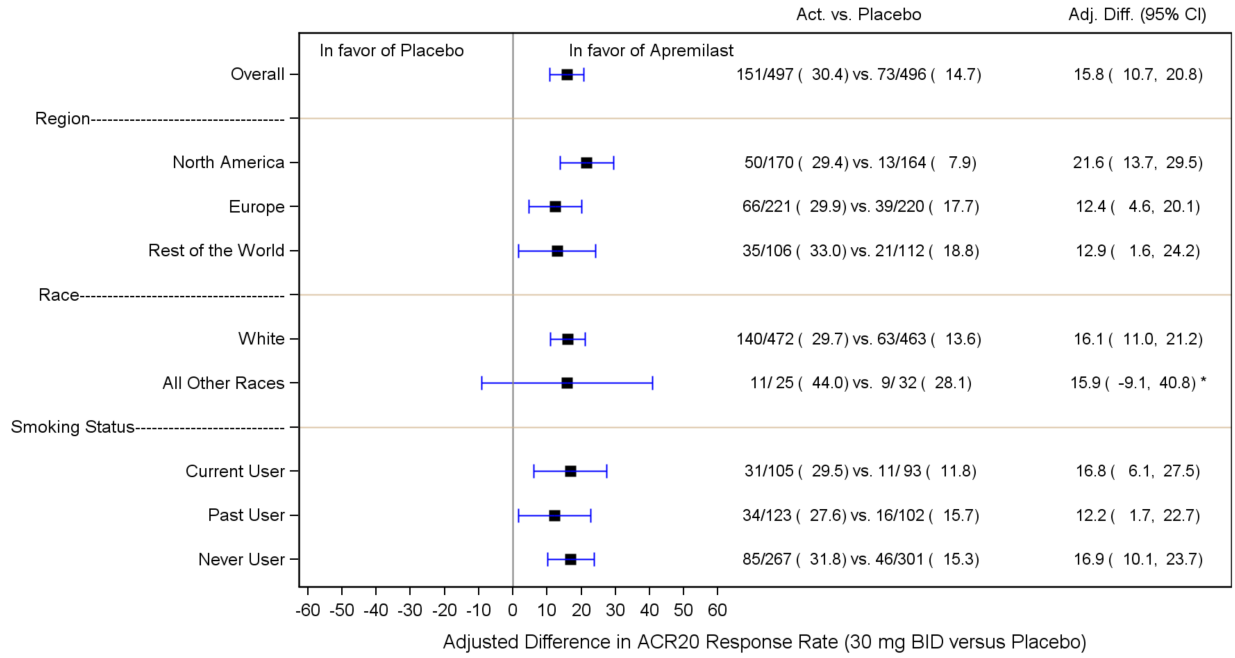
*= unadjusted difference and CI.

Note: Subjects who discontinued early prior to Week 24 and subjects who did not have sufficient data for a definitive determination of response status at Week 24 are counted as non-responders.

Source: 5.3.5.3.2 項 有効性併合解析（PsA） Table 2.1.2, Table 3.1.2.

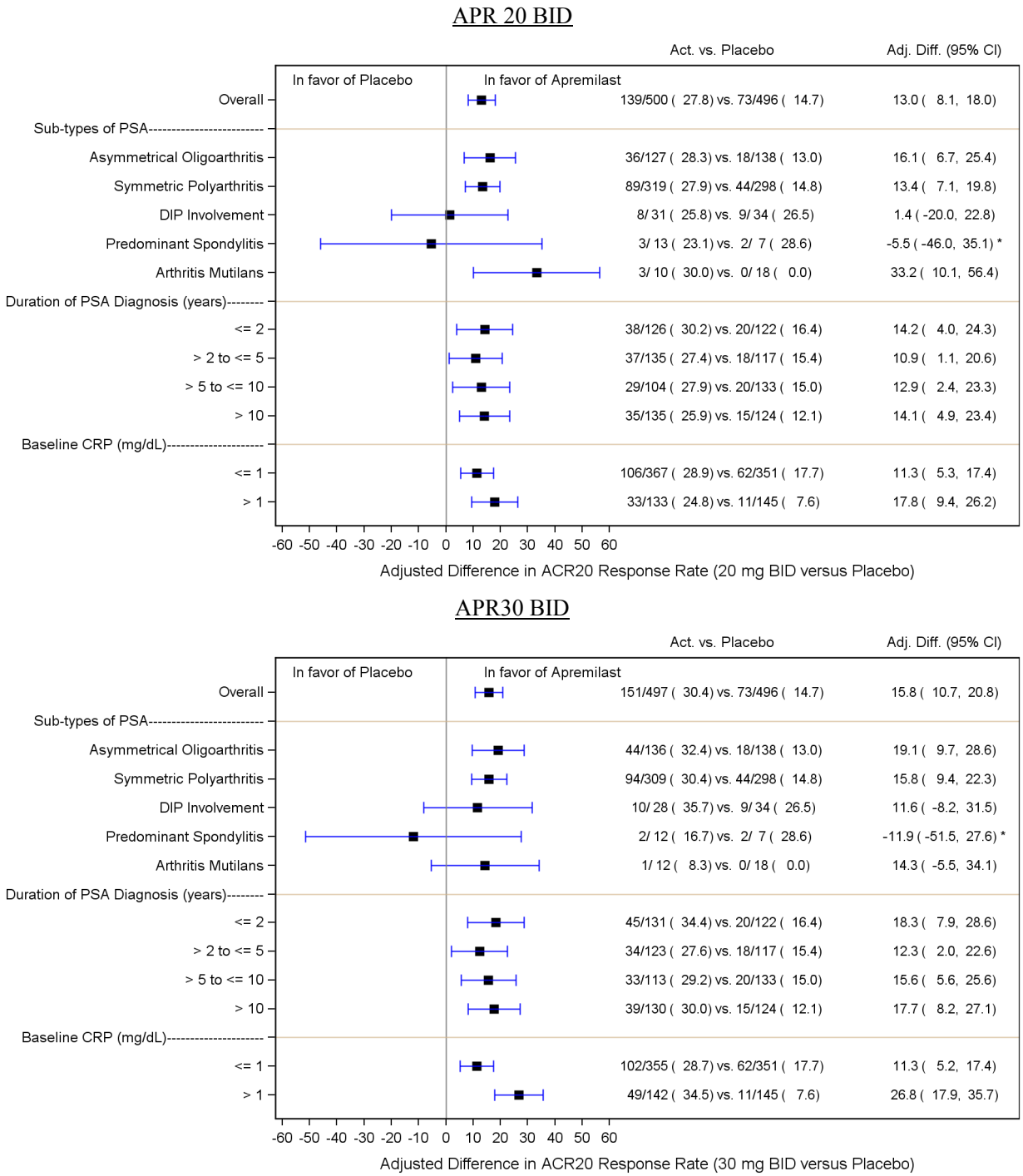
Figure 39: Modified ACR 20 Response in the APR 30 BID Treatment Group at Week 24 by Demographic Subpopulation (Pooled Analysis; FAS; NRI)





ACR 20 = 20% improvement in American College of Rheumatology response criteria; Act = active treatment; Adj = adjusted; APR = apremilast; BID = twice daily; BMI = body mass index; CI = confidence interval; Diff = difference; FAS = full analysis set; NRI = non-responder imputation; vs. = versus.
*= unadjusted difference and CI.
Note: Subjects who discontinued early prior to Week 24 and subjects who did not have sufficient data for a definitive determination of response status at Week 24 are counted as non-responders.
Source: 5.3.5.3.2 項 有効性併合解析（PsA） Table 2.1.2, Table 3.1.2.

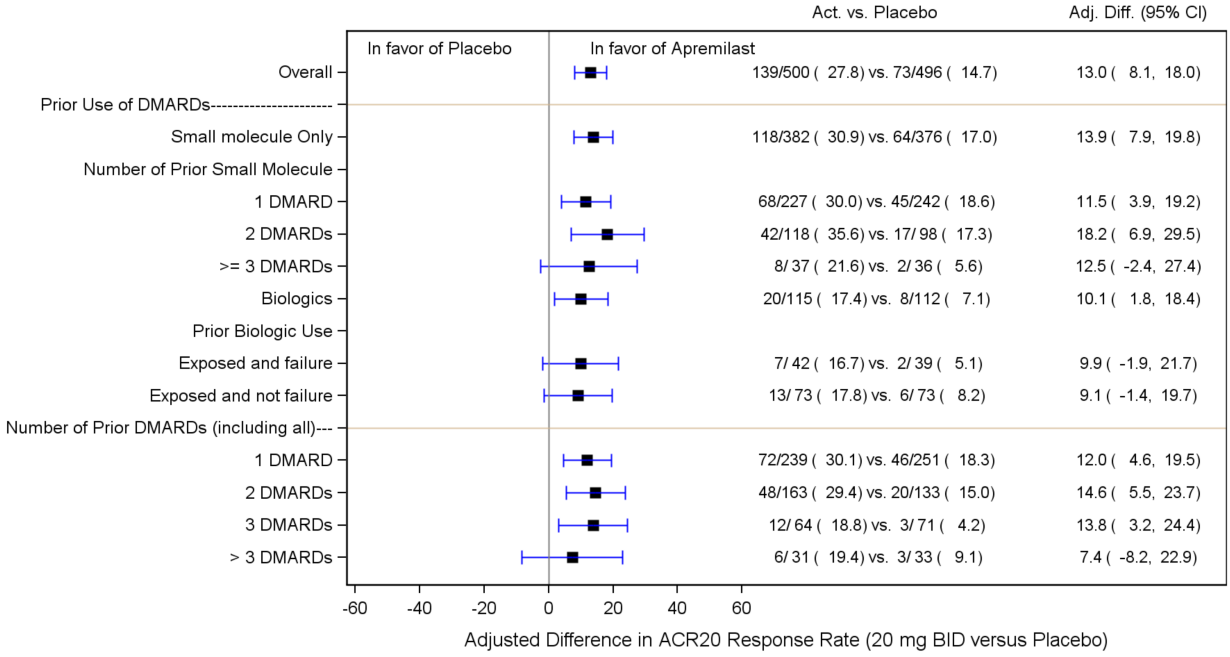
Figure 40: Modified ACR 20 Response at Week 24 by PsA Subtype, PsA Duration, and Baseline CRP (Pooled Analysis; FAS; NRI)



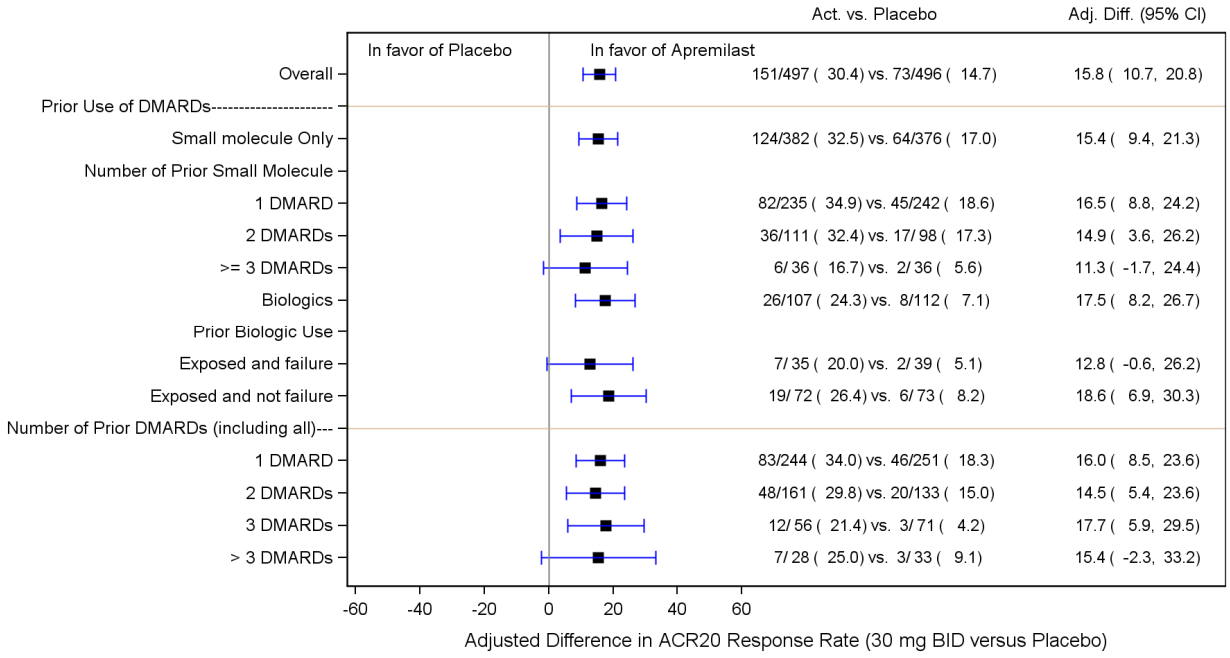
ACR 20 = 20% improvement in American College of Rheumatology response criteria; Act = active treatment; Adj = adjusted; APR = apremilast; BID = twice daily; CI = confidence interval; CRP = C-reactive protein; Diff = difference; DIP = distal interphalangeal; FAS = full analysis set; NRI = non-responder imputation; PsA = psoriatic arthritis; vs. = versus.
*=unadjusted difference and CI.
Note: Subjects who discontinued early prior to Week 24 and subjects who did not have sufficient data for a definitive determination of response status at Week 24 are counted as non-responders.
Source: 5.3.5.3.2 項 有効性併合解析（PsA） Table 2.1.2, Table 3.1.2.

Figure 41: Modified ACR 20 Response at Week 24 by Prior DMARD Use (Pooled Analysis; FAS; NRI)

APR 20 BID



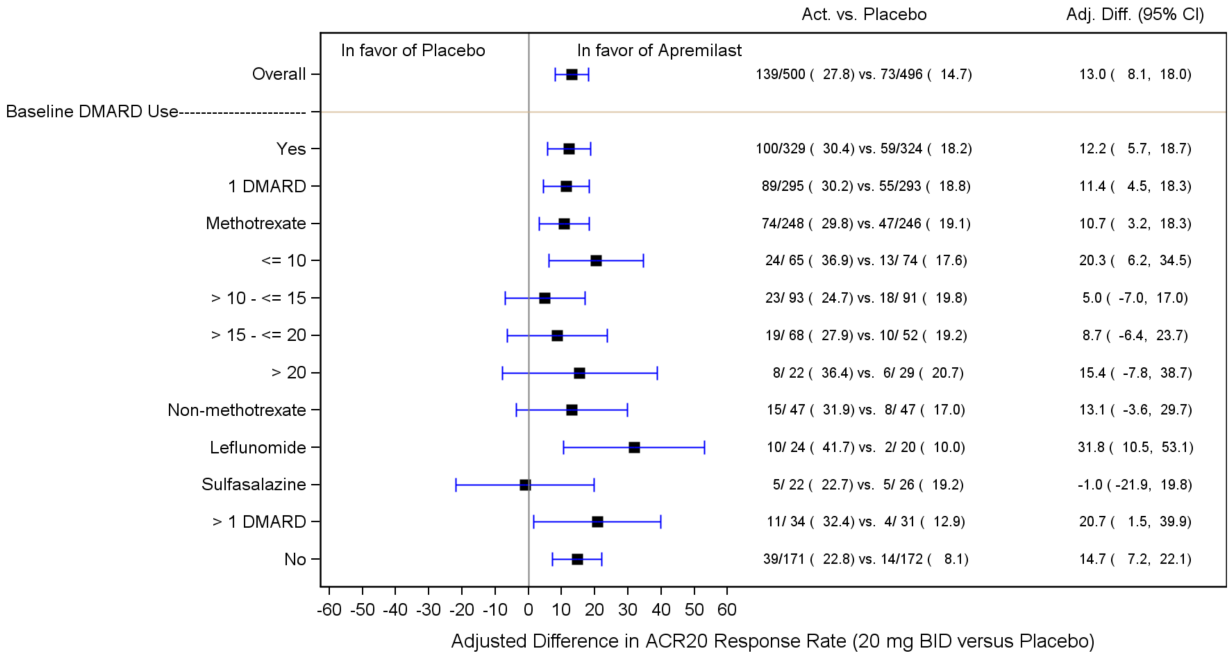
APR30 BID



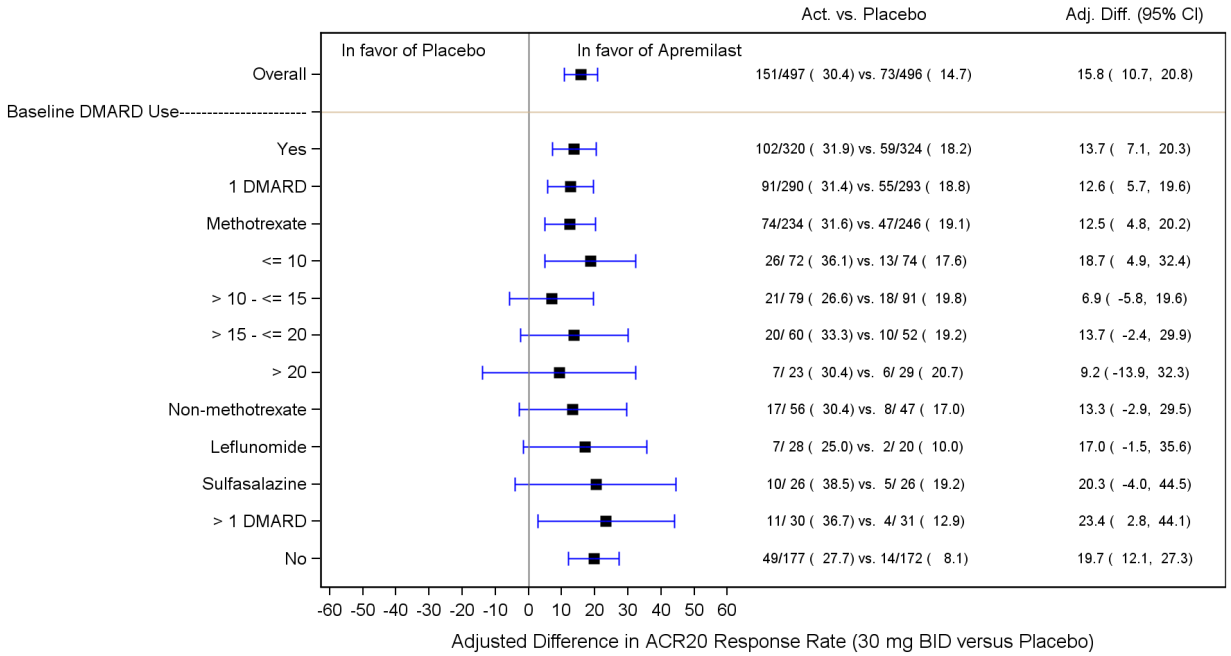
ACR 20 = 20% improvement in American College of Rheumatology response criteria; Act = active treatment; Adj = adjusted; APR = apremilast; BID = twice daily; CI = confidence interval; Diff = difference; DMARD = disease-modifying antirheumatic drug; FAS = full analysis set; NRI = non-responder imputation; vs. = versus.
*=unadjusted difference and CI.
Note: Subjects who discontinued early prior to Week 24 and subjects who did not have sufficient data for a definitive determination of response status at Week 24 are counted as non-responders.
Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 2.1.2, Table 3.1.2.

Figure 42: Modified ACR 20 Response at Week 24 by Baseline DMARD Use (Pooled Analysis; FAS; NRI)

APR 20 BID

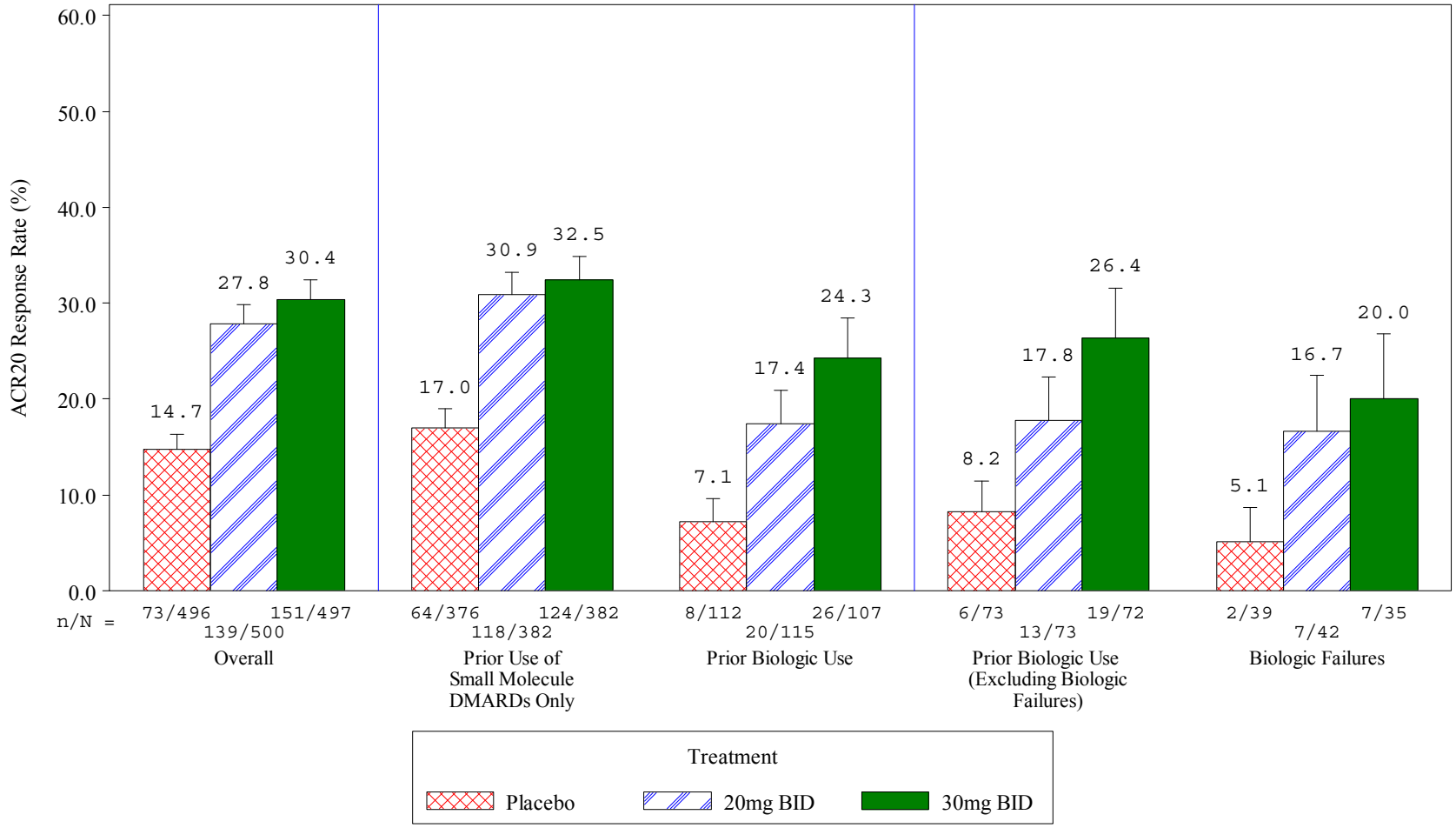


APR30 BID



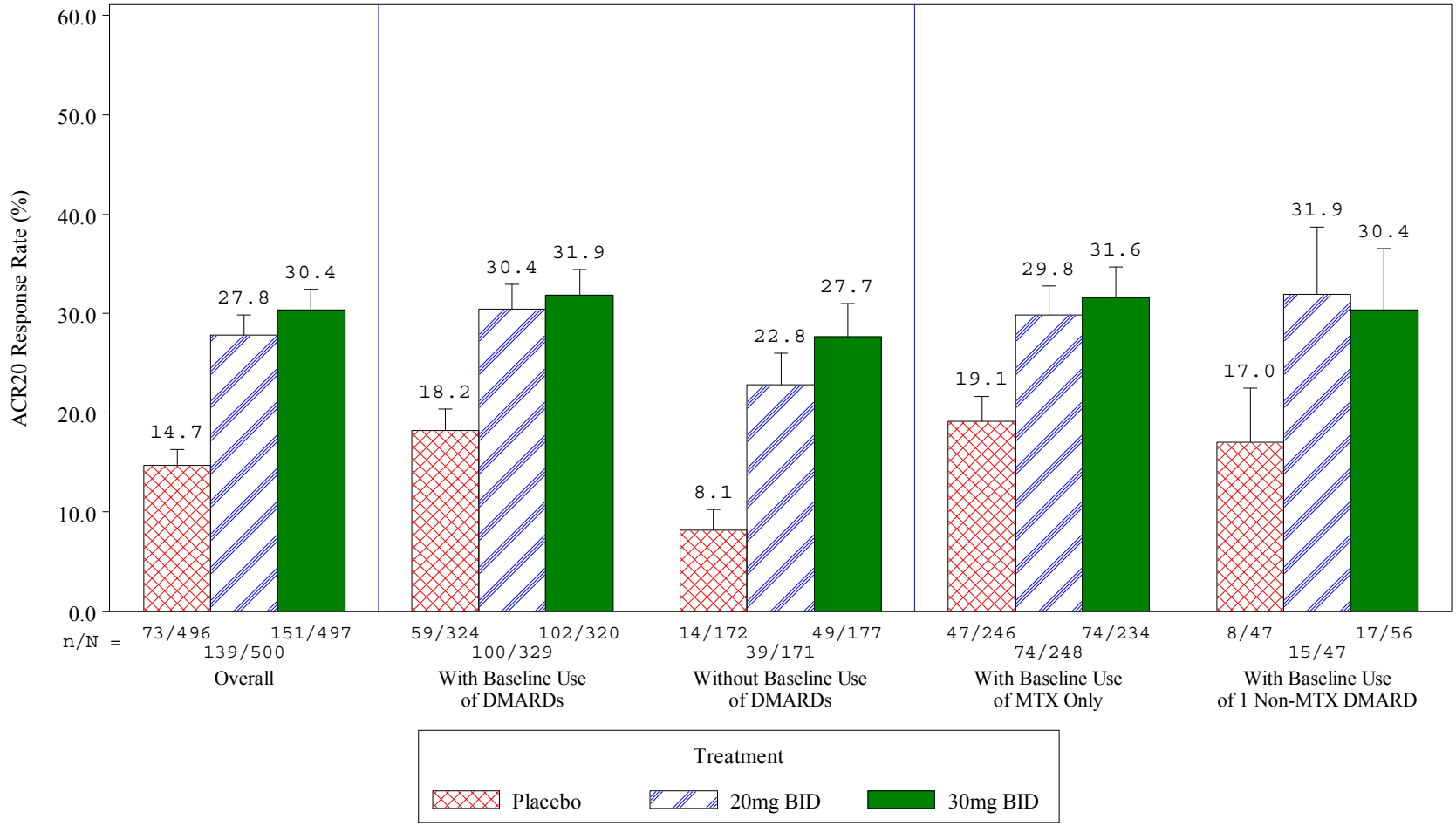
ACR 20 = 20% improvement in American College of Rheumatology response criteria; Act = active treatment; Adj = adjusted; APR = apremilast; BID = twice daily; CI = confidence interval; Diff = difference; DMARD = disease-modifying antirheumatic drug; FAS = full analysis set; NRI = non-responder imputation; vs. = versus.
*=unadjusted difference and CI.
Note: Subjects who discontinued early prior to Week 24 and subjects who did not have sufficient data for a definitive determination of response status at Week 24 are counted as non-responders.
Source: 5.3.5.3.2 項 有効性併合解析（PsA） Table 2.1.2, Table 3.1.2.

Figure 43:Modified ACR 20 Response at Week 24 by Prior Biologic DMARD Use (Pooled Analysis; FAS; NRI)



ACR 20 = 20% improvement in American College of Rheumatology response criteria; BID = twice daily; DMARD = disease-modifying antirheumatic drug; FAS = full analysis set; NRI = non-responder imputation.
Note: Error bars denote standard error.
Note: Subjects who discontinued early prior to Week 24 and subjects who did not have sufficient data for a definitive determination of response status at Week 24 are counted as non-responders.
Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 2.1.2, Table 3.1.2.

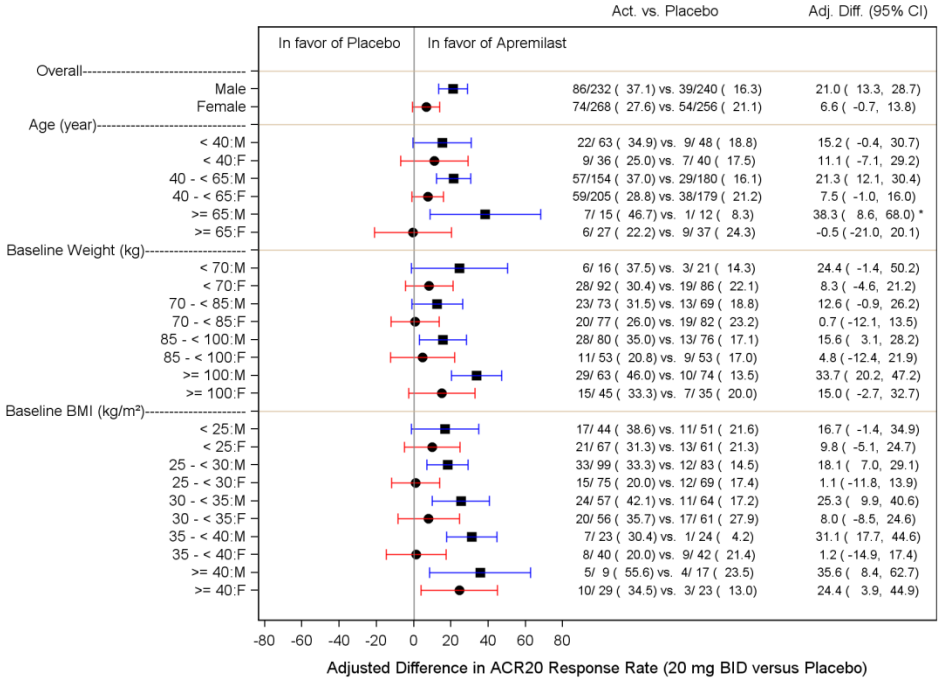
Figure 44: Modified ACR 20 Response at Week 24 by Baseline Use of Small-Molecule DMARDs (Pooled Analysis; FAS; NRI)



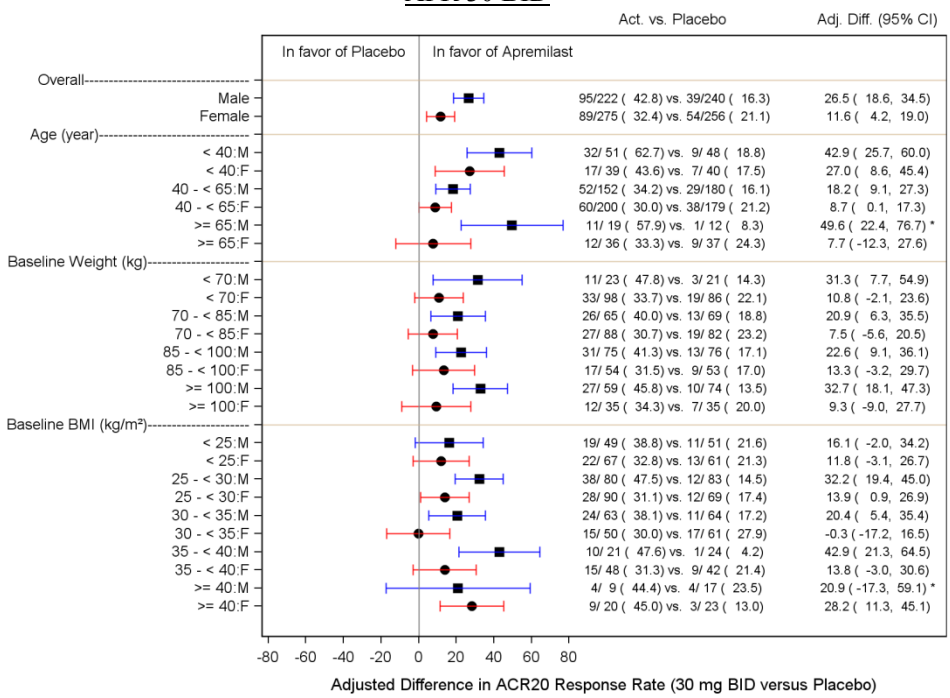
ACR 20 = 20% improvement in American College of Rheumatology response criteria; BID = twice daily; DMARD = disease-modifying antirheumatic drug; FAS = full analysis set; MTX = methotrexate; NRI = non-responder imputation.
Note: Error bars denote standard error.
Note: Subjects who discontinued early prior to Week 24 and subjects who did not have sufficient data for a definitive determination of response status at Week 24 are counted as non-responders.
Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 2.1.2, Table 3.1.2.

Figure 45: Analysis by Sex of Modified ACR 20 Response at Week 16 in Demographic Subgroups (Pooled Analysis; FAS; NRI) – Part 1

APR 20 BID



APR 30 BID



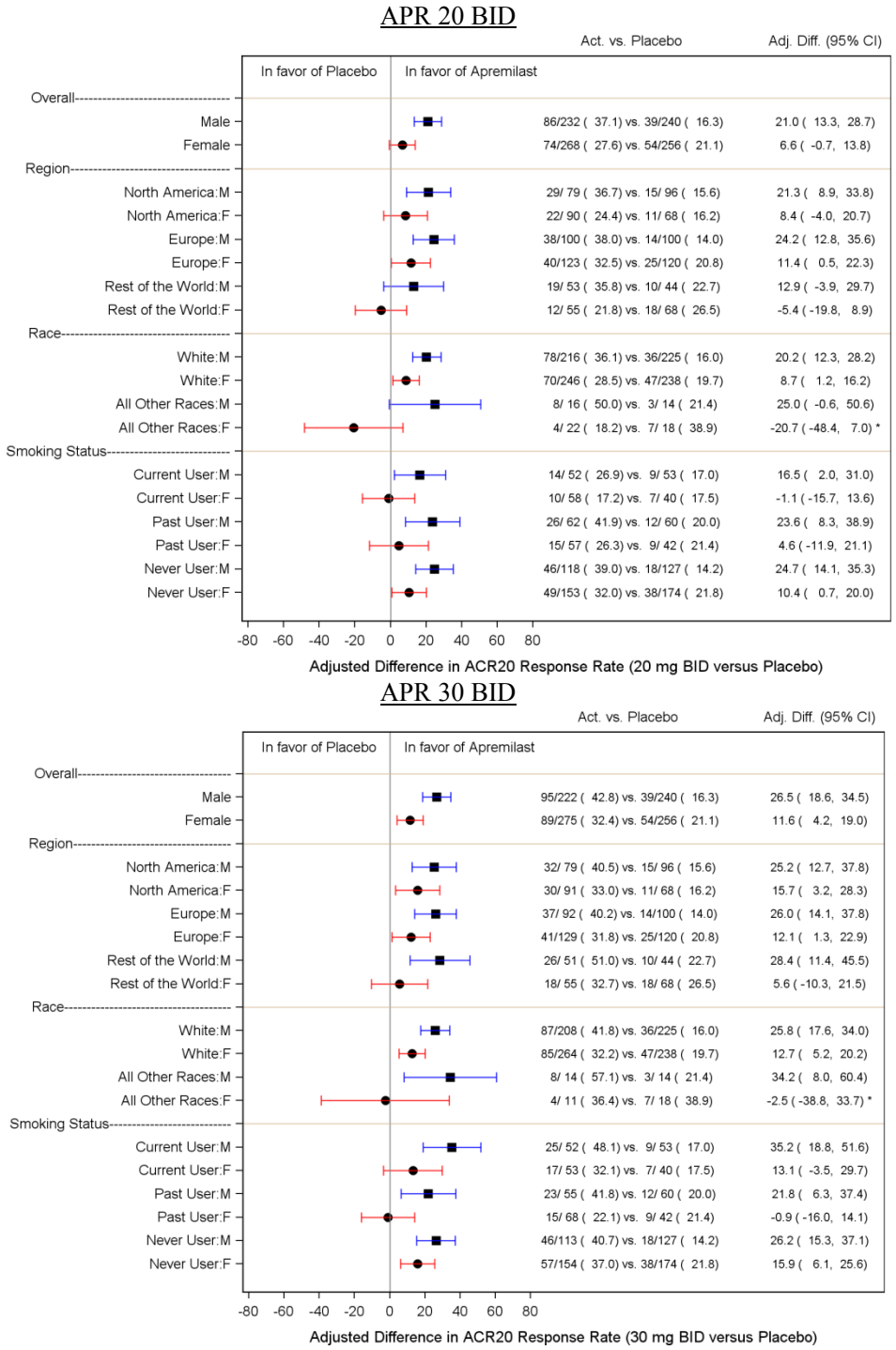
ACR 20 = 20% improvement in American College of Rheumatology response criteria; Act = active treatment; Adj = adjusted; APR = apremilast; BID = twice daily; BMI = body mass index; CI = confidence interval; Diff = difference; F = female; FAS = full analysis set; M = male; NRI = non-responder imputation; vs. = versus.

*=unadjusted difference and CI.

Note: Subjects who discontinued early prior to Week 16 and subjects who did not have sufficient data for a definitive determination of response status at Week 16 are counted as non-responders.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 3.1.1, Table 3.1.3, Table 3.1.4.

Figure 46: Analysis by Sex of Modified ACR 20 Response at Week 16 in Demographic Subgroups (Pooled Analysis; FAS; NRI) – Part 2



ACR 20 = 20% improvement in American College of Rheumatology response criteria; Act = active treatment; Adj = adjusted; APR = apremilast; BID = twice daily; CI = confidence interval; Diff = difference; F = female; FAS = full analysis set; M = male; NRI = non-responder imputation; vs. = versus.

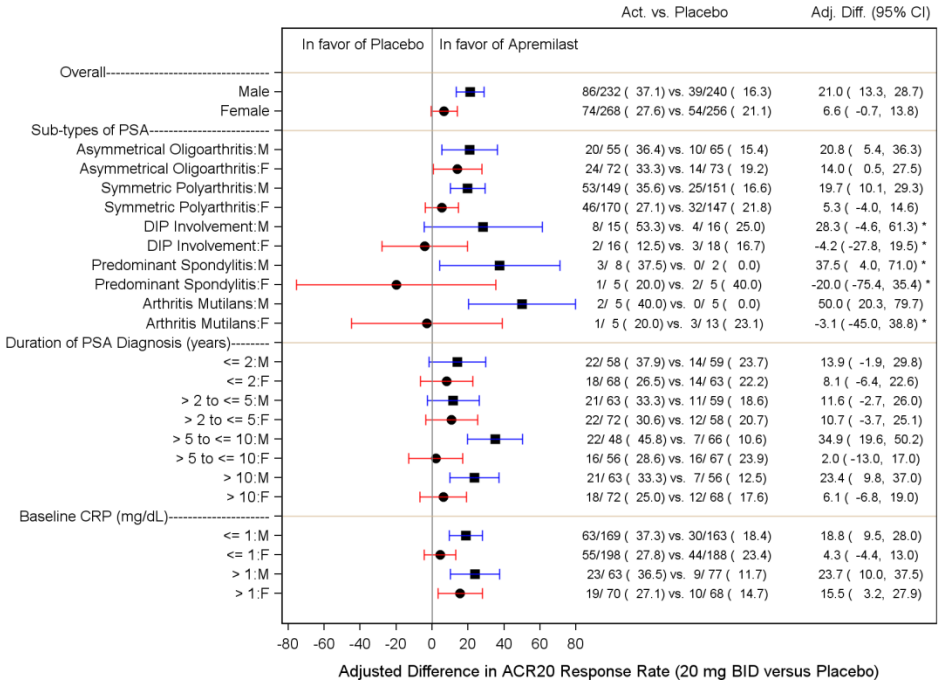
*=unadjusted difference and CI.

Note: Subjects who discontinued early prior to Week 16 and subjects who did not have sufficient data for a definitive determination of response status at Week 16 are counted as non-responders.

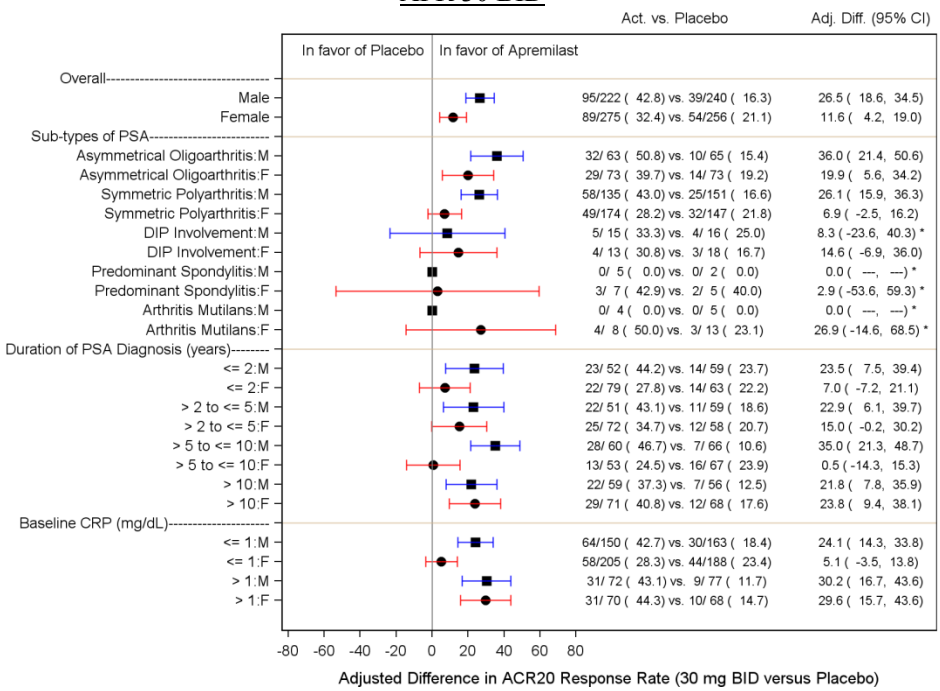
Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 3.1.1, Table 3.1.3, Table 3.1.4.

Figure 47: Analysis by Sex of Modified ACR 20 Response at Week 16 in Intrinsic Factor Subgroups (Pooled Analysis; FAS; NRI)

APR 20 BID



APR 30 BID



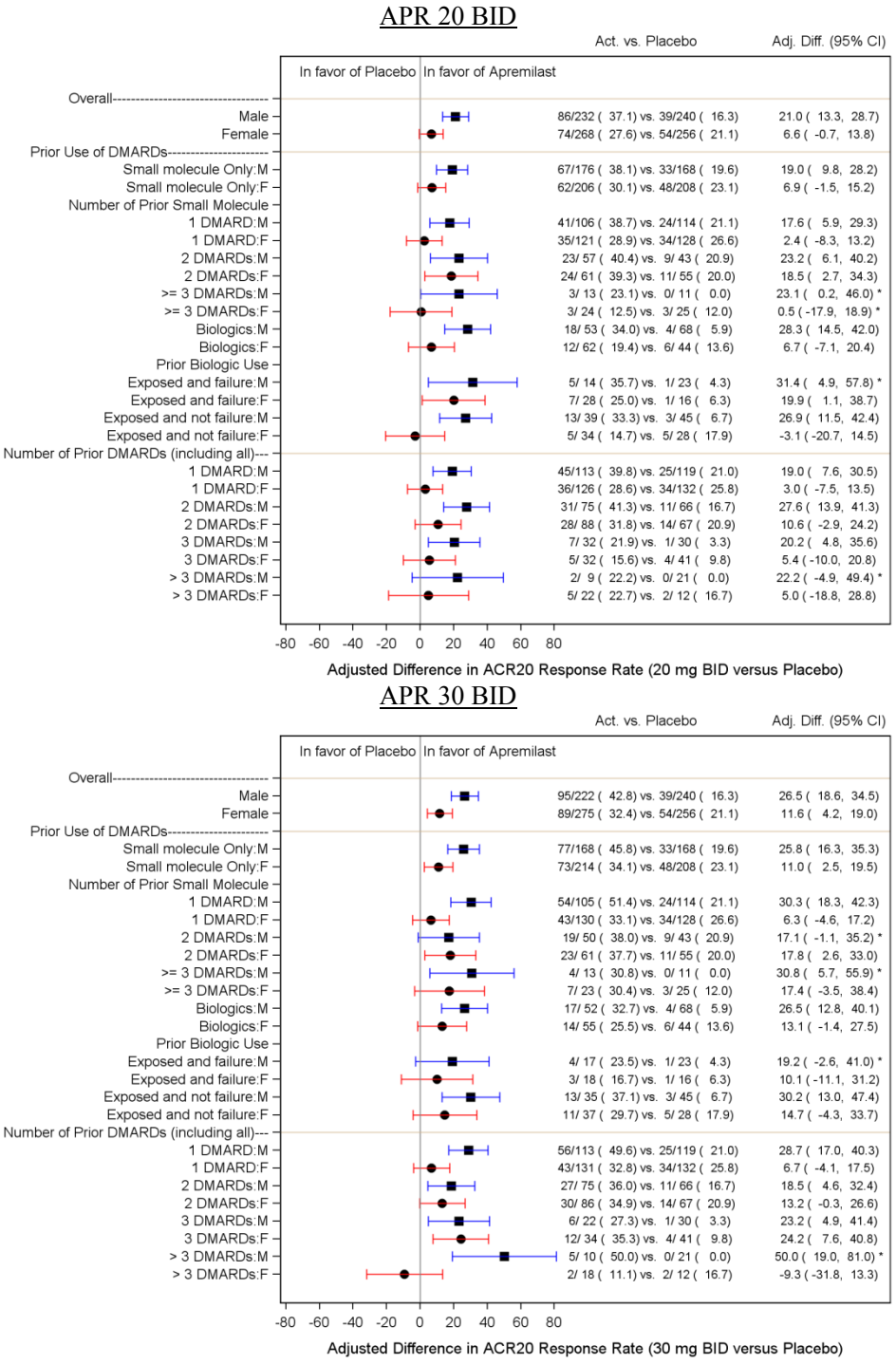
ACR 20 = 20% improvement in American College of Rheumatology response criteria; Act = active treatment; Adj = adjusted; APR = apremilast; BID = twice daily; CI = confidence interval; CRP = C-reactive protein; Diff = difference; F = female; DIP = distal interphalangeal; FAS = full analysis set; M = male; NRI = non-responder imputation; PsA = psoriatic arthritis; vs. = versus.

*=unadjusted difference and CI.

Note: Subjects who discontinued early prior to Week 16 and subjects who did not have sufficient data for a definitive determination of response status at Week 16 are counted as non-responders.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 3.1.1, Table 3.1.3, Table 3.1.4.

Figure 48: Analysis by Sex of Modified ACR 20 Response at Week 16 in Extrinsic Factor Subgroups – Prior DMARD Use (Pooled Analysis; FAS; NRI)



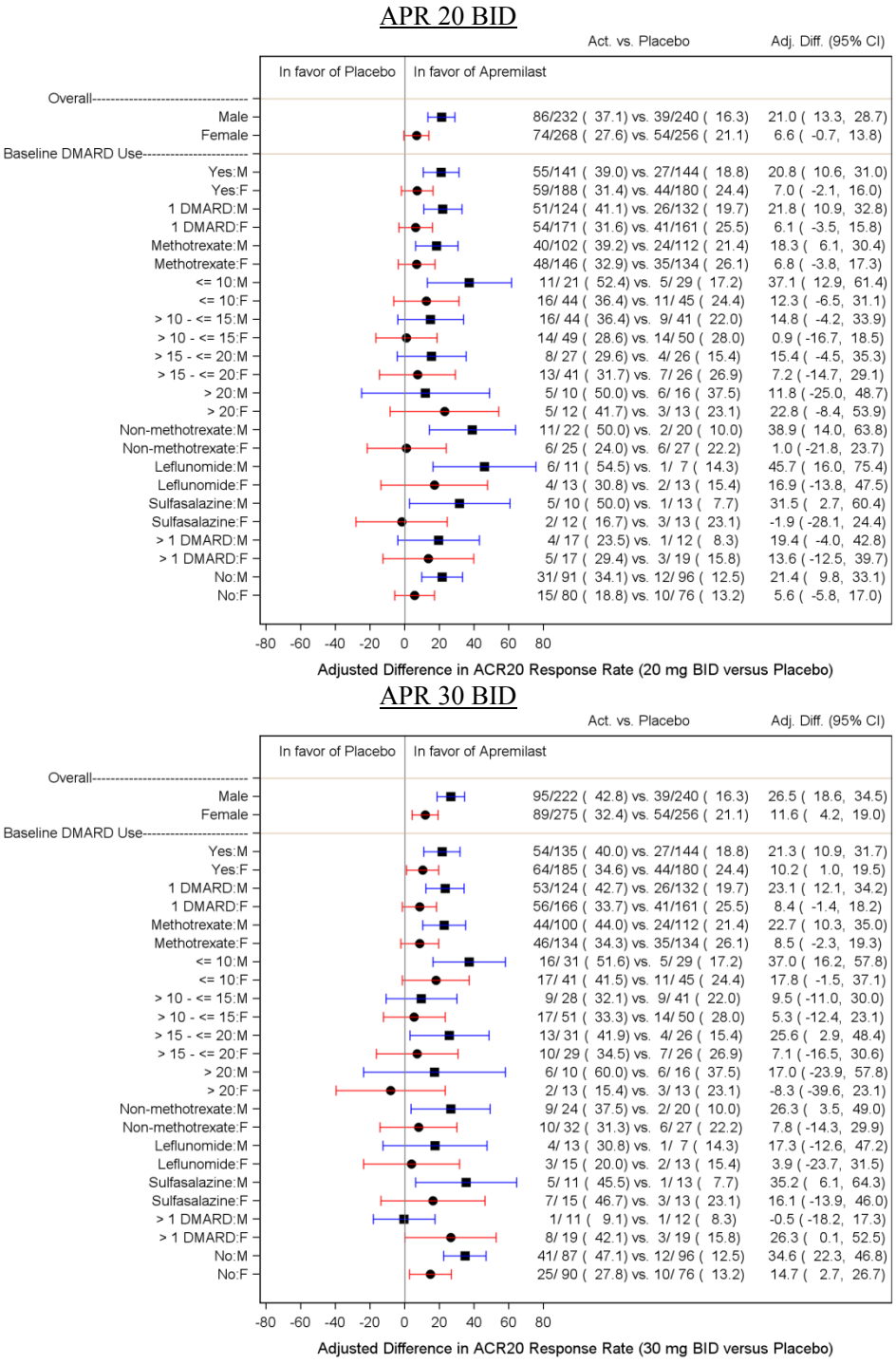
ACR 20 = 20% improvement in American College of Rheumatology response criteria; Act = active treatment; Adj = adjusted; APR = apremilast; BID = twice daily; CI = confidence interval; Diff = difference; DMARD = disease-modifying antirheumatic drug; F = female; FAS = full analysis set; M = male; NRI = non-responder imputation; vs. = versus.

*=unadjusted difference and CI.

Note: Subjects who discontinued early prior to Week 16 and subjects who did not have sufficient data for a definitive determination of response status at Week 16 are counted as non-responders.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 3.1.1, Table 3.1.3, Table 3.1.4.

Figure 49: Analysis by Sex of Modified ACR 20 Response at Week 16 in Extrinsic Factor Subgroups – Baseline DMARD Use (Pooled Analysis; FAS; NRI)



ACR 20 = 20% improvement in American College of Rheumatology response criteria; Act = active treatment; Adj = adjusted; APR = apremilast; BID = twice daily; CI = confidence interval; Diff = difference; DMARD = disease-modifying antirheumatic drug; F = female; FAS = full analysis set; M = male; NRI = non-responder imputation; vs. = versus.

*=unadjusted difference and CI.

Note: Subjects who discontinued early prior to Week 16 and subjects who did not have sufficient data for a definitive determination of response status at Week 16 are counted as non-responders.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 3.1.1, Table 3.1.3, Table 3.1.4.

Table 16: Demographic Characteristics by Sex: Pooled Analysis (FAS)

Demographic Characteristic	Placebo	APR 20 BID	APR 30 BID	Total
Age, years				
Male	n = 240	n =232	n = 222	n = 694
Mean ± SD	48.5 ± 10.66	47.7 ± 11.93	48.8 ± 11.74	48.3 ± 11.44
Median (min – max)	49.0 (19 – 75)	48.0 (20 – 75)	49.0 (21 – 77)	48.0 (19 – 77)
Female	n = 256	n = 268	n = 275	n = 799
Mean ± SD	52.5 ± 12.13	51.5 ± 11.13	52.1 ± 10.98	52.0 ± 11.41
Median (min – max)	53.5 (18 – 83)	52.0 (24 – 77)	53.0 (20 – 77)	53.0 (18 – 83)
Age Group, n (%)				
Male	n = 240	n = 232	n = 222	n = 694
< 65 years	228 (95.0)	217 (93.5)	203 (91.4)	648 (93.4)
18 to < 40 years	48 (20.0)	63 (27.2)	51 (23.0)	162 (23.3)
40 to < 65 years	180 (75.0)	154 (66.4)	152 (68.5)	486 (70.0)
≥ 65 years	12 (5.0)	15 (6.5)	19 (8.6)	46 (6.6)
65 to < 75 years	11 (4.6)	14 (6.0)	17 (7.7)	42 (6.1)
75 to < 85 years	1 (0.4)	1 (0.4)	2 (0.9)	4 (0.6)
≥ 85 years	0	0	0	0
Female	n = 256	n = 268	n = 275	n = 799
< 65 years	219 (85.5)	241 (89.9)	239 (86.9)	699 (87.5)
18 to < 40 years	40 (15.6)	36 (13.4)	39 (14.2)	115 (14.4)
40 to < 65 years	179 (69.9)	205 (76.5)	200 (72.7)	584 (73.1)
≥ 65 years	37 (14.5)	27 (10.1)	36 (13.1)	100 (12.5)
65 to < 75 years	27 (10.5)	24 (9.0)	34 (12.4)	85 (10.6)
75 to < 85 years	10 (3.9)	3 (1.1)	2 (0.7)	15 (1.9)
≥ 85 years	0	0	0	0

Table 16: Demographic Characteristics by Sex: Pooled Analysis (FAS)（つづき）

Demographic Characteristic	Placebo	APR 20 BID	APR 30 BID	Total
Geographic Region, n (%)				
Male	n = 240	n = 232	n = 222	n = 694
North America	96 (40.0)	79 (34.1)	79 (35.6)	254 (36.6)
Europe	100 (41.7)	100 (43.1)	92 (41.4)	292 (42.1)
Rest of world[a]	44 (18.3)	53 (22.8)	51 (23.0)	148 (21.3)
Female	n = 256	n = 268	n = 275	n = 799
North America	68 (26.6)	90 (33.6)	91 (33.1)	249 (31.2)
Europe	120 (46.9)	123 (45.9)	129 (46.9)	372 (46.6)
Rest of world[a]	68 (26.6)	55 (20.5)	55 (20.0)	178 (22.3)
Weight, kg				
Male	n = 240	n = 232	n = 222	n = 694
Mean ± SD	93.81 ± 20.525	92.00 ± 19.103	91.36 ± 18.783	92.42 ± 19.507
Median (min – max)	90.90 (60.0 – 173.0)	87.65 (57.0 – 180.6)	89.10 (50.0 – 180.2)	89.45 (50.0 – 180.6)
Female	n = 256	n = 267	n = 275	n = 798
Mean ± SD	79.48 ± 19.124	80.81 ± 21.517	79.00 ± 18.522	79.76 ± 19.750
Median (min – max)	77.95 (43.5 – 142.5)	77.00 (45.0 – 172.0)	76.20 (45.0 – 150.7)	77.00 (43.5 – 172.0)
BMI, kg/m^2				
Male	n = 239	n = 232	n = 222	n = 693
Mean ± SD	29.84 ± 5.871	29.47 ± 5.346	29.29 ± 5.409	29.54 ± 5.549
Median (min – max)	28.70 (18.2 – 51.0)	28.70 (17.2 – 50.2)	28.70 (16.6 – 49.7)	28.70 (16.6 – 51.0)
Female	n = 256	n = 267	n = 275	n = 798
Mean ± SD	30.22 ± 7.087	30.65 ± 7.747	29.97 ± 6.734	30.28 ± 7.195
Median (min – max)	29.55 (17.0 – 56.2)	29.50 (17.9 – 62.9)	28.90 (16.6 – 52.1)	29.40 (16.6 – 62.9)

Table 16: Demographic Characteristics by Sex: Pooled Analysis (FAS)（つづき）

Demographic Characteristic	Placebo	APR 20 BID	APR 30 BID	Total
BMI category, n (%)				
Male	n = 240	n = 232	n = 222	n = 694
< 25 kg/m^2	51 (21.3)	44 (19.0)	49 (22.1)	144 (20.7)
25 to < 30 kg/m^2	83 (34.6)	99 (42.7)	80 (36.0)	262 (37.8)
30 to < 35 kg/m^2	64 (26.7)	57 (24.6)	63 (28.4)	184 (26.5)
35 to < 40 kg/m^2	24 (10.0)	23 (9.9)	21 (9.5)	68 (9.8)
≥ 40 kg/m^2	17 (7.1)	9 (3.9)	9 (4.1)	35 (5.0)
Missing	1 (0.4)	0	0	1 (0.1)
Female	n = 256	n = 268	n = 275	n = 799
< 25 kg/m2	61 (23.8)	67 (25.0)	67 (24.4)	195 (24.4)
25 to < 30 kg/m2	69 (27.0)	75 (28.0)	90 (32.7)	234 (29.3)
30 to < 35 kg/m2	61 (23.8)	56 (20.9)	50 (18.2)	167 (20.9)
35 to < 40 kg/m2	42 (16.4)	40 (14.9)	48 (17.5)	130 (16.3)
≥ 40 kg/m2	23 (9.0)	29 (10.8)	20 (7.3)	72 (9.0)
Missing	0	1 (0.4)	0	1 (0.1)
Tobacco use, n (%)				
Male	n = 240	n = 232	n = 222	n = 694
Current user	53 (22.1)	52 (22.4)	52 (23.4)	157 (22.6)
Past User	60 (25.0)	62 (26.7)	55 (24.8)	177 (25.5)
Non-user	127 (52.9)	118 (50.9)	113 (50.9)	358 (51.6)
Missing	0	0	2 (0.9)	2 (0.3)
Female	n = 256	n = 268	n = 275	n = 799
Current user	40 (15.6)	58 (21.6)	53 (19.3)	151 (18.9)
Past User	42 (16.4)	57 (21.3)	68 (24.7)	167 (20.9)
Non-user	174 (68.0)	153 (57.1)	154 (56.0)	481 (60.2)

APR = apremilast; BID = twice daily; BMI = body mass index; FAS = full analysis set; min – max = minimum to maximum; SD = standard deviation.

[a] Rest of world countries included Australia, New Zealand, Republic of Korea, Russian Federation, South Africa, and Taiwan, province of China. A summary of subjects by country can be found in Table 14.1.3 of PSA-002 CSR, PSA-003 CSR, and PSA-004 CSR.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 1.1.1.a, Table 1.1.1.b.

Table 17: Baseline Disease History by Sex (Pooled Analysis; FAS)

Disease Characteristic	Placebo	APR 20 BID	APR 30 BID	Total
Duration of PsA, years since diagnosis				
Male	n = 240	n = 232	n = 222	n = 694
Mean ± SD	7.07 ± 6.817	7.72 ± 7.974	7.81 ± 7.462	7.53 ± 7.422
Median (min – max)	5.15 (0.1 – 44.4)	4.80 (0.2 – 41.3)	5.75 (0.5 – 43.4)	5.10 (0.1 – 44.4)
Female	n = 256	n = 268	n =275	n = 799
Mean ± SD	7.46 ± 7.720	7.46 ± 7.529	7.20 ± 8.037	7.37 ± 7.759
Median (min – max)	5.30 (0.5 – 54.4)	4.55 (0.5 – 39.0)	4.10 (0.4 – 57.3)	4.70 (0.4 – 57.3)
PsA type, n (%)				
Male	n = 240	n = 232	n = 222	n = 694
Symmetric polyarthritis	151 (62.9)	149 (64.2)	135 (60.8)	435 (62.7)
Asymmetrical oligoarthritis	65 (27.1)	55 (23.7)	63 (28.4)	183 (26.4)
Predominant DIP involvement	16 (6.7)	15 (6.5)	15 (6.8)	46 (6.6)
Predominant spondylitis	2 (0.8)	8 (3.4)	5 (2.3)	15 (2.2)
Arthritis mutilans	5 (2.1)	5 (2.2)	4 (1.8)	14 (2.0)
Female	n = 256	n = 268	n =275	n = 799
Symmetric polyarthritis	147 (57.4)	170 (63.4)	174 (63.3)	491 (61.5)
Asymmetrical oligoarthritis	73 (28.5)	72 (26.9)	73 (26.5)	218 (27.3)
Predominant DIP involvement	18 (7.0)	16 (6.0)	13 (4.7)	47 (5.9)
Predominant spondylitis	5 (2.0)	5 (1.9)	7 (2.5)	17 (2.1)
Arthritis mutilans	13 (5.1)	5 (1.9)	8 (2.9)	26 (3.3)

APR = apremilast; BID = twice daily; FAS = full analysis set; min – max = minimum to maximum; SD = standard deviation.
Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 1.1.2a, Table 1.1.2.b.

Table 18: Prior and Baseline Use of PsA-Related Therapies by Sex (Pooled Analysis; FAS)

Disease Characteristic	Placebo	APR 20 BID	APR 30 BID	Total
Prior DMARD use (small molecule or biologic), n (%)				
Male	n = 240	n = 232	n = 222	n = 694
Yes	236 (98.3)	229 (98.7)	220 (99.1)	685 (98.7)
Number of prior DMARDs used				
1 DMARD	119 (49.6)	113 (48.7)	113 (50.9)	345 (49.7)
2 DMARDs	66 (27.5)	75 (32.3)	75 (33.8)	216 (31.1)
3 DMARDs	30 (12.5)	32 (13.8)	22 (9.9)	84 (12.1)
> 3 DMARDs	21 (8.8)	9 (3.9)	10 (4.5)	40 (5.8)
Female	n = 256	n = 268	n =275	n = 799
Yes	252 (98.4)	268 (100.0)	269 (97.8)	789 (98.7)
Number of prior DMARDs used				
1 DMARD	132 (51.6)	126 (47.0)	131 (47.6)	389 (48.7)
2 DMARDs	67 (26.2)	88 (32.8)	86 (31.3)	241 (30.2)
3 DMARDs	41 (16.0)	32 (11.9)	34 (12.4)	107 (13.4)
> 3 DMARDs	12 (4.7)	22 (8.2)	18 (6.5)	52 (6.5)
Prior small-molecule DMARD use only				
Male	n = 240	n = 232	n = 222	n = 694
Yes	168 (70.0)	176 (75.9)	168 (75.7)	512 (73.8)
Number of prior DMARDs (small molecule) used				
1 DMARD	114 (47.5)	106 (45.7)	105 (47.3)	325 (46.8)
2 DMARDs	43 (17.9)	57 (24.6)	50 (22.5)	150 (21.6)
3 DMARDs	10 (4.2)	10 (4.3)	10 (4.5)	30 (4.3)
> 3 DMARDs	1 (0.4)	3 (1.3)	3 (1.4)	7 (1.0)
Female	n = 256	n = 268	n =275	n = 799
Yes	208 (81.3)	206 (76.9)	214 (77.8)	628 (78.6)
Number of prior DMARDs (small molecule) used				
1 DMARD	128 (50.0)	121 (45.1)	130 (47.3)	379 (47.4)
2 DMARDs	55 (21.5)	61 (22.8)	61 (22.2)	177 (22.2)
3 DMARDs	24 (9.4)	19 (7.1)	21 (7.6)	64 (8.0)
> 3 DMARDs	1 (0.4)	5 (1.9)	2 (0.7)	8 (1.0)

Table 18: Prior and Baseline Use of PsA-Related Therapies by Sex (Pooled Analysis; FAS)（つづき）

Disease Characteristic	Placebo	APR 20 BID	APR 30 BID	Total
Prior biologic DMARD use, n (%)				
Male	n = 240	n = 232	n = 222	n = 694
Yes	68 (28.3)	53 (22.8)	52 (23.4)	173 (24.9)
Number of prior biologic DMARDs used				
1 DMARD	40 (16.7)	32 (13.8)	39 (17.6)	111 (16.0)
2 DMARDs	21 (8.8)	16 (6.9)	8 (3.6)	45 (6.5)
≥ 3 DMARDs	7 (2.9)	5 (2.2)	5 (2.3)	17 (2.4)
Female	n = 256	n = 268	n =275	n = 799
Yes	44 (17.2)	62 (23.1)	55 (20.0)	161 (20.2)
Number of prior biologic DMARDs used				
1 DMARD	28 (10.9)	42 (15.7)	37 (13.5)	107 (13.4)
2 DMARDs	13 (5.1)	12 (4.5)	13 (4.7)	38 (4.8)
≥ 3 DMARDs	3 (1.2)	8 (3.0)	5 (1.8)	16 (2.0)
Baseline DMARD use, n (%)[a]				
Male	n = 240	n = 232	n = 222	n = 694
Yes	144 (60.0)	141 (60.8)	135 (60.8)	420 (60.5)
No	96 (40.0)	91 (39.2)	87 (39.2)	274 (39.5)
1 DMARD	132 (55.0)	124 (53.4)	124 (55.9)	380 (54.8)
2 DMARDs	12 (5.0)	16 (6.9)	11 (5.0)	39 (5.6)
3 DMARDs	0	1 (0.4)	0	1 (0.1)
> 3 DMARDs	0	0	0	0
Methotrexate	123 (51.3)	115 (49.6)	110 (49.5)	348 (50.1)
Leflunomide	10 (4.2)	18 (7.8)	17 (7.7)	45 (6.5)
Sulfasalazine	23 (9.6)	22 (9.5)	18 (8.1)	63 (9.1)
Other[b]	0	4 (1.7)	1 (0.5)	5 (0.7)

Table 18: Prior and Baseline Use of PsA-Related Therapies by Sex (Pooled Analysis; FAS)（つづき）

Disease Characteristic	Placebo	APR 20 BID	APR 30 BID	Total
Baseline DMARD use, n (%)[a] (cont'd)				
Female	n = 256	n = 268	n =275	n = 799
Yes	180 (70.3)	188 (70.1)	185 (67.3)	553 (69.2)
No	76 (29.7)	80 (29.9)	90 (32.7)	246 (30.8)
1 DMARD	161 (62.9)	171 (63.8)	166 (60.4)	498 (62.3)
2 DMARDs	19 (7.4)	15 (5.6)	19 (6.9)	53 (6.6)
3 DMARDs	0	2 (0.7)	0	2 (0.3)
> 3 DMARDs	0	0	0	0
Methotrexate	152 (59.4)	162 (60.4)	152 (55.3)	466 (58.3)
Leflunomide	23 (9.0)	21 (7.8)	21 (7.6)	65 (8.1)
Sulfasalazine	22 (8.6)	22 (8.2)	28 (10.2)	72 (9.0)
Other[b]	2 (0.8)	2 (0.7)	3 (1.1)	7 (0.9)
Baseline MTX dose, mg/week				
Male	n = 123	n = 115	n = 110	n = 348
Mean ± SD	16.00 ± 5.382	15.83 ± 4.644	15.51 ± 5.256	15.79 ± 5.098
Median (min – max)	15.00 (5.0 – 25.0)	15.00 (5.0 – 30.0)	15.00 (5.0 – 25.00)	15.00 (5.0 – 30.0)
Female	n = 152	n = 162	n = 152	n = 466
Mean ± SD	14.97 ± 5.155	15.39 ± 4.910	15.12 ± 5.003	15.16 ± 5.014
Median (min – max)	15.00 (2.5 – 25.0)	15.00 (7.5 – 25.0)	15.00 (5.0 – 25.0)	15.00 (2.5 – 25.0)
Baseline oral corticosteroids				
Male	n = 240	n = 232	n = 222	n = 694
Yes	21 (8.8)	39 (16.8)	31 (14.0)	91 (13.1)
No	219 (91.3)	193 (83.2)	191 (86.0)	603 (86.9)
Female	n = 256	n = 268	n =275	n = 799
Yes	27 (10.5)	56 (20.9)	33 (12.0)	116 (14.5)
No	229 (89.5)	212 (79.1)	242 (88.0)	683 (85.5)

Table 18: Prior and Baseline Use of PsA-Related Therapies by Sex (Pooled Analysis; FAS)（つづき）

Disease Characteristic	Placebo	APR 20 BID	APR 30 BID	Total
Baseline oral prednisone dose, mg/day[c]				
Male	n = 21	n = 39	n = 31	n = 91
Mean ± SD	6.37 ± 2.902	5.83 ± 2.585	6.82 ± 2.510	6.29 ± 2.643
Median (min – max)	5.00 (1.3 – 10.0)	5.00 (0.7 – 10.0)	5.00 (2.5 – 10.0)	5.00 (0.7 – 10.0)
Female	n = 27	n = 56	n = 33	n = 116
Mean ± SD	6.48 ± 2.525	6.69 ± 2.472	5.62 ± 2.267	6.34 ± 2.451
Median (min – max)	5.00 (2.5 – 10.0)	5.00 (1.3 – 10.0)	5.00 (1.0 – 10.0)	5.00 (1.0 – 10.0)

APR = apremilast; BID = twice daily; DMARD = disease-modifying antirheumatic drug; FAS = full analysis set; min – max = minimum to maximum; MTX = methotrexate; PsA = psoriatic arthritis; SD = standard deviation.

[a] Baseline DMARD use as recorded on case report form.

[b] Other DMARDs in Study PSA-002 included azathioprine, etanercept, hydroxychloroquine, and mesalazine. Other DMARDs in Study PSA-003 included chloroquine/hydroxychloroquine, tocanol, and ustekinumab. Other DMARDs in Study PSA-004 included azathioprine, etanercept, hydroxychloroquine, and mesalazine. Etanercept and ustekinumab are prior medications captured as baseline medications because the dates of last dose were incomplete and are therefore imputed as being used at baseline.

[c] Prednisone or equivalent (ie, normalized to prednisone).

Source: 5.3.5.3.2 項 有効性併合解析（PsA） Table 1.1.2a, Table 1.1.2.b.

Table 19: Baseline Disease Activity per the ACR Core Set Measures by Sex (Pooled Analysis; FAS)

Disease Characteristic	Placebo	APR 20 BID	APR 30 BID	Total
Tender joint count				
Male	n = 240	n = 232	n = 222	n = 694
Mean ± SD	19.3 ± 14.89	20.1 ± 16.04	20.9 ± 14.20	20.1 ± 15.06
Median (min – max)	15.0 (3 – 78)	15.0 (3 – 78)	17.0 (3 – 70)	16.0 (3 – 78)
Female	n = 256	n = 268	n = 275	n = 799
Mean ± SD	20.4 ± 14.66	21.9 ± 16.71	22.7 ± 16.01	21.7 ± 15.84
Median (min – max)	16.5 (3 – 78)	16.0 (3 – 78)	19.0 (3 – 78)	17.0 (3 – 78)
Swollen joint count				
Male	n = 240	n = 232	n = 222	n = 694
Mean ± SD	11.1 ± 7.74	12.0 ± 9.39	12.5 ± 8.87	11.9 ± 8.69
Median (min – max)	8.5 (3 – 42)	9.0 (3 – 58)	10.0 (3 – 55)	9.0 (3 – 58)
Female	n = 256	n = 268	n = 275	n = 799
Mean ± SD	11.0 ± 8.18	10.9 ± 8.35	10.8 ± 7.62	10.9 ± 8.04
Median (min – max)	8.0 (3 – 56)	8.0 (3 – 58)	9.0 (3 – 47)	8.0 (3 – 58)
Subject assessment of pain (VAS)				
Male	n = 239	n = 232	n = 221	n = 692
Mean ± SD	56.2 ± 21.58	55.1 ± 21.38	57.5 ± 20.71	56.2 ± 21.23
Median (min – max)	58.0 (5 – 100)	57.0 (3 – 99)	58.0 (1 – 100)	58.0 (1 – 100)
Female	n = 255	n = 267	n = 274	n = 796
Mean ± SD	58.7 ± 19.18	56.3 ± 21.97	56.8 ± 21.90	57.2 ± 21.09
Median (min – max)	58.0 (7 – 100)	58.0 (0 – 99)	60.0 (0 – 99)	59.0 (0 – 100)
Patient's (subject's) global assessment of disease activity (PGA)				
Male	n = 238	n = 232	n = 221	n = 691
Mean ± SD	56.4 ± 22.02	54.6 ± 21.82	55.6 ± 23.08	55.5 ± 22.28
Median (min – max)	58.0 (3 – 99)	55.0 (7 – 99)	58.0 (0 – 100)	57.0 (0 – 100)
Female	n = 255	n = 266	n = 273	n = 794
Mean ± SD	56.9 ± 20.39	56.5 ± 21.15	56.8 ± 21.75	56.8 ± 21.10
Median (min – max)	58.0 (3 – 100)	59.0 (1 – 100)	58.0 (1 – 99)	58.0 (1 – 100)

Table 19: Baseline Disease Activity per the ACR Core Set Measures by Sex (Pooled Analysis; FAS)（つづき）

Disease Characteristic	Placebo	APR 20 BID	APR 30 BID	Total
Evaluator's (physician's) global assessment of disease activity (EGA)				
Male	n = 233	n = 227	n = 214	n = 674
Mean ± SD	54.5 ± 18.12	53.4 ± 20.63	56.4 ± 19.70	54.7 ± 19.50
Median (min – max)	56.0 (17 – 93)	54.0 (2 – 98)	57.0 (10 – 96)	55.5 (2 – 98)
Female	n = 247	n = 261	n = 268	n = 776
Mean ± SD	53.8 ± 19.72	55.2 ± 18.46	55.7 ± 18.42	54.9 ± 18.85
Median (min – max)	53.0 (6 – 100)	56.0 (0 – 97)	57.0 (15 – 97)	55.0 (0 – 100)
HAQ-DI score				
Male	n = 239	n = 232	n = 221	n = 692
Mean ± SD	1.028 ± 0.5954	0.989 ± 0.6166	1.070 ± 0.6177	1.028 ± 0.6097
Median (min – max)	1.000 (0.00 – 2.63)	1.000 (0.00 – 2.63)	1.000 (0.00 – 2.75)	1.000 (0.00 – 2.75)
Female	n = 256	n = 267	n = 274	n = 797
Mean ± SD	1.324 ± 0.5890	1.263 ± 0.6219	1.337 ± 0.6258	1.308 ± 0.6130
Median (min – max)	1.375 (0.00 – 2.75)	1.250 (0.00 – 2.88)	1.375 (0.00 – 2.88)	1.375 (0.00 – 2.88)
CRP (mg/dL)[a]				
Male	n = 240	n = 232	n = 222	n = 694
Mean ± SD	1.096 ± 1.4200	1.015 ± 1.6240	1.118 ± 1.6697	1.076 ± 1.5702
Median (min – max)	0.538 (0.02 – 8.86)	0.411 (0.02 – 13.73)	0.537 (0.02 – 13.22)	0.491 (0.02 – 13.73)
Female	n = 256	n = 268	n = 275	n = 799
Mean ± SD	0.968 ± 1.4485	0.957 ± 1.8261	0.830 ± 1.1159	0.917 ± 1.4892
Median (min – max)	0.425 (0.02 – 11.49)	0.459 (0.02 – 23.99)	0.355 (0.02 – 8.13)	0.422 (0.02 – 23.99)

ACR = American College of Rheumatology; APR = apremilast; BID = twice daily; HAQ-DI = Health Assessment Questionnaire Disability Index; CRP = C-reactive protein; FAS = full analysis set; SD = standard deviation; VAS = visual analog scale.

[a] Normal range for CRP was < 0.5 mg/dL.

Note: Baseline data available for all subjects unless otherwise noted.

Source: 5.3.5.3.2 項 有効性併合解析（PsA） Table 1.1.2a, Table 1.1.2.b.

Table 20: Analysis by Sex of Modified ACR 20/50/70 Response, HAQ-DI Improvement, PsARC Response, SF-36v2 Physical Functioning Domain Score Improvement, and PASI-75 (Pooled Analysis; FAS)

	Male					Female				
	Placebo N = 240[a]	APR 20 BID N = 232[a]		APR 30 BID N = 222[a]		Placebo N = 256[a]	APR 20 BID N = 268[a]		APR 30 BID N = 275[a]	
Endpoint Visit	n/m (%)[b]	n/m (%)[b]	Treatment Difference[c]	n/m (%)[b]	Treatment Difference[c]	n/m (%)[b]	n/m (%)[b]	Treatment Difference[c]	n/m (%)[b]	Treatment Difference[c]
Modified ACR 20[d]										
Week 16	39/240 (16.3)	86/232 (37.1)	21.0 (13.3, 28.7)	95/222 (42.8)	26.5 (18.6, 34.5)	54/256 (21.1)	74/268 (27.6)	6.6 (-0.7, 13.8)	89/275 (32.4)	11.6 (4.2, 19.0)
Week 24	33/240 (13.8)	76/232 (32.8)	19.3 (12.0, 26.6)	75/222 (33.8)	20.0 (12.5, 27.6)	40/256 (15.6)	63/268 (23.5)	8.0 (1.4, 14.7)	76/275 (27.6)	12.5 (5.7, 19.2)
Modified ACR 50[d]										
Week 16	10/240 (4.2)	40/232 (17.2)	13.0 (7.6, 18.4)	38/222 (17.1)	12.8 (7.3, 18.3)	22/256 (8.6)	31/268 (11.6)	3.0 (-2.1, 8.1)	31/275 (11.3)	3.1 (-2.0, 8.1)
Week 24	15/240 (6.3)	41/232 (17.7)	11.4 (5.7, 17.1)	39/222 (17.6)	11.3 (5.5, 17.1)	19/256 (7.4)	29/268 (10.8)	3.4 (-1.5, 8.3)	39/275 (14.2)	7.1 (1.9, 12.2)
Modified ACR 70[d]										
Week 16	3/240 (1.3)	15/232 (6.5)	5.3 (1.9, 8.8)	8/222 (3.6)	2.3 (-0.5, 5.1)	4/256 (1.6)	9/268 (3.4)	1.9 (-0.7, 4.5)	7/275 (2.5)	1.1 (-1.3, 3.5)
Week 24	5/240 (2.1)	17/232 (7.3)	5.3 (1.5, 9.0)	16/222 (7.2)	5.2 (1.3, 9.0)	7/256 (2.7)	8/268 (3.0)	0.3 (-2.6, 3.1)	14/275 (5.1)	2.5 (-0.8, 5.8)
HAQ-DI[e]										
Week 16 LS Mean (SE)	-0.089 (0.0286)	-0.231 (0.0292)	-0.142 (-0.221, -0.062)	-0.273 (0.0299)	-0.184 (-0.265, -0.104)	-0.047 (0.0281)	-0.101 (0.0274)	-0.055 (-0.130, 0.021)	-0.158 (0.0272)	-0.112 (-0.187, -0.036)
Week 24 LS Mean (SE)	-0.105 (0.0297)	-0.260 (0.0303)	-0.154 (-0.236, -0.072)	-0.271 (0.0311)	-0.165 (-0.249, -0.082)	-0.035 (0.0292)	-0.092 (0.0284)	-0.056 (-0.135, 0.022)	-0.174 (0.0281)	-0.139 (-0.217, -0.061)

Table 20: Analysis by Sex of Modified ACR 20/50/70 Response, HAQ-DI Improvement, PsARC Response, SF-36v2 Physical Functioning Domain Score Improvement, and PASI-75 (Pooled Analysis; FAS)（つづき）

	Male					Female				
	Placebo N = 240[a]	APR 20 BID N = 232[a]		APR 30 BID N = 222[a]		Placebo N = 256[a]	APR 20 BID N = 268[a]		APR 30 BID N = 275[a]	
Endpoint Visit	n/m (%)[b]	n/m (%)[b]	Treatment Difference[c]	n/m (%)[b]	Treatment Difference[c]	n/m (%)[b]	n/m (%)[b]	Treatment Difference[c]	n/m (%)[b]	Treatment Difference[c]
PsARC[d]										
Week 16	62/240 (25.8)	103/232 (44.4)	18.7 (10.5, 27.0)	114/222 (51.4)	25.6 (17.1, 34.1)	87/256 (34.0)	104/268 (38.8)	4.9 (-3.3, 13.0)	130/275 (47.3)	13.6 (5.4, 21.8)
Week 24	41/240 (17.1)	85/232 (36.6)	19.8 (12.2, 27.3)	93/222 (41.9)	24.7 (16.7, 32.7)	68/256 (26.6)	86/268 (32.1)	5.6 (-2.0, 13.3)	105/275 (38.2)	12.3 (4.6, 20.1)
SF-36v2 PF[e]										
Week 16 LS Mean (SE)	1.62 (0.508)	4.06 (0.520)	2.44 (1.02, 3.85)	4.42 (0.534)	2.80 (1.37, 4.24)	0.90 (0.503)	1.41 (0.488)	0.51 (-0.84, 1.87)	2.81 (0.484)	1.91 (0.56, 3.26)
Week 24 LS Mean (SE)	1.53 (0.523)	4.48 (0.535)	2.95 (1.49, 4.40)	4.41 (0.549)	2.88 (1.40, 4.36)	1.05 (0.518)	1.76 (0.503)	0.70 (-0.69, 2.09)	3.47 (0.496)	2.42 (1.03, 3.80)

Table 20: Analysis by Sex of Modified ACR 20/50/70 Response, HAQ-DI Improvement, PsARC Response, SF-36v2 Physical Functioning Domain Score Improvement, and PASI-75 (Pooled Analysis; FAS)（つづき）

	Male					Female				
	Placebo N = 240[a]	APR 20 BID N = 232[a]		APR 30 BID N = 222[a]		Placebo N = 256[a]	APR 20 BID N = 268[a]		APR 30 BID N = 275[a]	
Endpoint Visit	n/m (%)[b]	n/m (%)[b]	Treatment Difference[c]	n/m (%)[b]	Treatment Difference[c]	n/m (%)[b]	n/m (%)[b]	Treatment Difference[c]	n/m (%)[b]	Treatment Difference[c]
PASI-75[f]										
Week 16	3/123 (2.4)	23/119 (19.3)	17.1 (9.4, 24.8)	20/133 (15.0)	12.7 (6.2, 19.3)	9/108 (8.3)	27/129 (20.9)	12.7 (4.0, 21.4)	35/116 (30.2)	21.5 11.9, 31.1)
Week 24	4/123 (3.3)	25/119 (21.0)	18.2 (10.2, 26.1)	26/133 (19.5)	17.1 (9.8, 24.4)	12/108 (11.1)	28/129 (21.7)	10.7 (1.5, 19.9)	35/116 (30.2)	19.0 (9.0, 29.1)

ACR 20/50/70 = American College of Rheumatology 20%/50%/70% response; APR = apremilast; BID = twice daily; FAS = full analysis set; HAQ-DI = Health Assessment Questionnaire Disability Index; LS Mean = least-squares mean; PsARC = Psoriatic Arthritis Response Criteria; SF-36v2 PF = 36-item Short Form Health Survey, version 2, physical functioning domain score; PASI-75 = Psoriasis Area and Severity Index score improvement ≥ 75%; SE = standard error.

[a] N reflects number of subjects randomized; the number of subjects evaluated may vary by endpoint and time point.

[b] n/m = number of responders/number of subjects in the subgroup. Subjects with a missing subgroup factor are not included.

[c] Treatment difference for categorical endpoints is the adjusted difference in proportions (weighted average of the treatment differences across the strata of baseline disease-modifying antirheumatic drug (DMARD) use and study with the Cochran-Mantel-Haenszel weights) and corresponding 2-sided 95% confidence interval based on a normal approximation to the weighted average. Treatment difference for continuous endpoints is the LS mean difference (based on an analysis of covariance model for the change from baseline, with treatment group, baseline DMARD use [yes/no], study, sex, and the treatment-by-sex interaction as factors and the baseline value as a covariate) and corresponding standard error.

[d] For modified ACR 20/50/70 and PsARC response, subjects who discontinued early prior to the respective visits, subjects who entered early escape (EE) at Week 16 (for the Week 24 analyses), and subjects who did not have sufficient data for a definitive determination of response status at the respective visits were counted as nonresponders. Joints temporarily or permanently not assessable at baseline were excluded from joint count. For other unassessed joints at baseline, the joint assessment at the Screening visit, if assessed, was used as the Baseline assessment; otherwise, the joint was excluded from joint count. The last observed joint assessment (at baseline or postbaseline) was used for joints unassessed at the respective visits. There was no imputation for other missing ACR component scores.

[e] For HAQ-DI and SF-36v2 PF, for subjects who discontinued from the study prior to Week 16, the last available postbaseline value observed prior to discontinuation was carried forward to Weeks 16 and 24. For subjects who entered EE at Week 16 or who did not enter EE but discontinued from the study between Weeks 16 and 24, the last available postbaseline value observed prior to EE or discontinuation, respectively, was carried forward to Week 24. Missing values for subjects who did not discontinue or enter EE were imputed using the latest available postbaseline value prior to the visit in question.

[f] For PASI-75, for subjects who discontinued from the study prior to Week 16, the last available postbaseline value observed prior to discontinuation was carried forward to Weeks 16 and 24. For subjects who entered EE at Week 16 or who did not enter EE but discontinued from the study between Weeks 16 and 24, the last available postbaseline value observed prior to EE or discontinuation, respectively, was carried forward to Week 24. Missing values for subjects who did not discontinue or enter EE were imputed using the latest available postbaseline value prior to the visit in question. Subjects who did not have sufficient data (observed or imputed) for a determination of response status at the respective visits were counted as nonresponders.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 3.1.1, Table 3.1.2, Table 3.2.1 through Table 3.6.2, Table 3.9.1, Table 3.9.2.

Table 21: Analysis of Change from Baseline in ACR Components by Sex at Week 16 (Pooled Analysis; FAS; LOCF)

Endpoint Sex	Placebo		APR 20 BID			APR 30 BID		
	n[a]	LS mean Change (SE)[b]	n[a]	LS mean Change (SE)[b]	LS Mean Difference (95% CI)	n[a]	LS mean Change (SE)[b]	LS Mean Difference (95% CI)
TJC								
Male	236	-0.4 (0.72)	226	-5.8 (0.74)	-5.4 (-7.4, -3.4)	214	-6.6 (0.76)	-6.2 (-8.3, -4.2)
Female	249	-2.3 (0.71)	260	-4.0 (0.70)	-1.7 (-3.6, 0.2)	266	-5.2 (0.68)	-2.9 (-4.8, -1.0)
SJC								
Male	236	-1.1 (0.47)	226	-3.6 (0.48)	-2.6 (-3.9, -1.3)	214	-4.1 (0.49)	-3.0 (-4.3, -1.7)
Female	249	-2.4 (0.46)	260	-3.5 (0.45)	-1.1 (-2.4, 0.1)	266	-4.3 (0.45)	-1.9 (-3.2, -0.7)
Pain VAS, mm								
Male	233	-5.7 (1.50)	223	-13.6 (1.54)	-7.9 (-12.1, -3.7)	210	-14.4 (1.59)	-8.7 (-13.0, -4.4)
Female	247	-5.9 (1.48)	260	-8.2 (1.44)	-2.3 (-6.3, 1.7)	262	-11.2 (1.43)	-5.4 (-9.3, -1.4)
PGA, mm								
Male	233	-3.5 (1.56)	223	-10.2 (1.60)	-6.7 (-11.0, -2.3)	210	-10.6 (1.64)	-7.2 (-11.6, -2.7)
Female	247	-3.5 (1.53)	260	-5.9 (1.49)	-2.4 (-6.5, 1.7)	262	-8.1 (1.48)	-4.6 (-8.7, -0.5)
EGA, mm								
Male	229	-6.4 (1.47)	217	-16.5 (1.51)	-10.1 (-14.2, -5.9)	205	-19.1 (1.55)	-12.7 (-16.9, -8.6)
Female	238	-9.9 (1.46)	255	-15.4 (1.41)	-5.5 (-9.4, -1.6)	256	-17.3 (1.40)	-7.4 (-11.3, -3.4)
HAQ-DI								
Male	234	-0.089 (0.0286)	225	-0.231 (0.0292)	-0.142 (-0.221, -0.062)	212	-0.273 (0.0299)	-0.184 (-0.265, -0.104)
Female	247	-0.047 (0.0281)	260	-0.101 (0.0274)	-0.055 (-0.130, 0.021)	261	-0.158 (0.0272)	-0.112 (-0.187, -0.036)
CRP, mg/dL								
Male	239	0.103 (0.0824)	231	-0.253 (0.0839)	-0.356 (-0.586, -0.127)	220	-0.031 (0.0859)	-0.134 (-0.367, 0.098)
Female	252	-0.067 (0.0812)	266	-0.110 (0.0791)	-0.043 (-0.261, 0.176)	273	-0.224 (0.0777)	-0.157 (-0.374, 0.061)

ACR = American College of Rheumatology; APR = apremilast; BID = twice daily; CI = confidence interval; EGA= Evaluator (Physician) global Assessment of Disease Activity; FAS = full analysis set; HAQ-DI = Health Assessment Questionnaire – Disability Index; CRP = C-reactive protein; LS = least squares; Pain VAS = subject's assessment of pain visual analog scale; PGA = Patient's (Subject's) Global Assessment of Disease Activity; SE = standard error; SJC = swollen joint count; TJC = tender joint count.

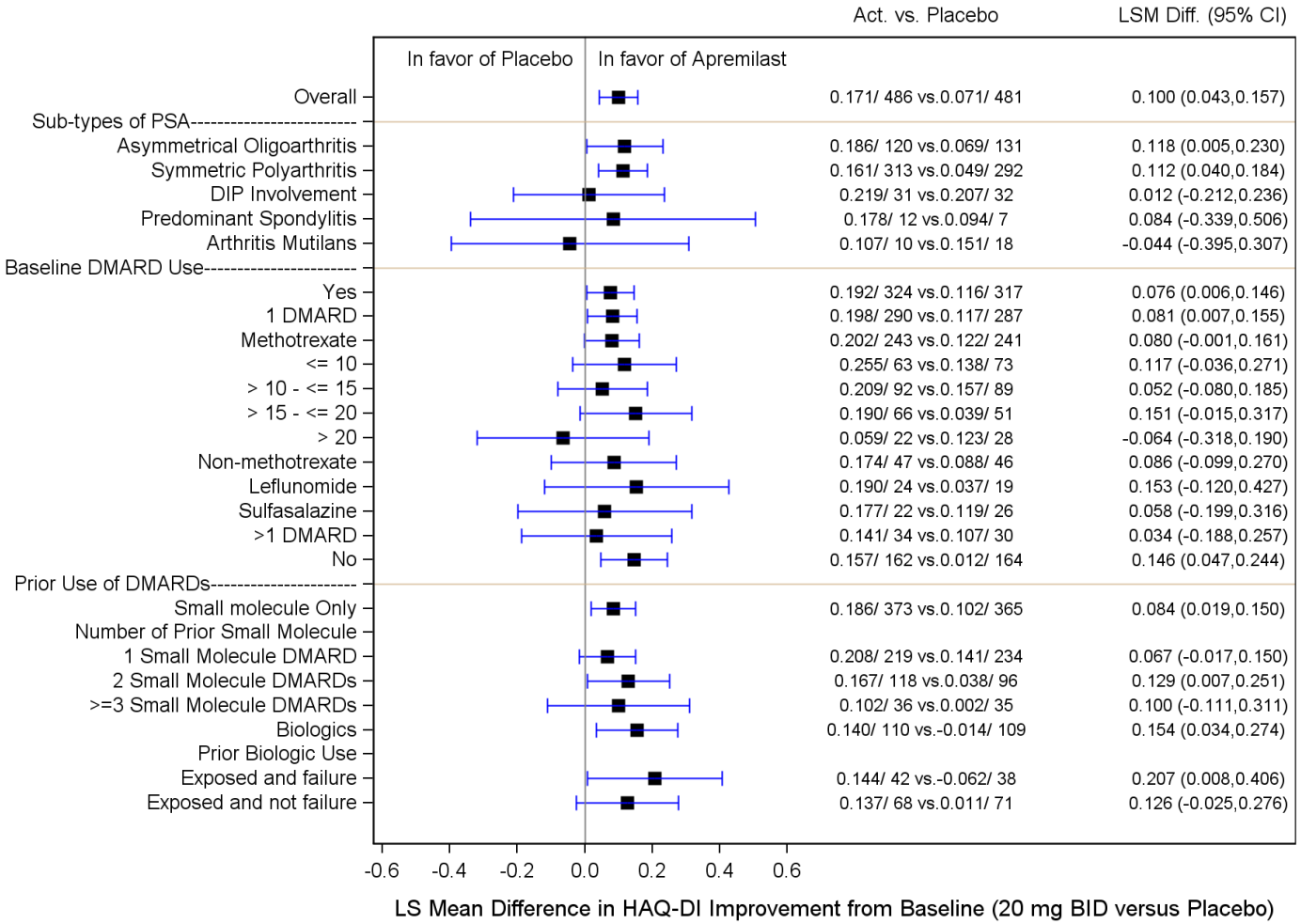
[a] Subjects with a baseline value and at least one postbaseline value at or prior to Week 16 are included. Subjects with a missing subgroup factor are not included.

[b] Estimates are based on an analysis of covariance model for the change from baseline, with treatment group, baseline disease-modifying antirheumatic drug (DMARD) (yes/no), study, the subgroup factor, and the treatment-by-subgroup-factor interaction as factors and the baseline value as a covariate.

Note: For subjects who discontinued from the study prior to Week 16, the last available postbaseline value observed prior to discontinuation was carried forward to Weeks 16 and 24. For subjects who entered early escape (EE) at Week 16 or who did not enter EE but discontinued from the study between Weeks 16 and 24, the last available postbaseline value observed prior to EE or discontinuation, respectively, was carried forward to Week 24. Missing values for subjects who did not discontinue or enter EE were imputed using the latest available postbaseline value prior to the visit in question.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 3.12.1.

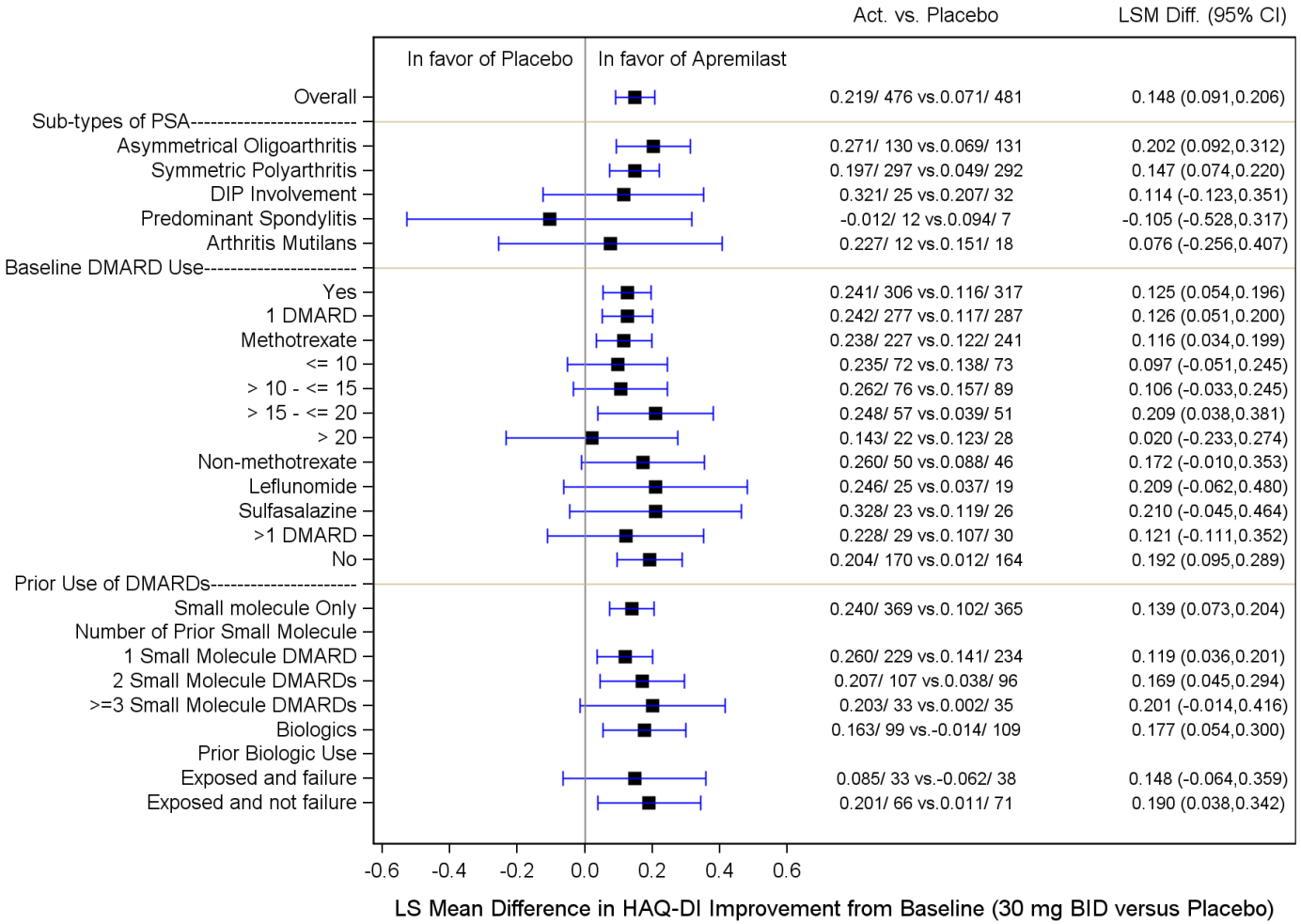
Figure 50: Mean Change from Baseline in HAQ-DI at Week 24 in the APR 20 BID Treatment Group by PsA Subtype, Prior DMARD Use, and Baseline (Concomitant) DMARD Use (Pooled Analysis; FAS; LOCF)



Act = active treatment; APR = apremilast; BID = twice daily; CI = confidence interval; Diff = difference; DIP = distal interphalangeal (joint); DMARD = disease-modifying antirheumatic drug; FAS = full analysis set; HAQ-DI = Health Assessment Questionnaire – Disability Index; LOCF = last observation carried forward; LS = least squares; LSM = least-squares mean; PsA = psoriatic arthritis; vs. = versus.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 2.5.2, Table 3.5.2.

Figure 51: Mean Change from Baseline in HAQ-DI at Week 24 in the APR 30 BID Treatment Group by PsA Subtype, Prior DMARD Use, and Baseline (Concomitant) DMARD Use (Pooled Analysis; FAS; LOCF)



Act = active treatment; APR = apremilast; BID = twice daily; CI = confidence interval; Diff = difference; DIP = distal interphalangeal (joint); DMARD = disease-modifying antirheumatic drug; FAS = full analysis set; HAQ-DI = Health Assessment Questionnaire – Disability Index; LOCF = last observation carried forward; LS = least squares; LSM = least-squares mean; PsA = psoriatic arthritis; vs = versus.

Source: 5.3.5.3.2 項 有効性併合解析（PsA）Table 2.5.2, Table 3.5.2.